

There is no overwhelming evidence that man's body and brain have not changed significantly during the past 10,000 years. The same set of genes that governed man's life when he was Paleolithic hunter or a Neolithic farmer still governs his anatomical development, physiological needs and emotional drives.<sup>30</sup>

Any stretch of DNA has two strands and, therefore, the capacity for holding two different sequences of bases, depending on which strand is read. That is not to say though both the strands are not used. Some genes will be on one strand while others will be on the other strand. Therefore, varied terms have been coined to refer to the strand, which hold sequence information and those which do not, such as sense and anti-sense, coding and non-coding. A gene sequence is always read from the 3' end to 5' end, and therefore genes which reside on different strands are read in opposite directions, again a fact that needs consideration when a researcher is trying to decipher the gene sequence.

### 7.3 Characteristics of Genome

Understanding the information contained in genome sequence was the major challenge of the early 21<sup>st</sup> century. The genome is the entire DNA content of a cell, including all the *genes* and all of the intergenic regions. Prokaryotic genomes are small with very little space between genes. The yeast genome contains 6000 genes and has a more compact organization.

Every organism is specified by genomes, which contain the biological information needed to construct and maintain a living organism. Most genomes, including those for all cellular life forms, are made of DNA (deoxyribonucleic acid) but a few viruses have RNA (ribonucleic acid) genomes. DNA and RNA are polymeric molecules made up of linear, unbranched chain of monomeric subunits called nucleotides.

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30 *Ibid*, p. 3

The biological information contained in a genome is encoded in the nucleotide sequence of its DNA or RNA molecules and is divided into discrete units called genes. The information in a gene is read by proteins attached to the genome at the appropriate positions and initiate a series of biochemical reactions referred to gene expression.

For organisms with DNA genomes, this process was originally looked on as comprising the following two stages:

- (i) **Transcription:** first producing an RNA copy of gene.
- (ii) **Translation:** resulting in synthesis of protein whose amino acid sequence is determined, via the genetic code, by the nucleotide sequence of the RNA transcript.

This is still an accurate description of *gene* expression in simple organisms such as bacteria, but it gives an incomplete picture of events involved in the conversion of genomic.<sup>31</sup>

### 7.3.1 GENETIC CODE—A BLUE PRINT

The genetic code (codon) has been compared to a blue print specifying the design of the organism that provides for the mechanisms needed to "read" the code and manufacture the components of the organisms as well as specifying the procedures needed for the life processes of the finished organisms. Simple organisms are completely defined genetically. Each tiny nematode worm has exactly 958 cells. Humans, on the other hand, have trillions of cells and 30 to 40000 genes so the genetic code is more of a general plan. For example, major blood vessels are genetically specified. Everybody has an aorta. But minor blood vessels grow where needed according to genetically defined rules.

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31 *Basic and Molecular Genetics*—by Parihar, Student edition, Jodhpur, 2004, p. 249.

Although all the somatic cells in an organism contain the complete code, in any given cell only a relatively few genes are active. The difference in the genes that are active determines the difference between, say, liver and brain cells. A complete gene logic determines when and where a particular gene will be “turned on.” The gene logic can accommodate varying amounts of positional detail. The eye which is complex requires less genetic information. The gene logic also controls when various activities take place. Cells divide rapidly in growing organisms but do not divide in adults unless needed to replace dead or discarded cells. Cancer involves a major breakdown in the gene logic in which cells grow in both an inappropriate time. Cancer is thought to require multiple mutations, some of which can be inherited.

### 7.3.2 WHAT ARE GENES FOR?

Somebody is naturally shy because of his genes, but genes are not the switches that indicate ones qualities. Genes are simply chemicals that direct the combination of more chemicals. The chemicals that make up genes is called deoxyribonucleic acid or DNA. It comprises simple building blocks called bases, of which there are four different varieties A, G, T and C. The bases come together in long strings, and each DNA molecule consists of two of these strings paired according to the rule that A matches T and G matches C. DNA stores information in the order of bases. The DNA sequence ‘AGCT’ means one thing and the sequence ‘TCGA’ means something else, as difference in meaning as ‘taps’ and ‘spat’.

The information in DNA is converted into proteins, which are made of amino acids. Proteins are there, where there the action is. The most important function of proteins is to act as enzymes that change one chemical into another. For example, it is an enzyme that converts tyrosene, as amino acid found in many foods, into dopamine, a brain chemical that can make you feel active and excited. A different enzyme breaks down the

dopamine into smaller molecules and thereby leaves you feeling more relaxed or even lazy. Different enzymes make and degrade more than 300 brain chemicals that influence thinking, acting and feeling.

The brain and body are built by DNA and everyone's DNA is pretty much the same. We have 99.9 per cent the same DNA as Michael Jordan, Albert Einstein, Elizabeth Taylor, Charles Manson, Julius Caesar, Julia Child and Jules Verne. All of them and every one who has ever lived have the same 1.0 lakh or so genes, which are organized into the same 23 chromosomes.

But pretty much the same is not exactly the same. There are differences in DNA. About 0.1 per cent or one bit out of every 1000. Considering that there are three billion chemicals based in question, the differences in matter, where Michael Jordan's DNA says "G," Michael Jackson's may say "C" and Andrew Jackson's said "T," while Jack the Ripper's said "A." There are roughly three million such differences between individuals, and these differences are responsible for all the inherited aspects, the variations among people from eye color to height to personality and intelligence. It is hard to believe that such a tiny difference—one-tenth of one per cent, could make such a great difference in how people vary from each other. Many of the three million variations do not mean anything as far as we know, so there are even fewer differences that matter.

If we do not believe that 0.1 per cent of DNA could be responsible for so many differences, consider the fact that human DNA differs from chimpanzee DNA by only 1 to 2 per cent; yours and a chimp's DNA is at least 98 per cent the same. Yet this seemingly "fine print" of DNA instructions is the reason why human can do calculus, compose poetry and build cathedrals, while chimps pick bugs of each other and eat them. Humans have pretty much the same DNA as a chimp because that is where we came from, and the chimp is close to

the ape because that is where he came from, and so down the line fish and reptiles and even upto single celled organism such as yeast. This evolutionary conservation has a beneficial side effect: we can often figure out what a human gene does by looking at a similar gene in simpler organisms.

One of the most common misconception about genetics is that there are genes 'for' things. Some people have the genes for breast cancer, shyness, blue eyes so they must have the disease, condition or trait. This is what people tend to think when they hear about a gene 'for' depression, or a 'gay gene' or 'obesity gene.' If that were true, it would be easily enough to undergo testing to see what genes you have, and, therefore, what you ought to worry about. That is not the way it works. Everyone has a "mood gene" and a "sexual orientation gene" and a gene that regulates body weight. The difference is that the genes come in different varieties or flavours.

For example, may be the "mood gene" which every one has a receptor, that responds to the hormones related under stress. May be the only difference between two people is that one has a gene with T at position 4,356 where as the other person has a C at the same spot. That might be enough to affect the strength of the electrical current flowing through the cells, so the same amount of hormone produces a gentle buzz in one person and a walloping jolt in another. That single detail—one letter out of three billion—could mean the difference between a mostly cheerful person and the one who is easily depressed. Both people have the same gene, but the fine print makes all the difference. Imagine a room filled with 30,000 books. Here the difference would be the equivalent of a single letter in a single book.<sup>32</sup>

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32 Bouchard, Thomas J. Jr. "Genes, Environment and Personality" science 264, 1700-1, 1994.

### 7.3.3 MODERN CONCEPT IN GENE

Mendel, while explaining the result of his breeding experiment, pointed out that hereditary characters were governed by some particular genetic determinants present in the germ cells. These genetic determinants of hereditary character are now called “genes.” The term gene was coined by the prominent geneticist Johansen Dauries (1990) used the term 'pangen' and perhaps from this word the term 'gene' was derived. In old books of genetics, the term 'gene' is treated as merely something which effects the phenotype and behaves as a particle. It should be noted here that nothing was said about the size, shape and chemical constitution of gene in old definition:

As per 'Morgan' theory of gene, it is stated that:

- (i) Chromosomes are bearers of hereditary units and each chromosome carries hundreds or thousands of genes.
- (ii) The genes are arranged on the chromosomes in linear order and on specific region or loci.

Genes can be defined best in terms of its effects. The gene is a unit of function. Gene is a unit of recombination. The gene is a unit of mutation. From the source of Scientists Limba Defira and Moses (1966), it is established that DNA is the essential genetic material. Here everybody seems generally agreed as the fact that the genetic material (genes) of lower organisms is similar to those of higher ones. Munteing (1961) defines a gene as a small segment of chromosome having a unitary bio-chemical function and specific step on the properties of individual.<sup>33</sup>

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33 *Cytogenetics Evolution and Plant Breeding*—by R.S. Shukla and P.S. Chandel, publisher—S. Chand and Co. Ltd. New Delhi, 1998 edition.



## Life in the Science of Genetics

Earlier, in chapter 2 we have discussed life in the science of *karma*. Now we shall deal with life in the science of genetics.

### 8.1 Characteristic of living being

There are many theories in vogue about the origin of life on the earth. Prominent among them are the theories of spontaneous generation, the Meteor Stone theory and the Creation theory, but the theory most widely accepted is given by the Russian bio-chemical scientist Operin. According to Operin, life on earth originated in three stages—(i) Physical evolution, (ii) Chemical evolution, and (iii) Biological evolution.

The earth was a ball of fire about five billion years ago. Whatever there was in its atmosphere all were in the form of mere elements. After the earth cooled down, the existing elements formed some compounds which contained carbohydrates. These complex carbohydrates may be taken as equivalent to the chemical compounds found in some viruses. These carbohydrates possessed the capacity for spontaneous generation. Then owing to mutation, there occurred some changes in them and there came in free chromosomes that are found in some bacteria too. With chromosomes coming into existence took shape of rudimentary cell nucleolus through complex structuring. Characteristic of living being appeared for the first time in these cell prototypes. The entire process spanned a period of about one billion years. Thus, life came into existence on the earth nearly four billion years ago.

There have been numerous experiments to prove scientist Operin's hypothesis. Scientists like Stanley Miller, Yuri, Calvin and Fox tried, through separate experiments, to prove Operin's theory of chemical evolution of life. They succeeded in producing the structural components of cell in their experiments in the laboratory under high temperature and high voltage. This confirmed Operin's hypothesis.<sup>1</sup> Through experiments in genetics, it was possible to show evolution in the laboratory. Such experimental evidences could be achieved in the field of animals and plant breeding. Through a cross-breeding between two species of a living being comes into being a totally new living creature. For instance, cross-breeding between a horse and a donkey produces a mule. In the same way, through cross-breeding between goat and sheep comes into being bhakari, one can bring desired variations also at will. Bull dogs and alsiesion etc., are good examples of such an artificial evolution. Various species of multicoloured roses available today are also examples of artificial breeding. Thus we can bring out novelties and variations among plants and creatures through cross-breeding with choice.

### 8.1.1 REFERENCE STANDARDS

Every living organism acts in a directed way, each moment of its life, this is because the highly stable DNA molecules give instructions and information indicating what to do. For humans, instructions of the genes provide, during embryonic development, the system of reference standards at which to aim, e.g. the cells of the hypothalamus ensure that the right amount of food and drink are taken and the right amount is incorporated to allow the body to grow to its proper size. Throughout life, the genes continue giving instructions to the cells as to how to select the right chemical action to fare the eventualities that are likely to

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1 *What is life?*—by Dr. Anil Kumar Jain, Vidyā Prakāśana Mandira, New Delhi.

cause the body to disintegrate. The information is embodied in an enormous long string described as genetic code, provided by the sequences of three nucleotide bases. The reference standards in our brains influence our wants and desires, our satisfactions and revulsions, our longings and fears. The causes of actions of a given man will include not only all the above variables but also his free will.<sup>2</sup>

### 8.1.2 SEX DETERMINATION

Sex is of two types, male is characterized by XY chromosomes constitution, secondary sex characters are masculine voice, muscular body with beard and moustache in mates, with male sex organs like penis, testicles etc. The female has XX chromosome constitution, secondary sex character like mammary glands meant to nurse the child assumed a different modulation in civilized society, feminine voice, fat at hips, sex organs, ovaries, uterus, vagina, etc. Sex is determined at the time of fertilization. Two types of gametes are produced by males in testicles, i.e. gametes with X chromosome and gametes with Y chromosome.

Female produces one type of egg (ova) with X constitution. When egg is fertilized by X chromosome sperm, it is female, XX or if it fertilized by Y chromosome sperm, it will be male, XY.

Ova		Sperm	Zygotes after fertilization
X	+	X	XX—female
X	+	Y	XY—male

A child is a product of the fusion of two cells from woman and man. Woman produces cells called ova from ovaries and man produces spermatozoa from testicles.<sup>3</sup>

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2 *Neuroscience and karma*—by late Jethālāla S., Zaverī & Muni Mahendrakumara, JVBI, Ladnun, Second edition, p. 15-16.

3 *Understanding Genetics*—by O.S. Reddi, publisher Allied Publishers Ltd., New Delhi, p. 52.

## 8.2 Organization of the cell

To know about the types of genes, first we shall have to understand biology of cell of structure. Each of 100 trillion cells in the human being is a living structure that can survive indefinitely and in most instances, can even reproduce itself, provided its surrounding fluids contain appropriate nutrients. To understand the function of the organs and other structures of the body, it is essential that first understand the basic organization of the cell and functions of its component parts.<sup>4</sup>

To summarize, the body is actually a social order of about 100 trillion cells organized into different functional structure provides its share in the maintenance of homeostatic conditions in the extra cellular fluid, which is called the internal environment, the cells of the body continue to leave and function properly. Thus each cell benefits from homeostatic, and in turn, each cell contributes its share towards the maintenance of homeostatic. This reciprocal interplay provides continuous automaticity of the body until one or more functional systems lose their ability to contribute their share of function. When this happens, all the cells of the body suffer. Extreme dysfunction leads to death, whereas moderate dysfunction leads to sickness.<sup>5</sup>

Cells are highly organized units of molecules and macromolecules in which chemical reactions are carried out that together produce a unique property we define as life. Another unifying principle in biology is the overall composition of cells which, regardless of type and function, are basically the same. Thus the unitary concept in biology is that all organisms are related to one another and have evolved from some common ancestor. Any cell except red blood cells contain a central

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4 Almers, W and Stirling, C, "Distribution of Transport Proteins over Animal Cell Membranes" J. Member, Biol 77: 169, 1984.

5 Yates, F.E. (ed.), "*Self organizing systems*," New York, Plenum Publishing Corp. 1987.

prominent nucleus and cytoplasm (fig. 8.6). The nucleus controls the cellular factory like the board of director.

**(a) Cell size**

Human egg x 100	=	0.1 mm.
Human egg: Amoeba	=	100 microns.
Sea urchin egg	=	70 microns.
Liver cell	=	20 microns.
RBC	=	7 microns.
Typhoid bacillus	=	2.4 x 0.5 microns.
Influenza bacillus	=	0.5 x 0.2 microns.
Small leukocyte	=	3 to 3 microns.

**(b) Cell diameter**—It varies as a square of its metabolism. Three factors govern the size of the cells:

- (i) Nucleus cytoplasm ratio,
- (ii) Ratio of cell surface area to cell volume, and
- (iii) Rate of cellular activity.

When a cell enlarges, the surface area of the nucleus across an interchange of material must pass increases only as the square of cell radius while the cell volume increases as the cube of cell volume. A disproportionate increase of cytoplasm will put the cell out of metabolic kilter. The nucleus can increase its surface area by changing shape or doubling the chromosome number. Air which contains 20 per cent oxygen, supplies the centre of the cell of 0.1 mm in diameter with sufficient oxygen to maintain metabolism.

**(c) Chemical nature of cell**—The abundant elements in the biological molecules are:

C = carbon

H = hydrogen

N = nitrogen

O = oxygen

P = phosphorus

S = sulphur

The trace elements needed for all cells to function are:

Na = sodium

K = potassium

Ca = calcium

Mg = magnesium

Mn = manganese

Fe = iron

Co = cobalt

Cu = copper

Zn = zinc

Cl = chlorine

Trace elements needed for some cells are:

B = boron

F = fluorine

Si = silicon

V = vanadium

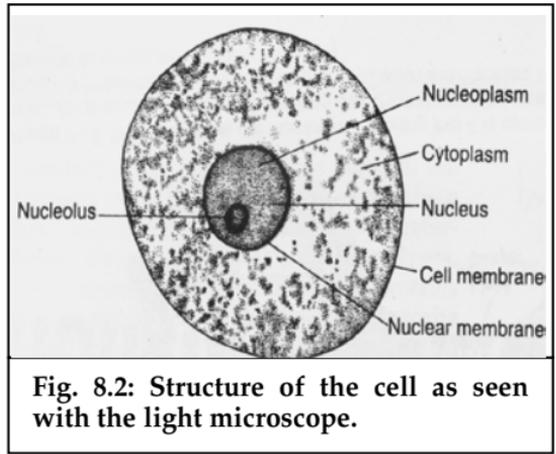
Cr = chromium

Se = selenium

Mo = molybdenum

I = iodine.<sup>6</sup>

A typical cell as seen by the light microscope is illustrated in fig. 8.2.<sup>7</sup> Its two major parts are the nucleus and cytoplasm. The



**Fig. 8.2: Structure of the cell as seen with the light microscope.**

6 *Understanding Genetics*—by O.S. Reddi, Allied publisher Ltd., New Delhi, p. 5-8.

7 *Medical Physiology*—by Guyton, Prism Books (P) Ltd., eighth edition, 1991.

nucleus is separated from the cytoplasm by a nuclear membrane, and the cytoplasm is separated from the surrounding fluids by a cell membrane. The different substances that make up the cell are collectively called protoplasm. Protoplasm is composed mainly of five basic substances—water, electrolytes (minerals), proteins, lipids (fats) and carbohydrates.

- (i) **Water**—The principal fluid medium of the cell is water, which is present in a concentration between 70 and 85 per cent. Many cellular chemicals are dissolved in the water, whereas others are suspended in particulate or membranous form. Chemical reactions take place among the dissolved chemicals or at the surface boundaries between the suspended particles or membranes and the water.
  - (ii) **Electrolytes (mineral)**—The most important electrolytes in the cell are potassium, magnesium, phosphate, sulphate, bicarbonate and small quantities of sodium, chloride and calcium. The electrolytes provide inorganic chemicals for cellular reactions and they are necessary for the operation of some of the cellular control mechanisms. For instance, electrolytes acting on cell membrane allow transmission of electrochemical impulses in nerve and muscle fibres, and the intra-cellular electrolytes determine the activity of different enzymatically catalyze reactions that are necessary for cellular metabolism.
  - (iii) **Proteins**—Next to water, the most abundant substance in most cells is proteins, which normally constitute 10 to 20 per cent of the cell mass. These can be divided into two different types:
    1. Structural proteins, and
    2. Globular proteins.
- (1) **Structural proteins:** To get an idea of what is meant by structural proteins, one needs to note that leather is composed principally of structural proteins and that hair is

almost entirely a structural protein. Proteins of this type are present in the cell in the form of long time filaments that themselves are polymers of many protein molecules. The most prominent use of such intracellular filament is to provide the contractile mechanism of all muscles.

- (2) **Globular proteins:** The globular proteins, on the other hand, are an entirely different type of proteins, composed usually of individual protein molecules or at most aggregates of a few molecules in a globular form rather than in a fibrillar form. These proteins are mainly the enzymes of the cell and in contrast to the fibrillar proteins, are often soluble in the fluid of the cell or are integral parts of or adherent to membranous structures inside the cell and catalyze chemical reactions. For instance, the chemical reactions that split glucose into its component parts and then combine these with oxygen to form carbon-di-oxide and water, while at the sametime providing energy for cellular function, are catalyzed by a series of protein enzymes.
- (iv) **Lipids (fats)**—Lipids are several different types of substances that are grouped together because of their common property of being soluble in fat solvents. The most important lipids in most cells are phospholipids and cholesterol, which constitute to about two per cent of the total cell of mass. The special importance of phospholipids and cholesterol is that they are mainly insoluble in water and, therefore, are used to form membranous barriers that separate the different intracellular components.

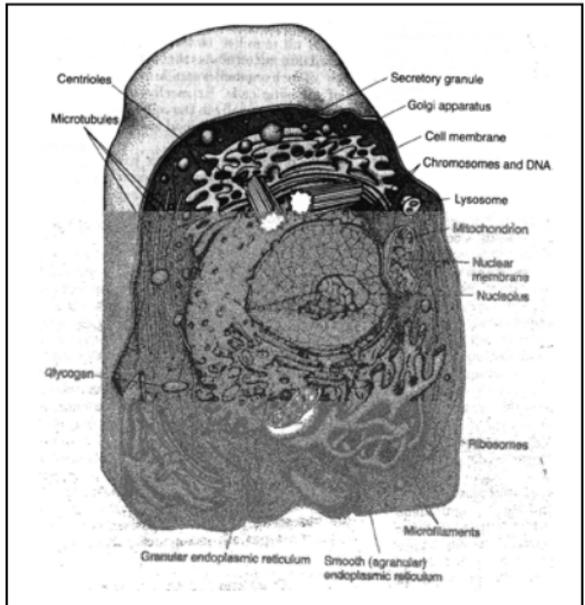
In addition to the phospholipids and cholesterol, some cells contain large quantities of triglycerides, also called neutral fat. In the so-called fat cells, triglycerides often account for as much as 95 per cent of the cell mass. The fat stored in these cells represents the body's main store house of energy giving nutrient

that can later be dissolved and used for energy where even in the body it is needed.

#### (iv) Carbohydrates

—In general, carbohydrates have very little structural function in the cell except as part of glycoprotein molecules, but they play a major role in

nutrition of the cell. Most human cells do not maintain large stores of carbohydrates, usually averaging about 1 per cent of their total mass. However, carbohydrate in the form of glucose, is always present in the surrounding extra cellular fluid so that it is readily available.<sup>8</sup>



**Fig. 8.3: Reconstruction of a typical cell, showing the internal organelles in the cytoplasm and in the nucleus.**

### 8.2.1 PHYSICAL STRUCTURE OF THE CELL

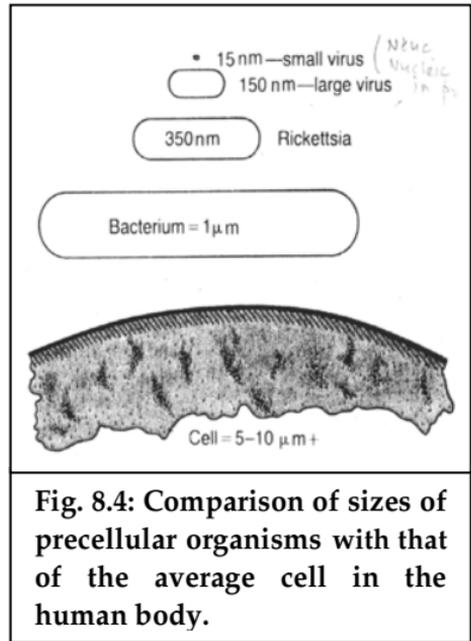
The cell is not merely a bag of fluid, enzymes and chemicals, it also contains highly organized physical structures of which are called organelles, and the physical nature of each of this is equally as important to the function of cell as the cell's chemical constituents. For instance, without one of the organelles, the mitochondria, more than 95 per cent of the energy supply of cell would cease immediately. Some principal organelles of structure of cell are

<sup>8</sup> Bettger, W.J. and Mc. Kechan, "W.L. Mechanism of Cellular Nutrition," *Physiol*, Rev. 66.1, 1986.

illustrated in figure 8.3.<sup>9</sup> Including the cell membrane, nuclear membrane, endoplasmic reticulum, Golgi apparatus, mitochondria, lysosomes and centrioles.

### (i) Comparison of the animal cell with precellular forms of life

Many of us think of the cell as the lowest level of life. However, the cell is a very complicated organism, which requires many million years to develop after the earliest form of life, an organism similar to the present day virus, first appeared on earth. Figure. 8.4.<sup>10</sup> illustrates the relative sizes of the smallest known virus, a large virus, a rickettsia, a bacterium and a nucleated cell. Showing that the cell has a diameter about 1000 times that of the smallest virus and, therefore, a volume about one billion times that of the smallest virus. Correspondingly, the functions and the anatomical organization of the cell are also far more complex than those of virus without nucleus.



**Fig. 8.4: Comparison of sizes of precellular organisms with that of the average cell in the human body.**

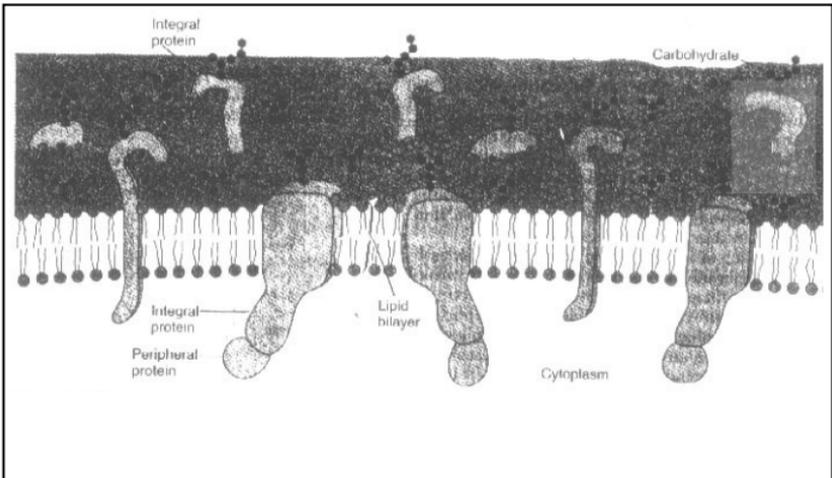
The essential life giving constituents of very small virus is a nucleic acid embedded in a coat of protein but without nucleus. This nucleic acid is composed of the same basic constituents (DNA and RNA) as found in mammalian cells, and it is capable of reproducing itself if appropriate conditions are available. Thus, the virus is capable of propagating its linkage from generation to generation and, therefore, is a living structure in the same way that the cell and the human beings are the living structures.

<sup>9</sup> *Medical physiology*, Guyton, p. 10.

<sup>10</sup> *Ibid*, p. 10.

As life evolved, other chemicals besides nucleic acid with specialized function began to develop in different parts of the virus. A membrane formed around the various parts, and inside the membrane a matrix appeared, specialized chemicals develop inside the matrix to perform special functions, many protein enzymes appeared, which are capable of catalyzing chemical reactions, and therefore, determining the organism's activities. In later stages, particularly in the rickettsial and bacterial stages, organelles developed inside the organism, representing physical structures of chemical aggregates that perform functions in a more efficient manner that can be achieved by dispersed chemicals throughout the fluid matrix. Finally, in the nucleated cell, still more complex organelles developed, the most important of which is the nucleus itself. The nucleus distinguishes this type of cell from all lower forms of life, this structure provides a control centre for all cellular activities, and it provides for exact reproduction of new cells generation after generation, each new cell having essentially the same structure as its progenitor.

- (ii) **Cell membrane**—Essentially all organelles of the cell are lined by membranes composed primarily of lipids and proteins. These membranes include the cell membrane, the nuclear membrane, the membrane of the endoplasmic reticulum, and the membranes of mitochondria, lysosomes, golgi apparatus as well as others (fig. 8.5). The lipids of the membranes provide a barrier that prevents free movement of water and water soluble substances from one cell compartment to another. The protein molecules in the membrane, on the other hand, often penetrate all the way through the membrane. Also, many of the membrane proteins are enzymes that catalyze a multitude of different chemical reactions.



**Fig. 8.5: Structure of the cell membrane, showing that it is composed mainly from a lipid bilayer but with large members of protein molecules protruding through the layer. Also, carbohydrate moieties are attached to the protein molecules on the outside of the membrane. An additional protein molecules on the inside. (from I. Adish and Rothman. *The Assembly of Cell Membranes Sci. Am.*, 240.48, 1979 © 1979 b Scientific American, Inc. All rights reserved.)**

The cell membrane, which completely envelopes the cell, is a very thin, elastic structure, only 7.5 to 10 nanometres thick. It is composed of proteins and lipids. The approximate composition is:

Proteins	=	55%
Phospholipids	=	25%
Cholesterol	=	13%
Other lipids	=	4%
Carbohydrates	=	3%

(iii) **Cytoplasm**—The cytoplasm is filled with both minute and large dispersed particles and organelles ranging in size from a few

nomometres to many micrometres (fig. 8.6). The clear fluid portion of cytoplasm in which the particles are dispersed is called cytosol. This contains many dissolved proteins, electrolytes, glucose and minute quantities of lipid compounds.

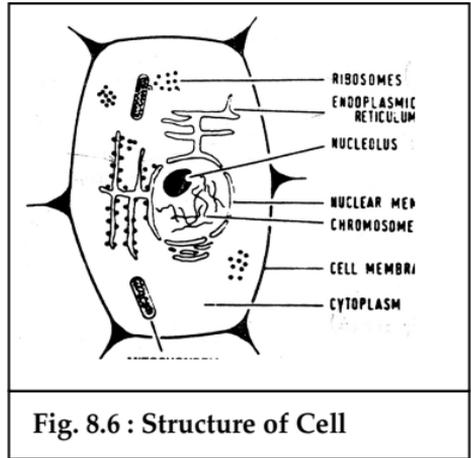


Fig. 8.6 : Structure of Cell

The portion of cytoplasm immediately beneath the cell membrane frequently contains an inter-woven net of microfilaments composed mainly of actin fibrillae. These provide a semi-solid gel-like support for the cell membrane. This zone of cytoplasm is called the ectoplasm. Dispersed in the cytoplasm are neutral fat globules, glycogen graunules, ribosomes, secretory granules, and five specially important organelles, the endoplasmic reticulum, the golgi apparatus the mitochondria, the lysosomes and peroxisomes.

(iv) **Endoplasmic Reticulum**—Figure 8.3 illustrates the cytoplasm, a network of tubular and flat vesicular structures called the endoplasmic reticulum. The tubules and vesicles all interconnect with each other. Also, their walls are constructed of lipid bilayer membranes containing large amount of proteins, similar to the cell membrane.

(v) **Ribosomes**—Attached to the outer surface of many parts of the endoplasmic reticulum are the large numbers of small granular

particles called ribosomes, where these are present. The ribosomes are composed of a mixture of ribonucleic acid (RNA) and proteins and they function in the synthesis of protein in the cells.

(vi) **Golgi apparatus**—The golgi apparatus, illustrated in fig. 8.7<sup>11</sup> is enclosed related to the endoplasmic reticulum. It has membranes similar to those of the angular endoplasmic reticulum. It is usually composed of four or more stacked layers of thin, flat enclosed vesicles lying near the nucleus.

The golgi apparatus functions in association with the endoplasmic reticulum. As illustrated in the figure 8.7, small "transport vesicles" also called endoplasmic reticulum vesicles or simply ER vesicles, continually pinch off from the endoplasmic reticulum and shortly thereafter fuse with the golgi apparatus. In this way, substances are transported from the endoplasmic reticulum to golgi apparatus. The transported substances are then processed in golgi apparatus to form lysosomes, secretory vesicles or other cytoplasmic components.

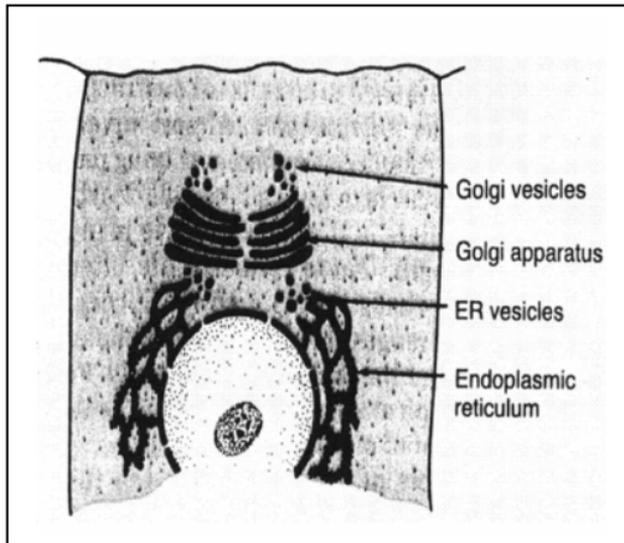


Fig. 8.7: A typical Golgi apparatus and its relationship to the endoplasmic reticulum and the nucleus.

(vii) **Lysosomes**—Lysosomes are vesicular organelles formed by the golgi apparatus that then become dispersed throughout the

cytoplasm. The lysosomes provide an intracellular digestive system that allows the cell to digest and thereby remove the unwanted substances and structures, especially the damaged or foreign structures such as bacteria. The lysosomes are illustrated in fig. 8.3.

- (viii) **Mitochondria**—The mitochondria are called the "power houses" of the cell. Without them, the cells would be unable to extract significant amounts of energy from the nutrients and oxygen, and as a consequence, all essential cellular functions would cease. As illustrated in the cell of figure 8.3, these organelles are present essentially in all proportions of the cytoplasm. Mitochondria are concentrated in those portions of cell which are responsible for the major share of its energy metabolism.

Mitochondria are self replicate, which means that one mitochondrion can form a second one, a third one and so on, whenever there is need in the cell for increased amounts of ATP. Indeed, the mitochondria contain deoxyribonucleic acid (DNA). Similar to that found in the nucleus. DNA is the basic substance of the nucleus that controls replication of the cell. This substance plays a similar role in the mitochondrion replication process. Many proteins and lipids that have already been formed in the cytoplasm are incorporated into the mitochondria as they enlarge and bud off to form new mitochondria.<sup>12</sup>

- (ix) **Nucleus**—The nucleus is the control

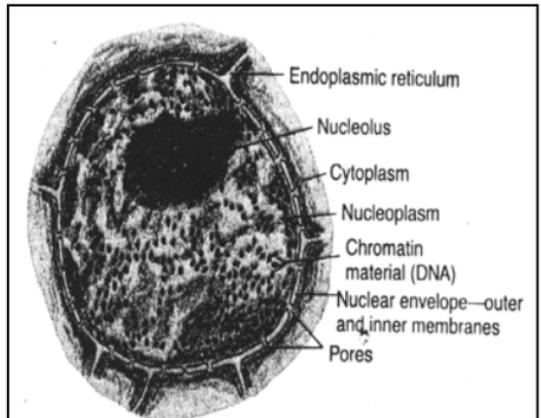


Fig. 8.8 (a): Structure of the nucleus

12 Lane, M.D. et al., "The Mitochondrion Updated," Science, 234, 1986, p. 566.

centre of the cell. Briefly, the nucleus contains large quantities of DNA which we call genes for many years. The genes determine the characteristics of the protein enzymes of the cytoplasm and in this way control cytoplasmic activities. They also control reproduction. The genes first reproduce themselves and after this the cell splits by a special process called mitosis to form two daughter cells, each of which receives one of the two sets of genes.

Fig. 8.8 (a) illustrates the light microscopic appearance of the interphase nucleus (period between mitosis) showing darkly staining chromatin material throughout the nucleoplasm. During mitosis, the chromatin material becomes readily identifiable as the highly structured chromosomes.

- (xi) **Nuclear membrane (envelop)**—The nuclear envelop is frequently called the nuclear membrane. However, it is actually two separate membranes, one inside the other. The outer membrane is continuous with the endoplasmic reticulum, and the space between the two nuclear membranes are also continuous with the compartment inside the endoplasmic reticulum.

## 8.2.2 Functions of different parts of the cells

Table 8.1

S.No.	Cell Component	Function
01.	Cell Walls	(i) It protects the protoplasm from injuries. (ii) Provides definite shape to the cell. (iii) It provides rigidity and strength to the cell.
02.	Plasma membrane	It is differentially permeable membrane through which translocation of material occurs.
03.	Cytoplasm	It is the executive centre of the cellular functions.
04.	Hyaloplasm or matrix	It contains substances and enzymes for the biochemical processes.

Contd..

05.	Cytoplasmic Organelles	
	(a) Plastids (In plantonly)	(i) Photo synthesis (ii) Storage of pigments, starch and some other cellular products.
	(b) Mitochondria	(i) Completion of Kreb's cycle. (ii) Synthesis of ATP—the energy rich compound. (iii) Electron transport chain. (iv) B-oxidation of fatty acids.
	(c) Golgi complex	(i) Storage of synthesis proteins and enzymes. (ii) Secretion of certain substances.
	(d) Endoplasmic reticulum	(i) Acts as ultra structural skeletal framework in the cell. (ii) Provides increased surface for the various enzymatic activities, which normally occur at a cross membrane surface. (iii) Transports extra cellular and intra cellular molecules. (iv) Forms nuclear envelop at the telophase.
	(e) Microsomes	The ribosome particles attached to the membranes of endoplasmic reticulum and microsomes are the main sites for protein synthesis in the cell.
	(f) Ribosomes	(i) These are the sites for protein synthesis in the cell.
	(g) Lysosome	(i) Acts as the store house for a number of hydrolysing enzymes which help in the digestion of intracellular particles. (ii) Destroys bacteria and other foreign bodies inside the cell.
	(h) Microbodies	(i) Contain enzymes of hydrogen peroxide for metabolism, purine metabolism, gluconogenesis and photo respiration.
		Contd...

	(i) Microtubules	(i) Transportation of water and small molecules of various substances. (ii) From structural units of centrioles, base grounds, cilia and flagella and mitotic spindles. (iii) Help in cytoplasmic movement.
	(j) Centrosome	The centrioles form the spindle and have a significant role in the movement of chromosomes during nuclear division.
	(k) Flagella & cilia	These are extra cellular projections which help in the movement of cell.
6.	Vacuoles	(i) Act as Osmoregulatory structures in the cell. (ii) Act as storage depots for excess water products, pigments, etc. (iii) Acts as excretory structures.
7.	Nucleus	It is the controlling centre for all the vital functions of the cell.
	(a) Nucleus envelop	It provides active continuity of ground plasm between nucleus and cytoplasm.
	(b) Nucleoplasm	It contains material for the synthesis of nucleic acids.
	(c) Chromatic reticulum and chromosomes	These are bearers of the hereditary instructions and for the regulation of cellular processes.
	(d) Nucleolus	(i) It disappears during nuclear division and forms matrix sheath around the chromosomes. (ii) Acts as a store house for ribosomal proteins and ribosomal RNA

**(a) Difference between plant cell and animal cell:**

S. No.	Plant Cell	Animal Cell
01.	Presence of cellulosic cell wall.	No cell wall of cellulose present.
02.	Presence of large vacuoles.	Vacuoles in animal cells are small.
03.	Plastids present in most cells.	Plastids absent in animal cells excepting some protozoa (euglenae).
04.	Centrioles are absent in the plant cells excepting a few algae.	Centrioles are common in all animal cells.

From the detailed study of different components of protoplasm, it is evident that each structure in the cell has to perform special vital activity. Thus the cell is actually an exceedingly complex factory in which a large number of chemical processes are going on simultaneously. The cytoplasm by virtue of its different organelles is regarded as execution centre for metabolic processes, and the nucleus by virtue of its genes can be regarded as the regulating or controlling centre of the cell.<sup>13</sup>

### 8.2.3 CELL DIVISION

For growth, cells have to be divided. In this process, they produce a replica of their own. All cells in the body except reproductive cells or germ cells multiply by a process called mitosis. This process has four stages as follows:--

(a) **Mitosis**—See fig. 8.8(b)

- (i) **Interphase**—Where the DNA has duplicated, chromatin material condenses.
- (ii) **Prophase**—Chromosomes seen as coils. Nuclear membrane and nucleolus disappear. The sister chromatids lie side by side.
- (iii) **Metaphase**—Chromosomes appear as rod like bodies with the centromere arranged on the equatorial plate attached by two spindle poles.

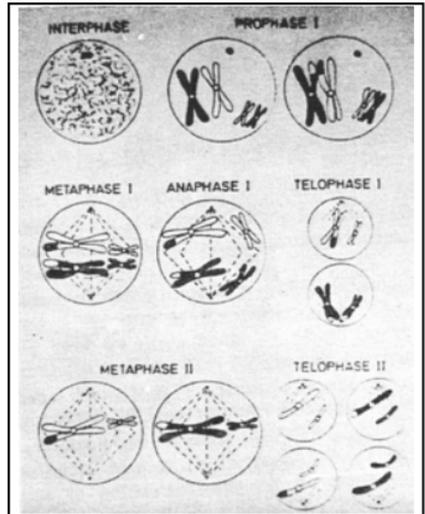


Fig. 8.9: Meiosis

13 *Cytogenetics evolution and plant breeding*—by R.S. Shukla and P.S. Chandel, published by S. Chand and Co. Ltd., New Delhi, 1998 edition.

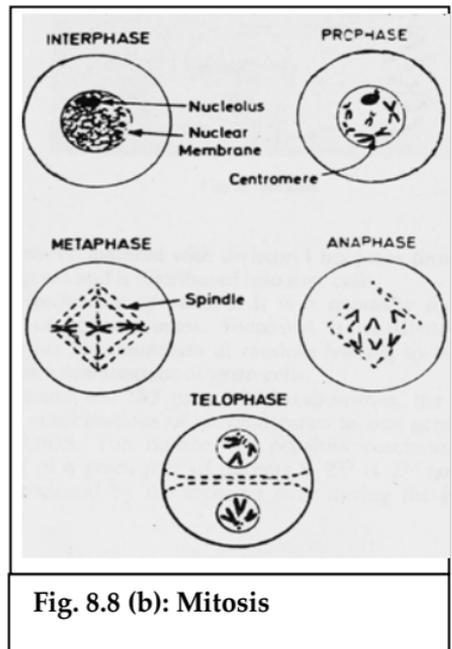
(iv) **Anaphase**—Disjunction occurs, each chromatid is pulled to poles.

(v) **Telophase**—Chromatids decendensed spindle fibres disintegrate. The nuclear membrane forms and cell division begins.

With the usual type of cell division or mitosis the number of chromosomes in daughter cells remain constant.

(b) **Meosis**—In the germ cells, there is another type of division called meosis which reduces the number of chromosomes, since the chromosome numbers should remain constant even after fusion of egg from female and spermatozoa from the male.

The division sequence is as follows: see fig(8.9)



(i) **Prophase-I**—Chromosome threads are visible homologous from mother and father pair (zygotene). When pairing is completed, chromosomes are shorten by contraction (pachytene). A longitudinal cleft can be seen in each pair of chromosome. Thus, four chromotids of each kind are seen side by side (diplotene). Then the non-sister chromotides separate, while sister chromotides remain paired, chromotin crossing between non-sister chromotids can be seen.

- (ii) **Metaphse-I**—As the centromeres are drawn to poles chromosomes arrange on the metaphase plane.
- (iii) **Anaphase-I**—Paired chromosomes separate and migrate to opposite poles. Daughter nuclei are formed.

The genetic material with division-I become four fold ( $2 \times 2$  homologous) and is divided into four cells.

- (c) **Significance of meiosis**—It is necessary to reduce the number of chromosomes. Secondly it distributes the non homologous chromosomes at random leading to large number of possible combinations of germ cells. In man, with 23 pairs chromosomes, the number of possible combinations of chromosomes in one germ cell is  $2^{23} = 83,88,608$ . The number of possible combination in offspring of a given pair of parents is  $2^{23} \times 2^{23}$  and is further highly enhanced by crossing over during the homologous pairing.<sup>14</sup>

#### 8.2.4 CELL REPRODUCTION

Cell reproduction is another example of the pervading iniquitous role that the DNA—genetic system plays in all life processes. The *genes* and their regulatory mechanisms determine the growth characteristics of the cells and also when or whether these cells divide to form new cells. In this way, all the important genetic system controls each stage in the development of the human being from the single cell fertilized ovum to the whole functioning body. Thus, if there is any central theme to life, it is the DNA-genetic system.<sup>15</sup>

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14 *Understanding Genetics*—by O.S. Reddi, Allied Publishers Ltd., New Delhi, p. 10.

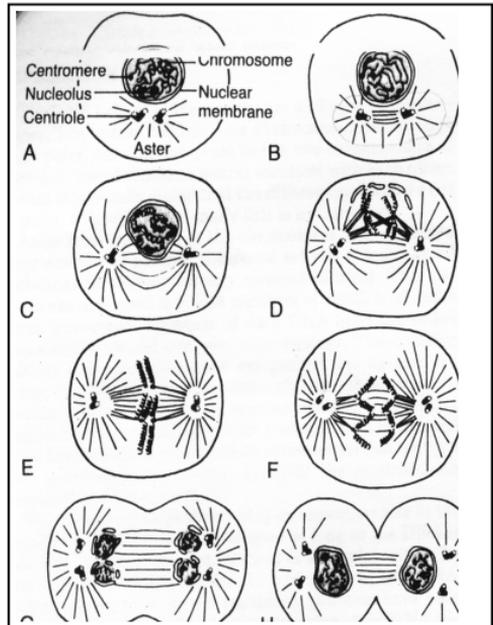
15 *Medical Physiology*—by Guyton, Prism Book (P) Ltd., eighth edition, 1991, p. 31.

## 8.2.5 THE LIFE CYCLE OF THE CELL

The life cycle of a cell is the period of time from cell reproduction to reproduction, when mammalian cells are not inhibited and are reproducing as rapidly as they can, this life cycle lasts for 10 to 30 hrs. It is terminated by a series of distinct physical events called mitosis that cause the division of the cell into two new daughter cells. The events of the life cycle of the cell are illustrated in figure 8.10.<sup>16</sup>

The actual state of mitosis, however, lasts for only about 30 minutes, so that more than 95 per cent of life cycle even of rapidly reproducing cells is

represented by the interval between mitosis called interphase. In fact, except in special conditions of rapid cellular reproduction, inhibitory factors almost always slow or stop the uninhibited life cycle of the cell. Therefore, different cells of the body have life cycle periods that vary from as little as 10 hrs. for stimulated bone marrow cells to an entire life time of the human body for nerve and striated muscle cells.



**Fig. 8.10:** Stages in the reproduction of the cell. A, B, and C, prophase; D, prometaphase; E, metaphase; F, anaphase; G and H, telophase. (Redrawn from Mazia : How cells divide. Sci. Am., 205 : 102, 1961. © by Scientific American, Inc. All rights reserved.)

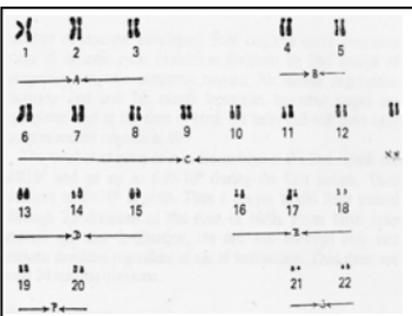
### 8.3 Characteristic of chromosomes

For understanding about life and functions of different organs of body, it is a must to understand about the characteristic of chromosomes.

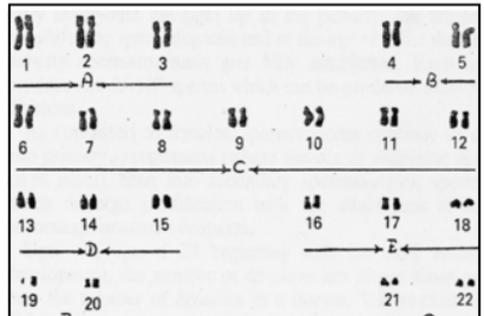
#### 8.3.1 WHAT IS A CHROMOSOME?

The basic structure of life is cell. The cell contains what is called cytoplasm and nucleus. The cytoplasm contains the machinery to manufacture all the chemical ingredients to sustain the processes of life. Some cells aggregate to form tissues which aggregate to form organs. These organs eventually make all the beings. These are brain, heart, lungs, kidneys, liver, pancreas, spleen, reproductive organs like ovaries and uterus in females and testicles and penis in males. Thus a human body is constructed by a diverse structure of tissues and organs with the basic unit of the cells. Thus we see unity in diversity of life.

The cytoplasm contains machinery to manufacture the chemicals to maintain life. It contains endoplasmic reticulum that contains ribosome to process the information transfer and



**Fig. 8.11: Chromosomes (female Karyotype)**



**Fig. 8.12: Chromosomes (Male Karyotype)**

mitochondria, the power plants of cells that supply energy. The nucleus contains rod like structure stainable with dyes called chromosomes. These chromosomes contain DNA, which is the store house of genetical information to be transmitted from

generation to generation. The chromosomes occur in pairs or in sets. In man and woman, there are 23 pairs, 22 sets are called autosomes and one pair called sex chromosome which determines the sex of child, designated as XX in woman and XY in man (fig. 8.11-8.12).<sup>17</sup> Thus any male will have chromosomal constitution of XY and female XX. Sex is primarily determined by sex chromosomes X and Y at the time of fertilization of egg.

### 8.3.2 MORPHOLOGY OF CHROMOSOMES

The term chromosome refers to the deeply staining DNA containing filamentous bodies observed in the dividing cells of nucleate organisms. The chromosomes are nuclear components possessing special organic individuality and functions. They bear genes or hereditary units and are capable of reproducing themselves without involving any change in morphology and physiology at successive generations. The chromosomes can be in reality stained with basic dyes. Such as basic fuchsin (fuelgen's stain) carmine, haematoxyline, crystal violet, etc.

The chromosomes are filamentous bodies found in the nucleus and are visible during cell division. They are linkage structures each consisting of a linear sequence of genetic information or genes. The chromosomes of prokaryotes and eukaryotes are essentially similar in two main activities—

- (i) They are concerned with transmission of genetic information from cell to cell and generation to generation.
- (ii) They are concerned with the release order of genetic information to control cellular functions and developments.

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<sup>17</sup> *Understanding Genetics*—by O.S. Reddi, Allied Publishers Ltd., New Delhi.

They are auto duplicating structures of differential complexity in eukaryotes and prokaryotes and their morphology and organization are organism specific. The chromosomes of prokaryotes are generally double stranded circular DNA molecules. But in some viruses, they may be single stranded. In eukaryotes, they present a complex structure. Most of the chromosomes in a cell are called autosomes which carry genes for most of the body characters.

Besides, there may be one, two or more chromosomes which carry genes for determination of sex as well as for sex linked character. They are called sex chromosomes (as for example X chromosome and Y chromosome).<sup>18</sup>

### 8.3.3 CHROMOSOMES IN SOME ANIMAL CELLS

Cells of the body are provided with a pocket of genetic material, the nucleus, which contains chromosomes. Normally, all the individuals of a species have fixed number of chromosomes in their nuclei. The characteristic group of chromosomes in a cell is spoken of its complement. Generally, the somatic cells of animal and higher plants are diploid (i.e., they have two sets of chromosomes  $2n$ ) while their gametes, as a rule, are haploid as they contain only one set of chromosomes. The number of chromosomes present in gametes is referred to as haploid or genetic chromosome number or 'n'. In diploid organisms, half of the chromosomes of a nucleus are contributed by the female gamete (maternal chromosome) in the sexual reproduction. The haploid set of chromosomes is also known as genome.

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18 *Cytogenetics Evolution and Plant Breeding*—by R.S. Shukla and P. S. Chandel, published by S. Chand and Co. Ltd., New Delhi, 1998 edition.

**(a) Table—Chromosome number of some animals**

S. No.	Name of animal	Diploid chromosome number (2n)
01.	Paramecium	30-40
02.	Hydra	32
03.	Round worm	2
04.	Silk worm	56
05.	House fly	12
06.	Fruit fly	8
07.	Honey bee	32, 16
08.	Mosquito	6
09.	Frog	26
10.	Chicken	78
11.	Pigeon	80
12.	Mouse	40
13.	Rabbit	44
14.	Common rat	42
15.	Guinea pig	64
16.	Dog	78
17.	Cat	38
18.	Horse	64
19.	Pig	40
20.	Goat	60
21.	Chimpanzee	48
22.	Man	46
S. No.	Name of plant	Diploid chromosome number (2n)
01.	Chlamydomonas	10, 12, 16 (haploid)
02.	Bread mold	2
03.	Yellow pine	24
04.	Cabbage	18
05.	Radish	18
06.	Papaya	18
07.	Cotton	52
		Contd...

08.	Coffee	44
09.	Sunflower	34
10.	Potato	48
11.	Tomato	24
12.	Tobacco	48
13.	Banana	22, 44, 55, 77, 88
14.	Garden pea	14
15.	Bean	22
16.	Orange	18, 27, 36
17.	Apple	34, 51
18.	Indian corn	20
19.	Barley	14
20.	Bread wheat	42
21.	Rice	20
22.	Bajra	10, 20, 40
23.	Sugarcane	80
24.	Field bean	12
25.	Onion	16

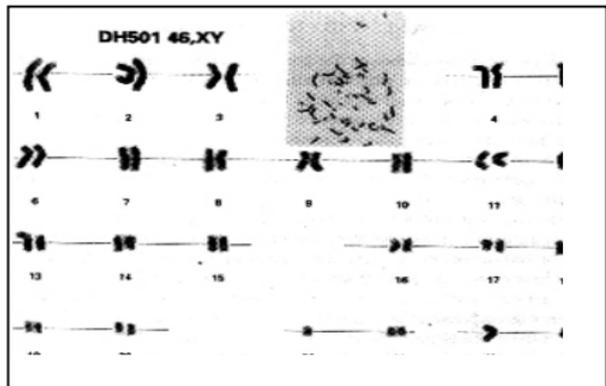
#### 8.3.4 GENES AND CHROMOSOMES

The root of all inheritance is the gene. In general, one *gene* encodes, or makes, one protein, which in turn catalyzes one biochemical reaction. Genes are so small that they cannot easily be divided, so they usually are passed on intact from parent to child. Genes are found on long, threadlike molecules called chromosomes, which are located within the nucleus of the cell. An average human chromosome, containing about 4000 genes, is large enough that it can be seen with a light microscope.

Humans have two copies of each chromosome. One number of each pair is inherited from the mother, the other from the father. Each person has twenty three pairs of chromosomes: twenty two pairs called autosomes and one pair of sex chromosomes. The two numbers of each pair of autosomes are virtually identical; looking in the microscope it is impossible to tell which was derived from the mother and which from the father. The two sex chromosomes known as "X" and "Y" are

noticeably different from one another; the X chromosome is relatively large and long whereas the Y chromosomes are small and dumpy. Men and women share almost the same genetic make up, but males have an X and Y sex chromosome, while females have two copies of the X. The sex of an individual is determined by the presence or absence of the Y chromosome, not by the number of X chromosomes.

Figure 8.13 shows the typical array of chromosomes found in the blood cells of a male, in this case a gay man. The chromosomes have been arranged into a karyotype, or a portrait of the chromosomes in the order of size.



**Fig. 8.13: A Male Karyotype** A typical male karyotype, or arrangement of chromosomes according to size, in the case of a gay man. The chromosomes are arranged in the order of size. The inset shows how the chromosomes were arranged when the cell was opened.

Almost every cell in the body contains the same set of forty-six chromosomes and thus the same genetic information, so each tiny cell contains all the information needed by the entire body. To make an analogy, each chromosome forms a single volume of a personalized set of encyclopaedias containing everything necessary to be human. The genes are like the individual articles found in each encyclopaedia.

Chromosomes from male and female come together during conception, when a sperm cell fertilizes an ovum. Sperm and ova are special types of cells, called germ cells that contain only one copy of each chromosome, instead of two. Only one of each pair of chromosomes—either the one inherited from the mother or the other from the father—can end up in a germ cell, and the selection is

determined purely by chance during a process called meiosis. Chance also dictates which of a large number of sperm cells will fuse with a particular ovum to form a fertilized egg cell. Once conception occurs and the male and female chromosomes have merged, all the cells in the new human will be almost exact copies of the original fertilized egg cell. Thus the genetic composition of a human depends on two throws of the dice, the first during the formation of the germ cells and the second at conception. These two actions suffle the genetic information so thoroughly that a child can have his\her father's nose and mother's eyes and the other traits that seem to be a combination of both parents' physical characteristics or characteristics that are 'gifts' from past generations.<sup>19</sup>

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19 *The Science of Desire*—by Dean Hamer and Peter Copeland, published by Simon and Schuster Rocke Feller Centre, 1230 Avenue of the Americas, New York, 10020, edition 1994, p. 75-77.

## 9

## Genetic Codes in DNA and RNA

## 9.1 DNA

DNA structure, its working, its importance and its role in bondage are briefed as follows:

## 9.1.1 CAUSE OF BONDAGE—DIFFERENCE OF GENES

Markers can help to find genes. But first the markers themselves have to be found. Genetically speaking, humans are nearly identical. Only about 0.1 per cent of human genome, or three million DNA base pairs out of the total three billion, varies from one person to the next (base pairs are chemicals that bind together to form the rugs on the spiral staircase that DNA resembles). Markers are found among the bits of DNA that differ from one person to the next. Such differences, called polymorphisms, can consist of deletion or insertions of genetic material or alteration in just a single base pair. Identifying, all three markers, these bits of DNA that vary from person to person, is the goal of Human Genome Project.<sup>1</sup>

All we could pick up were occasional bits of English words such as "trinucleotide repeat" and "PCR." These are the short stretches of DNA repeated again and again. The useful thing about them is that different people have different numbers of repeats on their chromosomes. For example, on the chromosome

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1 Lander E.S. 1988, "*Mapping complex genetic traits in humans*" in *Genome Analysis*, ed. K.E. Davis, 171-89, IRL Press, New York (U.S.A.).

the chemical sequence might be GGATTCA CA TT AC, which contains eleven repetition of the sequences CA, but in another person's chromosome same stretch of DNA might read GGATT CA CA, which has thirteen repeats of the phrase CA. These sequences serve as genetic finger prints found all over the genome, making it possible to map every bit of DNA.

From a practical point of view, the most important thing about these markers is that they can be detected easily and economically with a method called the polymerize chain reaction or PCR. Heating and cooling the DNA while mixing it with special enzymes and chemicals causes the short stretches of DNA markers to duplicate again and again. After forty cycles of heating and cooling the original target of DNA has a billion copies. The technique once dismissed as an academic exercise with no practical use has become one of the most powerful tools of molecular biology and won the inventor, Karry Mullis, a 1993 Nobel Prize winner. PCR works each of the four chemicals that form DNA can only make a ring on the ladder a base pair—with another chemical. So adenine (A) always pairs with thymine (T) and guanine (G) always pairs with Cytosine (C). That means knowing the pattern of chemicals on the side of the ladder automatically gives us the pattern on the other side. Working like a chemical Velcro, only with opposite stick together to form the DNA ladder.<sup>2</sup>

### 9.1.2 NUCLEIC ACID

DNA is made of nucleic acid, so defining DNA in detail needs the definition of nucleic acid on the first hand. The substance that was eventually proved to be genetic material was discovered in 1868, only four years after the announcement of laws of

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2 Botstein, D, R.L. White, M. Skolnick and R.W. Davis 1980, "Construction of a Genetic Linkage Map in Man using Restriction Fragment Length Polymorphism".

heredity by Mendel and 84 years before DNA became central issue of modern molecular biology following the publication of famous double helix model of DNA by Prominent Scientists Watson and Crick in 1953. By 1944, Capersson and Brachel independently suggested that the nucleic acids were directly connected with protein synthesis. In 1944, O.T. Avery, C.M. Macleod and M. Mc Carty conducted a remarkable experiment and suggested that bacteria could be genetically transformed by DNA. The nucleic acids are of two types—

- I. Deoxyribonucleic Acid (DNA).
- II. Ribonucleic Acid (RNA).

### 9.1.3 DNA STRUCTURE

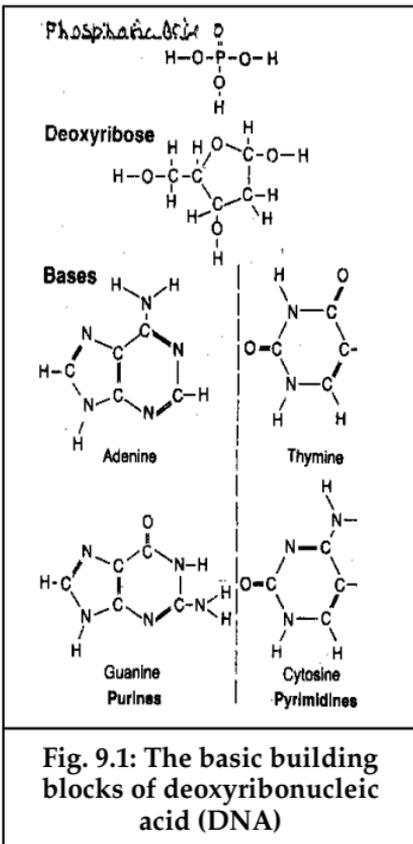


Figure 9.1 illustrates the basic chemical compounds involved in the formation of DNA. These include:

- (i) Phosphoric acid.
- (ii) A sugar called De-oxy-ribose.
- (iii) Four nitrogenous bases (two purines—adenine and guanine and two pyrimidines—thymine and cytosine). The phosphoric acid and deoxyribose form the two helical strands that are the backbone of the DNA molecule and the bases tie between the two strands and connect them.

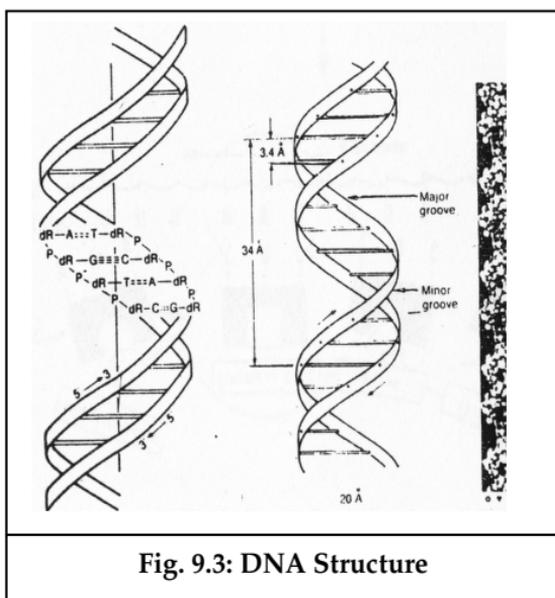
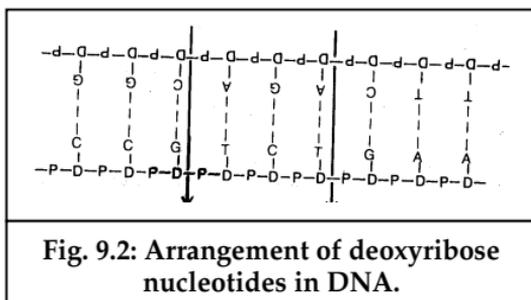
**Fig. 9.1: The basic building blocks of deoxyribonucleic acid (DNA)**

Figure 9.2 illustrates the manner in which multiple number of nucleotides are bound together to form DNA. Note that these are combined in such a way that phosphoric acid and de-oxy-ribose alternate with each other in the two separate strands, and these strands are held together by loose bonds between the purine and pyrimidine bases. But note carefully that—

- (i) The purine base—adenine always bonds with the pyrimidine base—thymine, and
- (ii) The purine base—guanine always bonds with the pyrimidine base—cytosine.

Thus in figure 9.2, the sequence of complementary pairs of bases is CG, CG, GC, TA, CG, TA, GC, AT and AT. However, the bases are bound together by very loose hydrogen bonding, represented in the figure by dashed lines. Because of the looseness of these bonds, the two strands can be pulled apart easily, and they do it so many times in the course of their function in the cell.

Now to put the DNA of figure 9.3 into its proper physical perspective, one needs merely to pick up the two ends and twist them into a helix. Ten



pairs of nucleotides are present in each full turn of the helix in the DNA molecule, as is illustrated in figure 9.4.<sup>3</sup>

Hershey and Chase Avery and others who worked with micro-organisms have proved that DNA is a genetic material. The structure of DNA was formulated by the prominent scientists Watson and Crick in 1953. We know that DNA carries the specifications of growth and differentiation. As stated earlier, we transfer biological inheritance by way of genes. These genes are chemical entities decided by a chemical called nucleic acid.

Thus the biological information is written in the form of chemical code. Watson and Crick (1953) determined the chemical molecule that is responsible for biological inheritance.

DNA has four bases with pairs of adenine and thymine (A-T pair) and cytosine and guanine (C-G pair) which are bound by hydroegn bonds with a backbone of sugar and phosphate structure. The chemical polymer is like a spiral or ascending staircase. *DNA represents life*. It is present in all the cells of body, except red blood cells which don't have a nucleus and hence cannot divide. We know that DNA is the basis of life of all organisms in nature—plants, animals and men.

**Table 9.1**

S. No.	Bases	Deoxyribonucleic Acid	Ribonucleic Acid
01.	(i) Pyrimidine bases (ii) Purine bases	(i) Cytosine (ii) Thymine (i) Adenine (ii) Guanine	(i) Cytosine (ii) Uracil (i) Adenine (ii) Guanine
02.	5c Sugars (pentoses)	Deoxyribose Sugar	Ribose Sugar

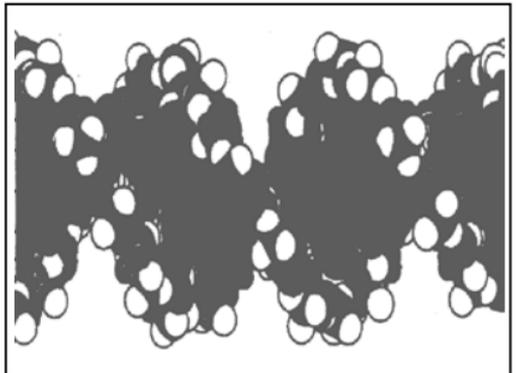
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<sup>3</sup> *Medical Physiology*—by Guyton, published by Prism Books (P) Ltd., eighth edition, 1991, p. 24.

DNA is present in the cells of plants, animals and prokaryotes and in a number of viruses. DNA molecule appears to be the most stable one present in the chromosome. It has also been reported in some cytoplasmic organelles like chloroplast, mitochondria and centrioles. The amount of DNA per set of chromosome is constant for a particular species. The DNA content of a diploid somatic cell ( $2n$ ) is exactly double that of haploid cells ( $n$ ). There is a close relationship between DNA content and chromosome size. It has been found that about 31 cms of double helix DNA is equal one pikogram ( $1\text{pg} = 10^{-12}\text{ gm}$ ). In man, a deploid cell contains about 5.6 pg of DNA which may correspond to about 174 cms of DNA.<sup>4</sup>

A deploid human cell contains  $7.1 \times 10^9$  nucleotide pairs. About 6-7 million genes are accommodated on this DNA. Forty-two per cent of DNA in the human genome consists of repetitive sequences of redundant DNA—that is non-coding DNA. Also, inter-spersed with coding DNA is non-coding DNA.<sup>5</sup>

Large number of genes attached end to end are contained in extremely long double stranded, helical molecules of DNA having molecule weights



**Fig. 9.4: The helical, double-stranded structure of the *gene*. The outside strands are composed of phosphoric acid and the sugar deoxyribose. The internal molecules connecting the two strands of the helix are punne and pyrimidine bases; these determine the "code" of**

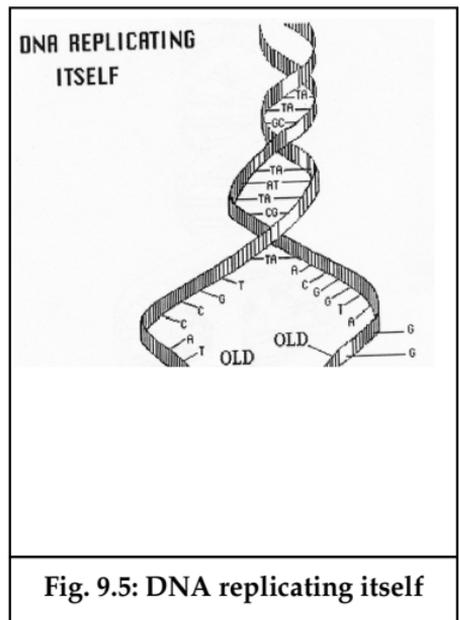
4 *Cytogenetic Evolution and Plant Breeding*—by R.S. Shukla and P.S. Chandel, p. 159.

5 *Understanding Genetics*—by O.S. Reddi, Allied Publishers, Ltd., New Delhi.

measured in the billion. A very short segment of such a molecule is illustrated in the above fig 9.4. This molecular is composed of several simple chemical compounds arranged in a regular pattern explained as follows:

The structure of DNA is illustrated by a right handed double helix, with about 10 nucleotide pairs per helical turn. Each spiral strand, composed of a sugar phosphate backbone and attached bases, is connected to a complementary strand by hydrogen bonding (non-covalent) between paired bases.

(a) DNA replicating itself (see fig. 9.5)—A simplified representation of a DNA molecule separating to form two new molecules. To reproduce, a cell must copy and transmit its genetic information (DNA) to all of its progenies. To do so, DNA replicates, following the process of semi-conservative replication. Each strand of the original molecule acts as a template for the synthesis of a new complementary DNA molecule.



**Fig. 9.5: DNA replicating itself**

The two strands of the double helix is first separated by enzymes. With the assistance of other enzymes, spare parts available inside the cell are bound to the individual strands following the rules of complementary base pairing:

Adenine (A) to Thymine (T) and Guanine (G) to Cytosine (C).

Two strands of DNA are obtained from one, having produced two daughter molecules which are identical to one another and to the parent molecules.<sup>6</sup>

As is true of almost all other important events in the cell, reproduction begins in the nucleus itself. In reproduction every gene plays an important role (see fig. 9.6

and 9.7). The first step is replication (duplication) of all DNA in the chromosomes. Only after this has occurred metosis can take place.

The DNA begins to be duplicated some 5 to 10 hrs. before metosis and this is completed in 4 to 8 hours. The DNA is duplicated only once so that the net result is two exact replicates of all DNA. These replicates, in turn, become the DNA in the two new daughter cells. There is another period of one to two hours before metosis begins abruptly. However, even during this period, preliminary changes are already by two hours before metosis begin

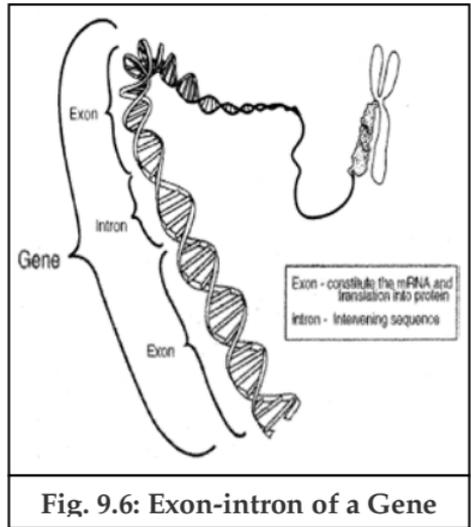


Fig. 9.6: Exon-intron of a Gene

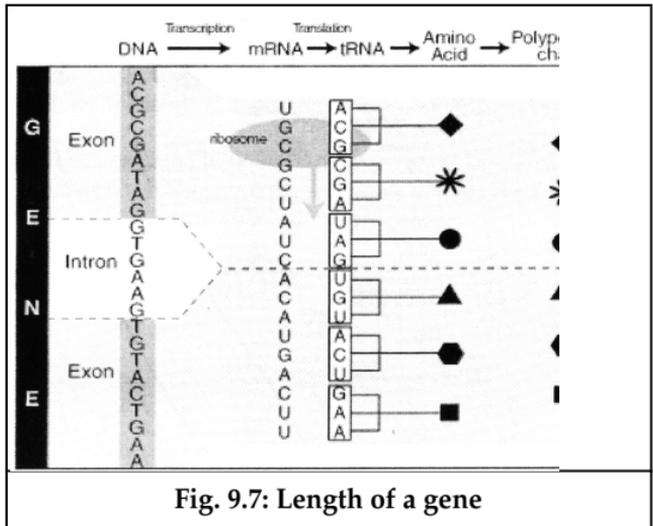


Fig. 9.7: Length of a gene

6 Website: [www.nationalhealth.com](http://www.nationalhealth.com) (Graphics gallery index, copy right, 1999).

abruptly. However, even during this period, preliminary changes are already beginning to take place that will lead to mitotic process.<sup>7</sup>

#### 9.1.4 HOW DOES THE DNA WORK?

The DNA influences many of our characteristics. Now it is explained how the DNA does this? The DNA looks like a large double stranded helix. Two strands are said to be complements—the "sequence" on one strand determines the "sequence" on the other. One reason for this is for protection against mutation. If something happens to one of the strands of the DNA, it is possible to read the opposite strand to make a new copy of the damaged strand. To simplify things, think of DNA as a long piece of ticker tape. Written on this ticker tape are all sorts of instructions or genes. Genes are discrete units of information that tell cells what to do. For example, there might be a *gene* for brown hair or gene for green eyes. Each one of our cells contain the exact same DNA sequences, or genes (with some exceptions). There are controls in place to make sure that the correct *genes* get exposed in the correct tissues—to ensure that you grow fingernails only on your fingers and hair only on specific parts of your skin, etc.

There are systems in our cells that read the DNA sequence and translate it into protein. Proteins are made by linking amino acids together. When you eat proteins, it gets broken down into amino acids—that is why, it is important to eat enough proteins. DNA contains the instructions and protein carry out the instruction.

So if DNA makes proteins and proteins perform functions, then the ultimate goal of genetic engineering is to alter proteins. Since proteins don't last very long they are only targets for genetic engineering. DNA is copied from one generation to the

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<sup>7</sup> *Medical Physiology*—by Guyton, Prism Books (P) Ltd., eighth edition, p. 32.

next, i.e., from parents to children. The changes in DNA can be carried over generations, making it a good target for lasting changes. There are two basic types of modifications—

1. To add a function to a cell, all you have to do is to introduce a new gene that codes off the given function.
2. Deletion of function can be performed either by "knocking out" a gene or introducing an "antisense" gene to interfere with the cell's ability to express a given gene.<sup>8</sup>

## 9.2 RNA

The basic building block of RNA is almost the same as those of DNA except two differences. First, the sugar deoxyribse is not used in the formation of RNA. In its place is used another sugar of very slightly different composition, ribose. Second, thymine is replaced by another pyrimide, uracil.

### 9.2.1 RNA—THE PROCESS OF TRANSCRIPTION

Because almost all the DNA are located in the nucleus of the cell and yet most of the functions of the cell are carried out in the cytoplasm, some means must be available for the genes of the nucleus to control the chemical reactions of cytoplasm. This is achieved through the intermediary of another type of nucleic acid, RNA, the formation of which is controlled by the DNA of the nucleus. In this process, the code is transferred to the RNA, which is called transcription. The RNA then diffused from the nucleus through the nuclear pores into the cytoplasm compartment, where it controls protein synthesis.

Assembly of the RNA molecule is accomplished in the manner illustrated in the figure 9.8 under the influence of the enzyme RNA polymerase. This is a very large enzyme that has many functional properties necessary for the formation of RNA molecule.

It should be remembered that there are four different types of DNA base and also four different types of RNA nucleotide bases. Further more, these always combine with each other and are specifically transmitted in a complimentary form to the RNA molecule. The ribose nucleotide bases always combine with the deoxyribose bases in the following combination:

**Table 9.2**

S. No.	DNA base	RNA base
01.	Guanine	Cytosine
02.	Cytosine	Guanine
03.	Adenine	Uracil
04.	Thymine	Adenine

After the RNA molecules have been released into the nucleoplasm, they still must be processed further before entering the cytoplasm. The reason for this is that the newly transcribed RNA contains many unwanted sequences of RNA nucleotides. Some of them occur at both ends of the RNA strand, and many other occur in the middle of the strand, this unwanted material probably constitutes more than 90 per cent of the total strand. Fortunately, a series of enzymes within the nucleoplasm has the capability to cutout these unwanted sequences and then re-splicing the RNA strand, a process called RNA splicing. The RNA is now ready to be used for the formation of proteins.

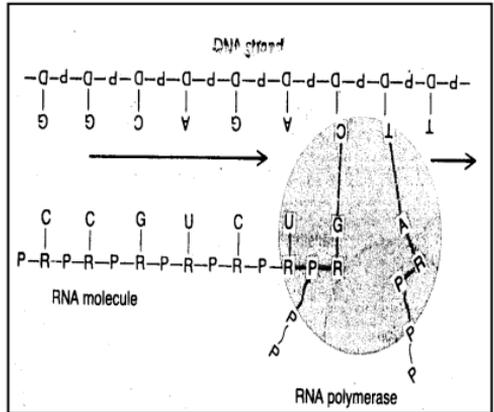
There are three separate types of RNA and each of them plays independent and entirely different role in protein formation. These are:

- (i) Messenger RNA, which carries the genetic code to the cytoplasm for controlling the formation of proteins.
- (ii) Transfer RNA, which transports activated amino acids to the ribosomes to be used in assembling the protein molecules, and

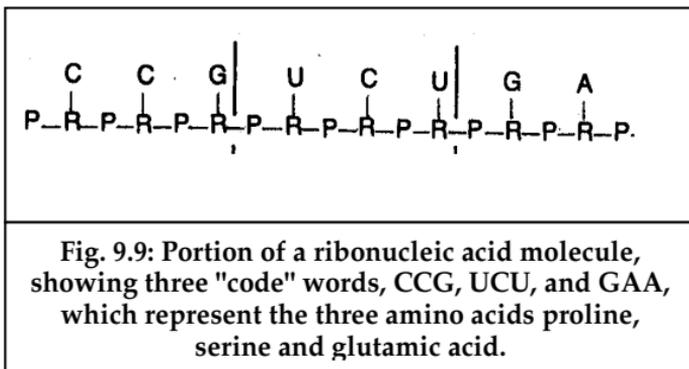
(iii) Ribosomal RNA, which along with about 75 different proteins, forms the ribosomes, the physical and chemical structure on which protein molecules are actually assembled.

### 9.2.2 MESSENGER RNA—"THE CODONS"

Messenger RNA molecules are long single RNA strands that are suspended in the cytoplasm. These molecules are composed of several hundreds to several thousand nucleotides in unpaired strands and they contain 'codons' that are exactly complementary to the code triplets of the genes. Figure 9.9 illustrates small segment of a molecule of messenger RNA. Its codons are CCG, UCU and GAA. These are codons for the amino acids proline,



**Fig. 9.8: Combination of ribose nucleotides with a strand of DNA to form a molecule of RNA that carries the DNA code from the gene to cytoplasm. The RNA polymerase moves along the DNA strand and builds the RNA molecule along the DNA strand.**



**Fig. 9.9: Portion of a ribonucleic acid molecule, showing three "code" words, CCG, UCU, and GAA, which represent the three amino acids proline, serine and glutamic acid.**

serine and glutamic acid. The transcription of these codons from the DNA molecule is demonstrated in Fig. 9.8.

The following table gives the RNA codons for 20 common amino acids found in protein molecules. Note that most of the amino acids are presented by more than one codons, also one

codon represents the signal "start manufacturing a protein" and three codons represent "stop manufacturing a protein molecule." In Table 9.3 these two types of codons are designated; CI for "Chain Initiating" and CT for "Chain Terminating."

**Table-9.3: RNA codons for the different amino acids and for start and stop**

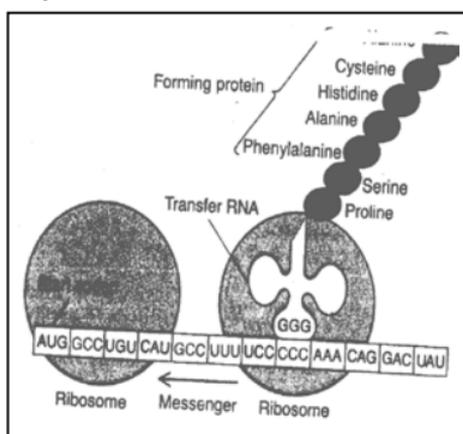
Amino Acid	RNA Codons					
Alanine	GCU	GCC	GCA	GCG		
Arginine	CGU	CGC	CGA	CGG	AGA	AGG
Asparagines	AAU	AAC				
Aspartic acid	GAU	GAC				
Cysteine	UGU	UGC				
Glutamic acid	GAA	GAG				
Glutamine	CAA	CAG				
Glycine	GGU	GGC	GGA	GGG		
Histidine	CAU	CAC				
Isoleucine	AUU	AUC	AUA			
Leucine	CUU	CUC	CUA	CUG	UUA	UUG
Lysine	AAA	AAG				
Methionine	AUG					
Phenylalanine	UUU	UUC				
Proline	CCU	CCC	CCA	CCG		
Serine	UCU	UCC	UCA	UCG	AGC	AGU
Threonine	ACU	ACC	ACA	ACG		
Tryptophan	UGG					
Tyrosine	UAU	UAC				
Valine	GUU	GUC	GUA	GUG		
Start (CI)	AUG					
Stop (CT)	UAA	UAG	UGA			

### 9.2.3 TRANSFER RNA—"THE ANTICODONS"

Another type of RNA that plays an essential role in protein synthesis is called transfer RNA because it transfers amino acid molecules to protein molecules as the protein is synthesized. Each type of transfer RNA combines specifically with one of the amino acids that are to be incorporated into proteins. The transfer RNA then acts as a carrier to transfer its specific type of amino acid to ribosomes, where protein molecules are forming. In ribosomes, each specific type of transfer RNA recognizes a particular codon on the messenger RNA, as is described subsequently, and thereby delivers the appropriate amino acid to the approximate place in the chain of newly forming molecule.

Transfer RNA, containing only about 80 nucleotides, is a relatively small molecule in comparison with messenger RNA. Since the function of transfer RNA is to cause attachment of a specific amino acid to forming protein chain, it is essential that each type of transfer RNA also have specificity for a particular codon in the messenger RNA. The specific code in the transfer RNA that allows it to recognize a specific codon is again a triplet of nucleotide bases and is called an anticodon. This is located approximately in the middle of transfer RNA molecule at the bottom of the cloverleaf configuration illustrated in fig. 9.10.

During formation of a protein molecule, the anticodon bases combine loosely by hydrogen bonding with the codon bases of the messenger RNA. In this way, the respective amino acids are lined up one after another along the messenger RNA chain, thus establishing the appropriate sequence of amino acids in the protein molecule.



**Fig. 9.10: Mechanism by which a protein molecule is formed in ribosomes in association with messenger RNA and transfer RNA**

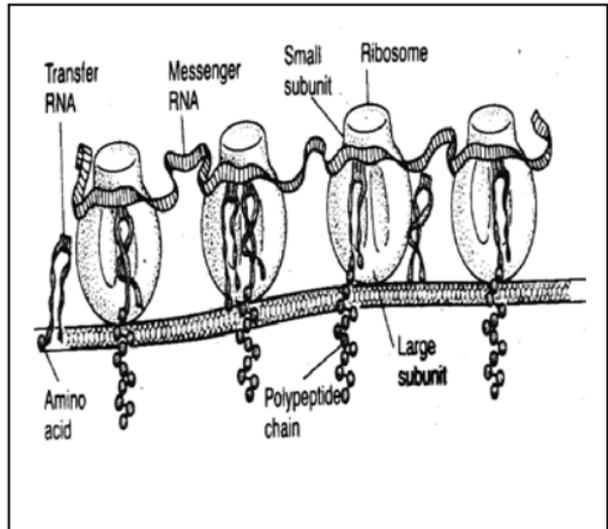
Deming formation of a protein molecule, the anticodon bases combine loosely by hydrogen bonding with the codon bases of the messenger RNA. In this way, the respective amino acids are lined up one after another along the messenger RNA chain, thus establishing the appropriate sequence of amino acids in the protein molecule.

### 9.2.4 PROCESS OF TRANSLATION

The third type of RNA in the cell is ribosomal RNA, it constitutes about 60 per cent of the ribosome. The remainder of the ribosome is protein, containing about 75 different types of proteins that are both structural proteins and enzymes needed in the manufacturer of protein molecules.

The ribosome is the physical structure in the cytoplasm on which protein molecules are actually synthesized. However, it always functions in association with both the other types of RNA as well.

Transfer RNA transports amino acids to the ribosomes for incorporation into the developing protein molecules, whereas messenger RNA provides the information necessary for sequencing the amino acids in proper order for each specific type of protein to be manufactured.



**Fig. 9.11: An artist's concept of the physical structures of the ribosomes as well as their functional relationship to messenger RNA, transfer RNA and the endoplasmic reticulum during the formation of protein molecules.**

The ribosomes of nucleated cells are composed of two physical subunits, called the small sub-unit, containing one RNA molecule and 33 proteins and the large sub-units containing 30 RNAs and more than 40 proteins. Although we have only partial knowledge of the mechanism of protein manufacture in the ribosome, it is known that messenger RNA and transfer RNA

first complex with the small sub-unit. Then the large sub-unit provides most of the enzymes that promote peptide linkage between the successive amino acids. Thus the ribosome act as a manufacturing plant in which the protein molecules are formed.

The ribosome is simply the structure in which the chemical reactions take place for manufacture of proteins. As illustrated in figure 9.10, while the messenger RNA travels along the ribosome, a protein molecule is formed through a process called "translation." Thus, the ribosome reads the code of the messenger RNA in much the same way that a tape is "read" as it passes through the playback head of a tape recorder. Then when a "stop" (or chain terminating) codon slips past the ribosome, the end of a protein molecule is signaled, and the protein molecule is freed into the cytoplasm. Figure 9.11 shows the functional relationship of messenger RNA to the ribosomes and also the manner in which the ribosomes attach to the membrane of the endoplasmic reticulum. Note the process of translation occurring in several ribosomes at the same time in response to the some strand of messenger RNA. Also note the newly forming polypeptide chains passing through the endoplasmic reticulum membrane into the endoplasmic matrix.

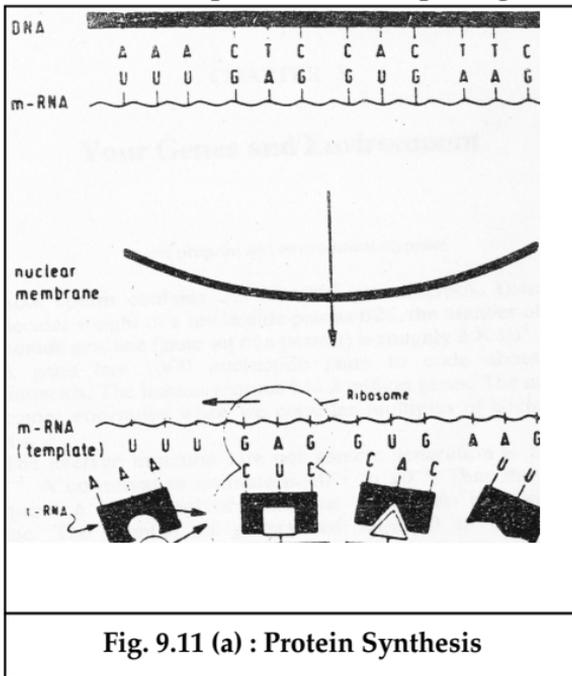
Yet it should be noted that except in glandular cells that form large amounts of protein—containing secretory vesicles, most proteins, formed by the ribosomes are released directly to the cytosol. These are enzymes and the internal structural proteins of the cell.

### 9.2.5 PROTEIN SYNTHESIS

Proteins are made in a living cell as per the information encoded in the genes of the cell. Genes consist of specific sequences of DNA in the nucleus of the cell. The genetic code is written in the form of four letters (representing bases) A, T, G, C which stand for Adenine, Thymine, Guanine and Cytosine. This code is read in three letter sets called "codon" which specify the amino acids

which get linked to form proteins. The order of base, besides determining the sequence of amino acids, is proteins also regulatory compounds. In human beings, a structural sequence or a gene consists of what are called Exons and Introns (fig. no. 9.6)—that is stretch of utilizable and non-utilizable sequences. The genetic information is translated directly into proteins.

First, the entire sequence of bases of DNA are transcribed into RNA as per the base pairing rule. Adenine to thymine, guanine to cytosine in



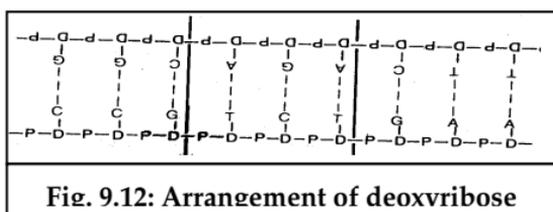
DNA. In RNA copies of introns are exercised from the message and all the remaining exons are joined together end to end. The reassembled strand of RNA then moves out of nucleus into cytoplasm when the manufacture of proteins take place (fig. 9.11 (a)). What is the quantity of DNA in a human being? A

diploid human cell contains  $7.3 \times 10^{12}$  (with a range of 6.6 to 8.0) with  $7.1 \times 10^9$  nucleotide pairs. About 6-7 million genes are accommodated on this DNA. Forty-two per cent of DNA in the human genome consists of repetitive sequences of redundant DNA—that is non coding DNA. Also interspersed with coding DNA is non coding DNA.<sup>9</sup>

### 9.3 Genetic codes

The importance of DNA lies in its ability to control the formation of other substances in the cell. It does this by means of the so-called genetic code. When the two strands of DNA molecule are split apart, this exposes the purine and pyrimidine bases projecting to the side of each strand. It is these projecting bases that form the code.

Research studies in the past few years have demonstrated that the genetic code consists of triplets of bases—that is, each three successive bases, is a code word. The successive triplets eventually control the sequence of amino acids in a protein molecule during its synthesis in the cell. Note (in figure 9.12) that each of the two strands



of the DNA molecule carries its own genetic code. For instance, the top strand reading from left to right, has the genetic code CGC, AGA, CTT, the triplets being separated from each other by the arrows. As we follow these genetic codes through figures 9.8, 9.9, we see that these three respective triplets are responsible for successive placement of the three amino acids—proline, serine and glutamic acid, in a molecule of protein.<sup>10</sup>

There are more than 20 different amino acids and only four bases, so the code cannot be based on a one-to-one correspondence between amino acids and bases. Biochemical investigations have revealed that the messenger RNA code is a triplet code that is, each successive frame of three nucleotides. Sometimes called a codon of the messenger RNA, it corresponds to one amino acid of the protein. This rule of correspondence is the genetic code. The genetic code consists of 64 entities—the 64 triplets possible when there are four possible nucleotides, each of which can be at any of the three places ( $4 \times 4 \times 4 = 64$ ).<sup>11</sup> (See Table 9.4)

10 *Medical Physiology*—by Guyton, publisher Prism Books (P) Ltd., eighth edition, 1991.

11 *Britanica Encyclopaedia*—topic gene, p. 337.

		Second letter			
		U	C	A	G
First letter	U	UUU } Phenylalanine (Phe)	UCU } Serine (Ser)	UAU } Tyrosine (Tyr)	UGU } Cysteine (Cys)
		UUC } Phenylalanine (Phe)	UCC } Serine (Ser)	UAC } Tyrosine (Tyr)	UGC } Cysteine (Cys)
		UUA } Leucine (Leu)	UCA } Serine (Ser)	UAA } Stop	UGA } Stop
		UUG } Leucine (Leu)	UCG } Serine (Ser)	UAG } Stop	UGG } Tryptophane (Tryp)
	C	CUU } Leucine (Leu)	CCU } Proline (Pro)	CAU } Histidine (His)	CGU } Arginine (Arg)
		CUC } Leucine (Leu)	CCC } Proline (Pro)	CAC } Histidine (His)	CGC } Arginine (Arg)
		CUA } Leucine (Leu)	CCA } Proline (Pro)	CAA } Glutamine (GluN)	CGA } Arginine (Arg)
		CUG } Leucine (Leu)	CCG } Proline (Pro)	CAG } Glutamine (GluN)	CGG } Arginine (Arg)
	A	AUU } Isoleucine (Ileu)	ACU } Threonine (Thr)	AAU } Asparagine (AspN)	AGU } Serine (Ser)
		AUC } Isoleucine (Ileu)	ACC } Threonine (Thr)	AAC } Asparagine (AspN)	AGC } Serine (Ser)
		AUA } Isoleucine (Ileu)	ACA } Threonine (Thr)	AAA } Lysine (Lys)	AGA } Arginine (Arg)
		AUG } Methionine (Met)	ACG } Threonine (Thr)	AAG } Lysine (Lys)	AGG } Arginine (Arg)

**Table-9.4:** The genetic code is a triplet code, consisting of 64 entries. Each triplet, called a codon, represents a frame of these nucleotides (U = uracil, C = cytosine, A = adenine, G = guanine) on messenger RNA. At least one codon, and usually more than one codes, for each of the 20 amino acids. A few triplets signal the "stop" of protein assembly and at least one—methionine—may signal the "start."

Amino acids specified by each codon sequence on messenger RNA key for the above table:

Ala: Alanine	Cys: Cysteine	Asp: Aspartic Acid	Glu: Glutamic Acid
Phe: Phenylalanine	Gly: Glycin	His: Histidine	Ile: Isoleucine
Lys: Lysine	Leu: Leucine	Met: Methenine	Asn: Asparagine
Pro: Proline	Gin: Glutamine	Arg: Arginine	Ser: Serine
Thr: Threonine	Val: Valine	Trp: Tryptophane	Tyr: Tyrosine

A = Adenine, G = Guanine, C = Cytosine, T = Thymine, U = Uracil.

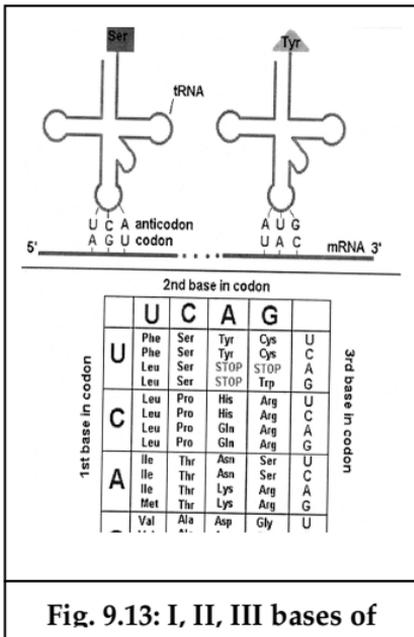


Fig. 9.13: I, II, III bases of

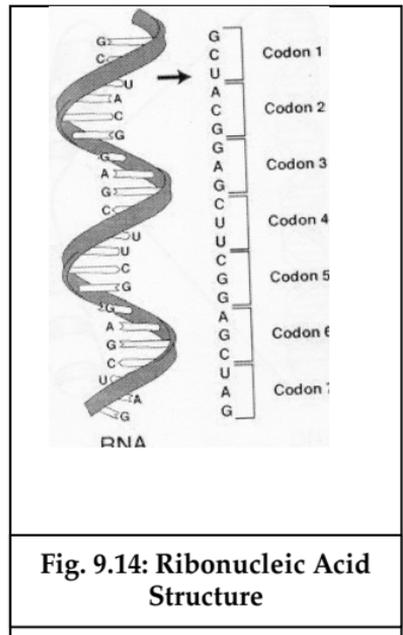


Fig. 9.14: Ribonucleic Acid Structure

DNA transfers information to messenger RNA in the form of a code defined by a sequence of nucleotides.

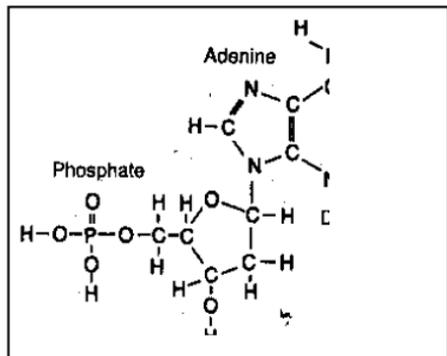
### 9.3.1 FOUNDERS OF GENETIC CODES

The concept of genetic code was anticipated by the American biologist James D. Watson and the British biologist Francis H.C. Crick as an extrapolation of the structural model of DNA that they proposed in 1953. For this work, they, along with the British biophysicist Maurice Wilkins, were awarded the Noble Prize for physiology or medicine in 1963.

The concept was bolstered by the indirect evidence for a messenger RNA put forward by two French Nobel Laureates, immediately corroborated by the demonstration of a message functioning RNA by Sydney Brenner, Francois Jacob and Matthew. S. Meselson in the same year. Marshall Nirenberg (1968 Nobel Prize winner) opened a door to a direct attack on the code by showing that a synthetic RNA containing only the nucleotide chain UUUU..... could function as a message for the synthesis of amino acid phenylalanine.

Subsequent by many other biochemists, especially the Americans, Severo Ochoa, Nobel Prize winner, 1959 and Gobind Khurana, Nobel Prize winner, 1968 used more complex synthetic messages pinned down the code as a triplet code. Using the fact that the triplet UUU coded for phenylalanine as a starting point, many investigators went to determine the code and by 1968 the entire code was broken (see table-19.3).

The successful work on the genetic code led to the research on the artificial synthesis of RNA molecules that would code for specific protein synthesis. The American biologist, Charles Yan, supported the code breaker's work, an entirely different line of research. He showed that the code was corroborated by the patterns of mutation and the recombination of mutants affecting single amino acids of the protein tryptophane synthetase in the Bacterium *E. Coli*.<sup>12</sup>

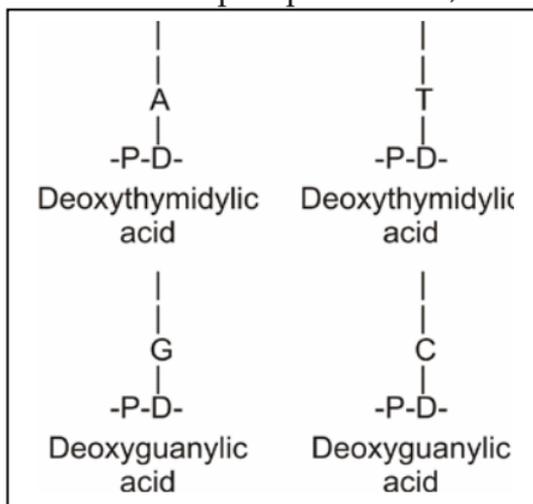


**Fig. 9.16: Deoxyadenylic acid, one of the nucleotides that make up DNA.**

<sup>12</sup> *Ibid*, p. 378.

### 9.3.2 THE NUCLEOTIDES

The first stage in the formation of DNA is the combination of one molecule of phosphoric acid, one molecule of deoxyribose and one of the four bases to form a nucleotide. Four separate nucleotides are thus formed into one for each of the four bases:



**Fig. 9.15: Combinations of the basic building blocks of DNA to form nucleotides (P, phosphoric acid; D, deoxyribose) The four nucleotide bases are A, adenine. T, thymine; G,**

deoxyadenylic, deoxythymidylic, deoxyguanylic, and deoxycytidylic acids. Figure 9.16 illustrates the chemical structure of adenylic acid while Figure 9.15 illustrates simple symbols for all the four basic nucleotides that form the DNA.

### 9.4 Classification of Genes

Genes are classified as follows:

#### Types of Gene

Genes may function in more ways than known. However, the following categories, which are not necessarily mutually exclusive, can be recognized.

- i. **Message or structural genes**—These codes for the amino acid sequence of a specific protein through a messenger RNA (mRNA) copy. This carries the coded instructions from the nucleus to the ribosomes, which are the sites of protein assembly in the cell.

- ii. **Operator genes**—These signal instructions to regulate the read out or transcription of adjacent message genes. The operator genes in turn may be switched on and off in response to repressor substances, which are products of regulatory genes.
- iii. **Ribosomal RNA genes**—These are transcribed into the structural RNA of the ribosomal particles (rRNA) on which protein assembly occurs.
- iv. **Transfer RNA gene**—These are transcribed into the diverse transfer RNA (tRNA) molecules that are responsible for tagging and carrying individual amino acids to the ribosome for protein assembly. There are at least 20 kinds of transfer RNA, one for each of 20 amino acids. A specific transfer RNA binds to a specific amino acid and carries it to that part of the messenger RNA that codes for the particular amino acid in the ribosome.
- v. **Regulatory genes**—These are structural genes whose products are repressors. These act on operator to control the transcription of other genes.
- vi. **Suppressor genes**—These reverse the phenotypic of observable, effects of mutations in other genes by a variety of mechanisms.
- vii. **Kinetic genes**—These are mixed bag of genes that regulate chromosome movement at cell division. For example, they regulate the centromere of the chromosomes and the initiation of chromosomes replication.
- viii. **Synaptic recognition genes**—These drive the unknown mechanism by which homologous chromosome synapse (pair off) during the reduction division in higher organisms.
- ix. **Inert genes**—In addition to the genes described above, the chromosomes contain DNA whose function, if any, has not been determined. This DNA may constitute functionless inert genes. It may constitute redundant genes that duplicate other genes in the chromosome. Out of all the genes, the "message gene" is the best understood and most simply explained of all the genes. To most people, "gene" means message genes. It was

only after the discovery of other types of genes that the term "message gene" was adopted. If a protein chain contains 100 amino acid units, the messenger RNA coding for that protein chain would have to be 300 nucleotide pairs long. Such a nucleotide chain would have a molecular weight 2,00,000.<sup>13</sup>

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13 *Britanica Encyclopaedia-chapter-gene*, p. 377-78.

## 10

## Gene Mutation

The off-springs resemble their parents in one or several respects, yet there are differences between the two. These differences, whether large or small, are called variations. Some of the variations may be induced by environment while other may be hereditary. Generally, the variations caused by environment are not permanent, hence non-heritable. But the variations which appear due to the changes in the hereditary mechanism are permanent and heritable. Sudden appearance of marked heritable variation in the nature of any organism in ordinary sense is known as mutation and the offsprings with unusable variability in characters are called mutants. A mutant individual or cell is one in which the changed phenotype is attributable to mutated gene or genes.

Many other definitions for mutation from time to time by different biologists have been given below:

1. Sudden appearance of new hereditary character in the progenies of plants and animals was referred to as "sport" or mutation by Darwin.
2. In the broad sense, it covers any "heritable change in the genotype" (micro mutation) and in the narrower sense "mutation is a change of *gene*."
3. According to Bateson, "mutation is a discontinuous variation."

4. According to Devries "mutations are sudden and drastic heritable changes not traceable or ascribable to segregation or recombination."
5. Stabbins describes mutation as a discontinuous chromosomal change with genetic effect. He further states that the chromosomal change refers to chemical change in a small part of its chromosome, as well as to alteration of its physical structure.
6. Amatto and Otto (1956) have defined mutation as a change in the hereditary constitution of a given species.<sup>1</sup>

### 10.1 Factors causing mutations

Mutations are of many types depending upon whether they are caused by natural factors or by artificial means—

- (a) Natural mutations (Spontaneous mutations), and
- (b) Induced mutations (Artificial mutations)

**(a) Natural Mutations (spontaneous mutations)** —Natural variations observed in nature are caused by natural factors. They are governed by internal factors and not by environment. Natural mutation may occur in a gene or chromosome at any time in the development and nothing is fixed about it. As per the Jaina doctrine of *karma*, this happens due to the fruition (rise) of *karma* of that living organism. The ultimate causes of natural mutations are not definitely known but it is known that the frequency of such mutations may be considerably increased by artificial means.

**(b) Induced Mutations (Artificial mutations)** —The induced mutations are caused artificially by mutagenic factors. The agents, which induce mutations, are known as mutagenes. Artificial mutagenic agents of mutations are as follows—

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1 *Cytogenetics Evolution and Plant Breeding*—by R.S. Shukla and P.S. Chandel, publisher—S. Chand and Company Ltd., New Delhi, 1998 Edition.

- i. Temperature,
- ii. Physical mutagenes,
- iii. Chemical mutagenes, and
- iv. Age effect.

Some of the important chemical mutagenes are enlisted below:<sup>2</sup>

**Table 10.1**

S.No.	Chemical mutagene	Abbreviations
01.	Ethyleneimine	EL
02.	Nitrogen mustard	
03.	Sulphur mustard	
04.	Dimethyl nitrosamine	DMN
05.	Nitroso guanidine	NG
06.	Nitroso methyl urea	NMU
07.	Ethylene oxide	EO
08.	Diepoxybutane	DEB
09.	Methyl methane sulphonate	NMS
10.	Ethyl methane sulphonate	EMS
11.	Diethyl sulphonate	DES
12.	Hydrazine	
13.	Nitrous acid	
14.	Maleic hydrazide	
15.	Hydroxylamine	

#### 10.1.1 MUTATIONS IN THE CODE

The DNA content of the cell must accurately replicate itself prior to mitosis or meiosis. Given complexity of the DNA molecule and the vast number of cell divisions that take place within the life time of a multi-cellular organism, it is obvious that copying errors are likely to occur. If unrepaired errors change the linear order of the DNA bases and produce mutation in genetic code, many mutations arise from unknown causes. These are perhaps

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<sup>2</sup> Ibid.

due to the fruition (rise) of *karma* of individual organism. In addition to these so-called spontaneous mutations, researchers have demonstrated that a variety of environmental agents including ionizing radiation, toxic chemicals and certain viruses can induce mutations.<sup>3</sup>

#### 10.1.2 GENE DAMAGE, MUTATION AND REPAIR

The remarkable properties of DNA come from the evolution of cellular mechanisms for its accurate replication and transcription into a protein molecule. Errors in the replication or transcription of DNA do occasionally occur, however, and these are known as mutations.

Like the letter of an alphabet, the single units of the DNA molecule are much less specific or interesting than the words they can compose. This is in contrast with the lack of any reliable evidence that a specific gene ever “knows how to mutate” in response to the needs of the organism in a new environment. Genes do not mutate to adopt to new environment conditions. Instead, mutations occur as random errors, and evolution operates retrospectively on the results of the random errors, which are usually disastrous. A previously mutated gene may prove beneficial in a new environment and the organisms, carrying such a gene will then be successfully reproduced.

The human genetic disease xeroderma pigmentosum has been described as a defect in the repair mechanism possibly a miscoding in the message gene for one of the repair enzymes. Afflicted patients are extremely sensitive to sunlight, suffer unrepaired damage to DNA in their cells, and are prone to develop multiple tumours.

In normal individuals, a certain number of DNA errors still escape the repair mechanism. This fact imposes on us the obligation to protect our genetic endowment from unnecessary exposure to possible mutagenes, such as ionizing radiation. In

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<sup>3</sup> *Britanica Encyclopaedia*, deluxe edition, 2005.

addition to the inherited defects produced when the DNA of the germ cells is injured, mutations in tissue cells are probably a part of the normal aging process and one of the mechanisms for initiation of cancer (Joshua Lederberg, Noble Prize winner in physiology or medicine, Stanford University School of Medicine).

### 10.1.3 EFFECT OF GENES OVER GENES

Genes and environment don't compete but are complimentary. Genes are like the tools of a painter, the lighting in the garret, palette brushes and paints. They cannot operate in a vacuum. They require external catalysts before they function. The environment provides the needed boost. It continues the artistic effort itself. It takes the preferred genetic tools and works with them to provide a finished portrait. Like the artist, it operates within a range defined by these tools. No matter how powerful it is, the environment cannot force genes to manufacture products they are not designed to manufacture.

The difference between seeing heredity and environment as competitors and recognizing their supportive relationship is a critical one not only to understand the concepts behind genetic prophecy but in realizing how we, living organisms, adopt in order to survive in a changing world.

*Genes* often act in concert with other *genes*. They can be influenced, altered, modified, triggered or shut down by these actions—and production by their neighbours. Such as, they not only help control the impact of environment but actually constitute a part of that environment for the genes they influence.

*Genes* can affect the genes in various ways, for instance, each of us inherits one of the two genes. The first makes us particularly susceptible to arsenic poisoning and the second confers resistance. The dose needed to poison someone, who has the *genes* for susceptibility, might be so small that it has no effect on someone who is resistant.

A person's height, for instance, is closely linked both to his genetic heritage and to the environment in which he grows. Genetically, tall people tend to be born into tall families and shorter into short families. The same holds true for entire population like seven feet giants of the Ibo tribe of Nigeria or the short stocky people of the South East Asia. Average stature in population tends to remain more or less constant. When it increases, it is mainly due to environment like improvement in nutrition and health during the first year of life which has significant effect on height in the later years.

The change in the average stature is the production of improvement in environment but individuals grow only within the ranges permitted by their genetic heritage. Height is influenced by a broad range of genetic and environment potential. The same kind of balance exists through the biology. We can track them down to the molecular level to the regulation of a single gene product.

#### 10.1.4 MUTATION—CHANGES IN GENETIC MATERIAL

A sudden variation, which is transmissible to generations, is called mutation. Mutations are produced by chemicals and radiations. Energy rich radiations are of two types:

- (i) **Electromagnetic Radiation**—To produce a mutation, the energy provided should at least to lift an electron from an inner to outer shell rendering the atoms unstable and more prone to chemical reactions. Ultraviolet radiation has this property and cause point mutations. Ultraviolet rays cannot penetrate the human epidermis and reach germ cells. Hence, it is not dangerous to human life. However, it can produce mutations in skin cells leading to skin cancer. X rays and Gamma rays have high energy electrons, which ionize cellular components and disrupt cell structure. These rays thus destroy living cells on contact and they are far more dangerous to life.

(ii) **Corpuscular radiations**—It consists not of energy photons but of particles. They may be charged like electrons and protons or uncharged like neutrons. Their physical effects depend upon their kinetic energy. These radiations cause not only point mutations but break chromosomes causing death of embryos.<sup>4</sup> Nothing is permanent and immutable in the universe.

## 10.2 Genes and diseases

In living organisms, cell is a living substance, which carries a nucleus. In nucleus of a cell chromosomes are made of DNA. There are *genes* lying on chromosomes in linear order (see fig. 10.1). *Genes* remain on DNA (de-oxyribonucleic Acid). *Gene* consists of genetic code made of three bases out of four bases ACGU, which are called nucleotides or triplet like ACG, GGU, GUA. Genetic science has searched out all number of *genes*, base pairs and diseases associated with each chromosome as follows:<sup>5</sup> (see Table 10.2.1)

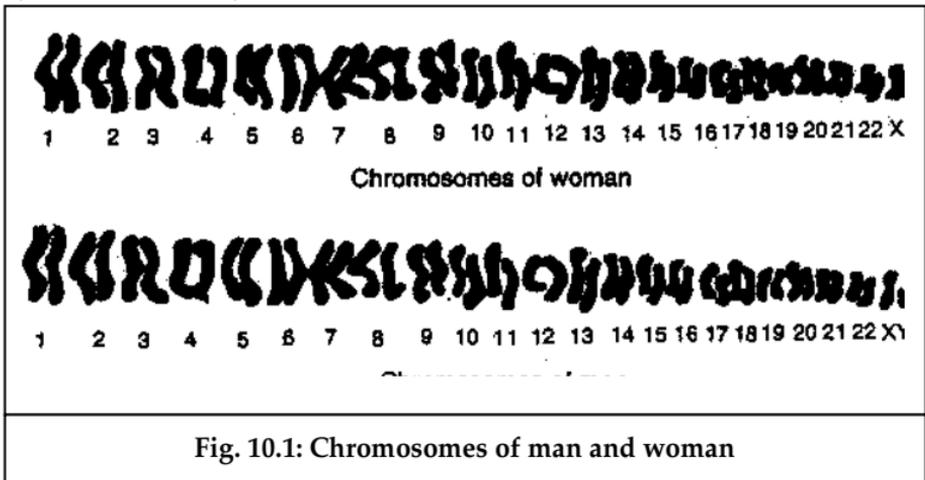


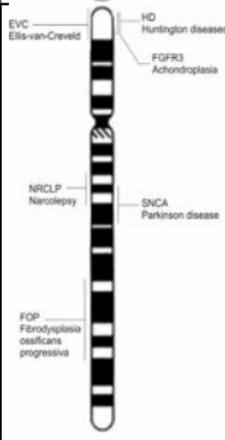
Fig. 10.1: Chromosomes of man and woman

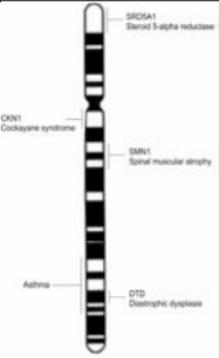
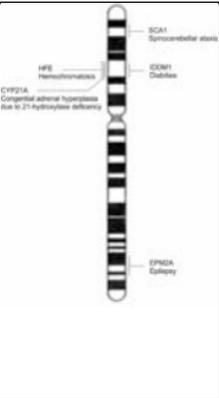
4 *Understanding Genetics*—by O.S. Reddi, Allied Publishers Ltd., New Delhi.

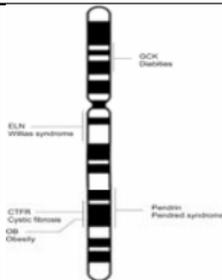
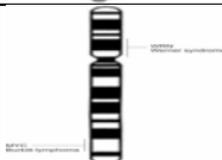
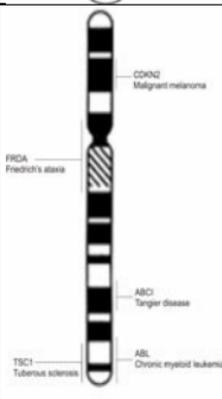
5 Website : [www.otherbooks.ncbi](http://www.otherbooks.ncbi).

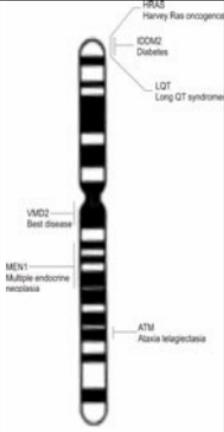
## 10.2.1 Diseases associated with chromosomes

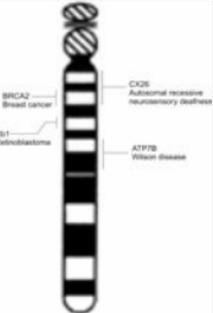
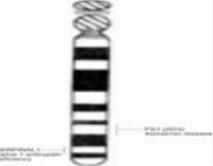
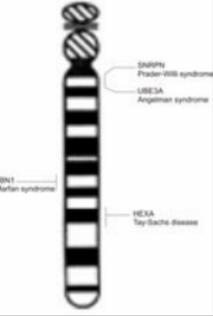
S. No.	Chromosome Number	No. of Genes contained by Chromosome	No. of base pairs in million contained by chromosome	Percentage of determination of base pairs	Diseases associated with chromosome	Photo
1.	1	3000	240	90%	(1) UROD Porphyria Cutanea tarda (2) GBA Gaucher disease (3) GLC1A Glaucoma (4) HPC1 Prostate Cancer (5) PS2 Alzheimer disease	<p>The image shows a vertical ideogram of chromosome 1. It is a black and white representation of the chromosome's structure. Several specific bands are highlighted and labeled with lines pointing to them. From top to bottom, the labels are: UROD (Porphyria cutanea tarda) at the very top; GBA (Gaucher disease) and HPC1 (Prostate cancer) in the middle section; PS2 (Alzheimer disease) in the lower middle section; and GLC1A (Glaucoma) at the bottom section.</p>
2.	2	2500	240	95%	(1) ETM2 Essential tremor (2) MS6 Colon Cancer (3) PAX3 Wardenberg Syndrom	<p>The image shows a vertical ideogram of chromosome 2. It is a black and white representation of the chromosome's structure. Three specific bands are highlighted and labeled with lines pointing to them. From top to bottom, the labels are: ETM2 (Essential tremor) at the top; MS6 (Colon Cancer) in the middle; and PAX3 (Wardenberg Syndrom) at the bottom.</p>

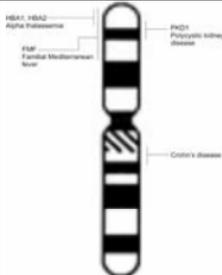
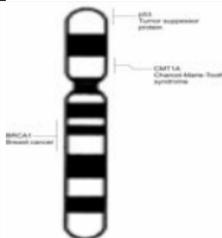
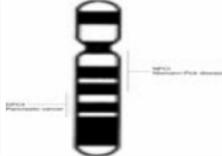
3.	3	1900	200	95%	<p>(1) UHL Von Hippel Lindau  (2) MLH1 Colon Cancer  (3) SCLC1 Lung Cancer  (4) ETM1 Essential tremor</p>	
4.	4	1600	190	95%	<p>(1) EVC Ellis-Van-Creveld  (2) HD Huntington disease  (3) FGFR3 Achondroplasia  (4) NRCPL Narcolepsy  (5) SNCA parkinson disease  (6) FOP Fibrodysplasia Ossificans progressiva</p>	

5.	5	1700	180	95%	<p>(1) SRD5A1 Steroid 5-alpha reductase1</p> <p>(2) CKN1 Cockayne syndrome</p> <p>(3) SMN1 Spinal muscular atrophy</p> <p>(4) Asthma</p> <p>(5) DTD Diastrophic dysplasia</p>	
6.	6	1900	170	95%	<p>(1) SCA1 Spinocerebellar ataxia</p> <p>(2) HFE Hemo Chromatosis</p> <p>(3) IDDM1 Diabetes</p> <p>(4) CYP21A Congenital adrenal hyperplasia due to 21-hydroxylase deficiency</p> <p>(5) EPM2A Epilepsy</p>	

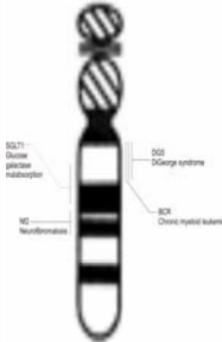
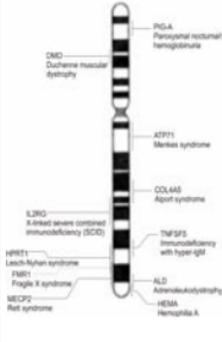
7.	7	1800	150	95%	<p>(1) GCK Diabetes</p> <p>(2) ELN Williams syndrome</p> <p>(3) CTFR fibrosis</p> <p>(4) Pendrin Pendred syndrome</p> <p>(5) Obesity</p>	
8.	8	1400	140	95%	<p>(1) WRN Werner syndrome</p> <p>(2) MYC Barkitt lymphoma</p>	
9.	9	1400	130	85%	<p>(1) CDKN2 Malignant melanoma</p> <p>(2) FRDA Friedrich's ataxia</p> <p>(3) ABCI Tangier disease</p> <p>(4) TSC1 Tuberosclerosis</p> <p>(5) ABL Chronic myeloid Leukemia</p>	

10.	10	1400	130	95%	(1) PAHX Refsum disease (2) OAT Gyrate atrophy	
11.	11	2000	130	95%	(1) HRAS Harvey Ras Oncogene (2) IDDM2 Diabetes (3) LQT Long QT syndrome (4) VMD2 Best syndrome (5) MEN1 multiple endocrine neoplasia (6) ATM Ataxia telangiectasia.	
12.	12	1600	130	95%	(1) PXR1 Zellweger syndrom (2) PAH Phenylketonuria	

13.	13	800	110	80%	<p>(1) BRCA2 Breast Cancer</p> <p>(2) CX 26 Autosomal recessive neurosensory deafness</p> <p>(3) RB1 Retinoblastoma</p> <p>(4) ATP7B Wilson disease</p>	
14.	14	1200	100	80%	<p>(1) PS1 (AD3) Alzheimer disease</p> <p>(2) SERPINA1 alpha-1-antitrypsin deficiency</p>	
15.	15	1200	100	80%	<p>(1) SNRPN prader-willi syndrome</p> <p>(2) UBE Angelman syndrome</p> <p>(3) FBN1 Marfan syndrome</p> <p>(4) HEXA Tay-sachs disease</p>	

16.	16	1300	90	85%	<p>(1) HBA1, HBA2 Alpha thalassemia</p> <p>(2) PKD1 Polycystic kidney disease</p> <p>(3) FMF Familial mediterranean fever</p> <p>(4) Crohn's disease</p>	
17.	17	1600	80	95%	<p>(1) PS3 Tumor suppressor protein</p> <p>(2) CMT1A (Charcot-marie-tooth syndrome)</p> <p>(3) BRCA1 Breast Cancer</p>	
18.	18	600	70	95%	<p>(1) NPC1 Niemann-pick disease</p> <p>(2) DPC4 Pancreatic cancer</p>	

19.	19	1700	60	85%	<p>(1) JAK2 Severe combined immunodeficiency</p> <p>(2) BCKDHA Maple syrup urine disease</p> <p>(3) DMPK Myotonic dystrophy</p> <p>(4) APOE Atherosclerosis</p>	<p>A vertical chromosome with four distinct bands. Labels on the right side point to these bands: JAK2 (Severe combined immunodeficiency), BCKDHA (Maple syrup urine disease), DMPK (Myotonic dystrophy), and APOE (Atherosclerosis).</p>
20.	20	900	60	90%	<p>(1) ADA Severe combined immunodeficiency</p>	<p>A vertical chromosome with a single prominent band. A label on the right side points to this band: ADA (Severe combined immunodeficiency).</p>
21.	21	400	40	70%	<p>(1) SOD1 Amyotrophic lateral sclerosis.</p> <p>(2) APS1 (Autoimmune polyglandular syndrome.)</p>	<p>A vertical chromosome with two distinct bands. Labels on the right side point to these bands: SOD1 (Amyotrophic lateral sclerosis) and APS1 (Autoimmune polyglandular syndrome.).</p>

22.	22	800	40	70%	<p>(1) SGLT1 Glucose galactase malabsorption.</p> <p>(2) DGS Digcorge syndrome.</p> <p>(3)NF2 (Neurofibromatosis.)</p> <p>(4) BCR Chronic myeloid leukemia.</p>	
X	X	1400	150	95%	<p>(1) PIGA Paroxysmal nocturnal hemoglobinuria.</p> <p>(2) DMD Duchenne Muscular Dystrophy.</p> <p>(3) ATP7A Menkes syndrome.</p> <p>(4) COL4AS Alport syndrome.</p> <p>(5) IL2RG X-Linked Severe Combined Immunodeficiency</p>	

					<p>(SCID).                      (6) TNFSF5 Immunodeficiency with hyper 19m.                      (7) HPRT1 Lesch-nyhan syndrome.                      (8) FMR1 Fragile X syndrome.                      (9) MEC P2 Rett syndrome.                      (10) ALD Adrenoleukodystrophy.                      (11) HEMA hemophilia A.</p>	
Y	Y	200	5	50%	<p>(1) SRY Testes determining factor.</p>	
Grand Total	23	34300	2935	-	92 types of diseases	

## 10.2.2 CHROMOSOME MAP

Our genetic information is stored in 23 pairs of chromosomes that vary widely in size and shape. Chromosome 1 is the largest and is over three times bigger than chromosome 22. The 23<sup>rd</sup> pair of chromosomes are two special chromosomes, X and Y, that determine our sex. Females have a pair of X chromosome (46, XX), where as males have one X and one Y chromosomes (46, XY). Chromosomes are made of DNA, and genes are special units of chromosomal DNA. Each chromosome is a very long molecule so it needs to be wrapped tightly around the protein for

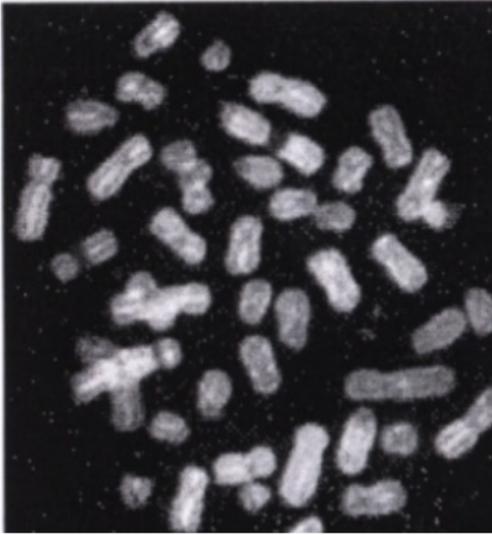


Fig. 10.1a This photograph shows a complete set of chromosomes from an acute promyelocytic leukemia (APL) patient. A new technique called chromosome painting allows visual distinction between chromosomes and can be used to show the chromosome translocations that frequently occur in human cancers. In the case of APL, chromosome 13 is lost, there is a translocation between chromosomes 7 and 15, translocation between chromosomes 11, 15, 17, and between chromosomes 9 and 18. (Look for chromosomes painted with more than one color.) With thanks to Thomas Ried, National Human Genome Research Institute, NIH, for supplying the picture.

efficient packaging. See fig. 10.1a

Near the centre of each chromosome is its centromere, a narrow region that divides the chromosome into a long arm (q) and a short arm (p). We can further divide the chromosomes using special stains that produce strips known as banding pattern. Each chromosome has a distinct banding pattern, and each band is numbered to help identify a particular region of a

chromosome. This method of mapping a gene to a particular band of chromosome is called cytogenetic mapping. For example, the hemoglobin beta gene (HBB) is found on chromosome 11p 15.4. This means that the HBB gene lies on the short arm (p) of chromosome 11 and is found at the band labelled 15.4.

With the advent of new techniques in DNA analysis, we are able to look into chromosome in a much greater detail. Whereas cytogenetic mapping gives a bird's eye view of the chromosomes. More modern methods show DNA at a much higher resolution. The Human Genome Project aims to identify the sequence of 30,000 genes in human DNA.

### 10.2.3 DISEASE OF EYES

The function of our eyes is to allow us to see the objects in our surroundings or variable distances and under various conditions of lights. This function is achieved by a very complex arrangement of layers and structures found in the eye. In addition, two pockets of

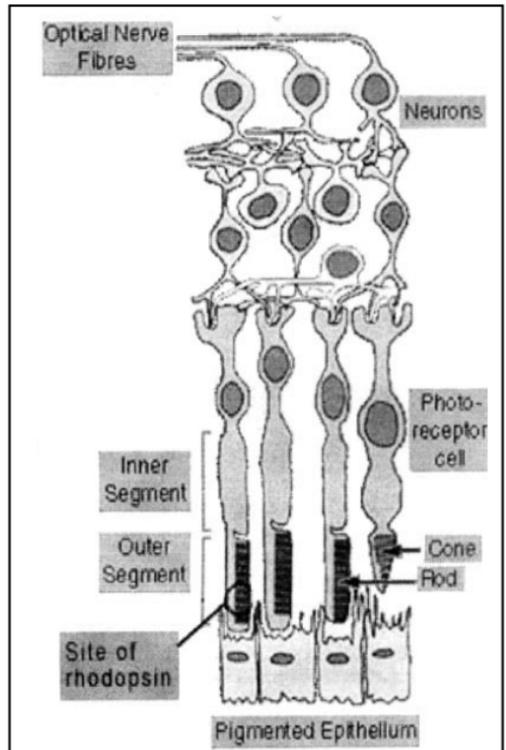


Fig. 10.2: In the eye, light enters the pupil is focused and inverted by the cornea and lens, and then is projected onto the retina at the back of the eye. The retina consists of several layers of cells, shown above. The only light-sensitive step during vision takes place in the outer segment of photoreceptor cells, and is catalyzed by the molecule rhodopsin. Light causes rhodopsin to change shape, which then triggers a signal to be sent through the layers of cells that make up the retina, resulting in a neural signal to the brain. (Adapted from Gebhard Schertler's web page, MRC-LMB, Cambridge, UK, with permission).

transparent fluid—the aqueous and vitreous humors—nourish eye tissues and help maintain constant eye shape. See fig 10.2

With the recent advances in molecular genetic techniques, new genes that cause eye disease are rapidly being identified, such as for those diseases discussed here. In many instances, these findings allow researchers to develop innovative strategies for preventing or slowing down the progress of genetic diseases of eyes.

#### 10.2.4 DISEASE OF THE IMMUNE SYSTEM

The immune system is a complex and highly developed system yet its mission is simple, to seek and kill invaders. If a person is born with a severely defective immune system, death from infection by a virus, bacterium, fungus or parasite may occur. In severe combined immunodeficiency, lack of an enzyme means toxic waste builds-up inside immune system cells, killing them and thus devastating the immune system. A lack of immune system cells is also the basis for Di George Syndrome, improper development of the thymus gland means the T cell production is diminished.<sup>1</sup> See fig. 10.3

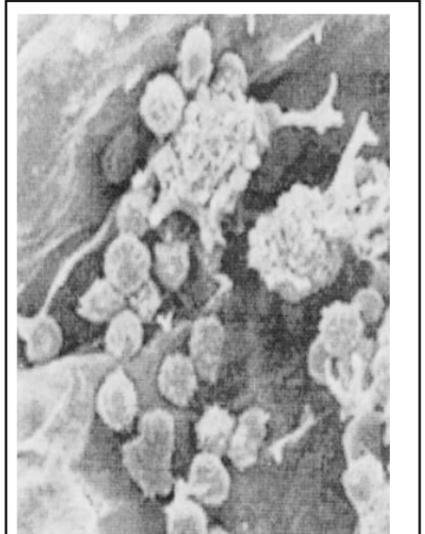


Fig. 10.3: Scanning electron micrograph of a lymph node. The large cells with multiple protrusions are macrophages; the smaller round cells are lymphocytes. A biconcave red blood cell can be seen on the left. (Micrograph by Willem van Ewijk, Dept Immunology, Erasmus University of Rotterdam, The Netherlands.)

1 Website: [www.otherbooks.ncbi](http://www.otherbooks.ncbi).

## 10.2.5 DISEASE OF EAR, NOSE AND THROAT

Within the structures of the ear, nose and throat are complex and interrelated mechanisms that allow a person to hear, maintain balance, smell, breathe and swallow. Traditionally, treatment of otology was associated with that of the eye in medical practice. With the development of laryngology, the study of the throat in the late 19<sup>th</sup> century, the connection between the ear and throat became known. Thus, occurred the birth of a discipline called otolaryngology. (See fig. 10.5)

When diagnosing ear, nose and throat disorders, it is important to differentiate genetic disorders from those due to environment influences. This is often difficult as similar clinical features may be produced by different environment factors or by different genes or groups of genes.

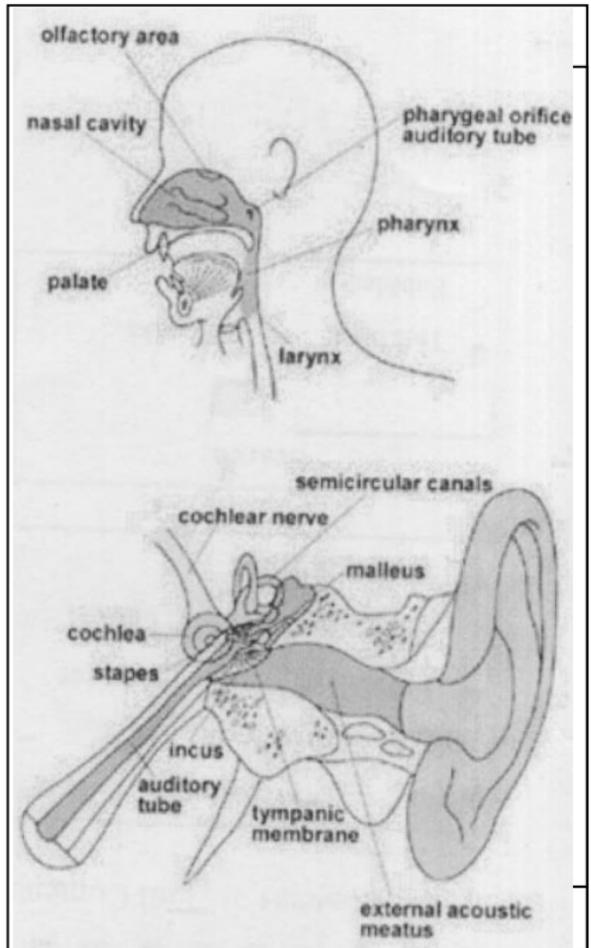


Fig. 10.5: The human ear, nose and throat are related in their functions, and thus often in the disorders that affect them. The ear is connected with the nose and throat by the auditory (or Eustachian).

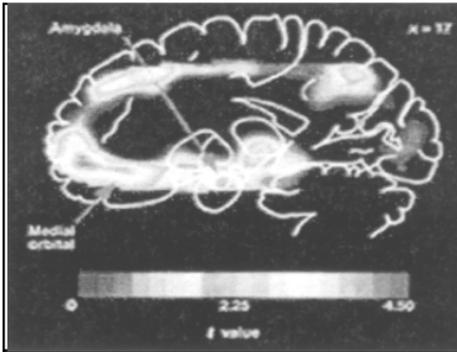


Fig. 10.6 : One of the major areas in which molecular genetics will play an important role in the future is in complex disorders like schizophrenia and depression. The figure shows areas of increased blood flow (red hotspots) in the left amygdala and the medial orbital cortex of a person with familial, major depressive disorder. The molecular basis for this observation, and others like it, remain a challenge for the future. [Reproduced from Andreasen, NC (1997) Science 275, . . . 1586-1593, with

## 10.2.6 DISEASE OF NERVOUS SYSTEM

The brain and nervous system form an intricate network of electrical signals that are responsible for co-ordinating muscles, the senses, speech, memories, thoughts and emotions. (See fig. 10.6)

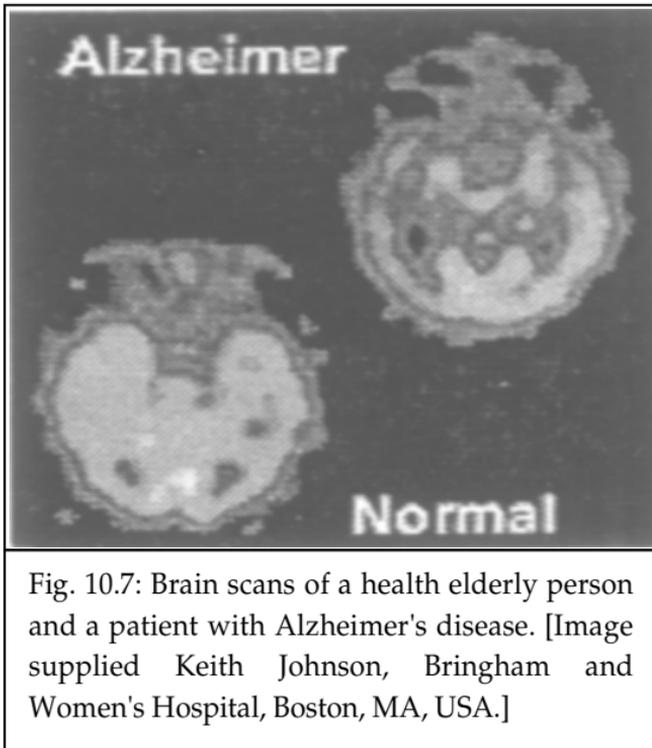
Several diseases that directly affect the nervous system have a genetic component, some are due to a mutation in a single *gene* and others are due to more complex mode of inheritance. Alzheimer brain plaques and the inclusion of bodies found

in Parkinson's disease contain at least one common component, while Huntington disease, fragile X syndrome and spinocerebellar atrophy are all "dynamic mutation" diseases in which there is an expansion of several neurodegenerative diseases, as other specific, intracellular signaling events. The bio-synthesis of myelin and the regulation of cholesterol traffic also figure in Charcot-marie-tooth and Neimann-Pick diseases, respectively.

## 10.2.7 ALZHEIMER'S DISEASE

Alzheimer's disease (AD) is the fourth leading cause of death in adults. The incidence of the disease rises steeply with age. Alzheimer's disease is twice more common in women than in men, although former President Ronald Reagan is a well known Alzheimer's patient. Some of the most frequently observed symptoms of the disease include a progressive inability to

remember facts and events and later to recognize friends and family. (see fig. 10.7)



Alzheimer's disease tends to run in families, currently mutations in four genes, situated on chromosomes 1, 14, 19 and 21, are believed to play a major role in the disease. Currently, scientists are studying the interrelationship between the various genes loci (particularly the mutation on chromosome 21) and how environmental factor could effect a person's susceptibility to Alzheimer's disease Recently, the use of mouse model of the disease identified an enzyme that may be responsible for the increase in amyloid production characteristic of the disease. If a way to regulate this enzyme could be found, then Alzheimer's disease may be slowed or halted in some people.<sup>2</sup>

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2 Website : [www.otherbooks.ncbi](http://www.otherbooks.ncbi).

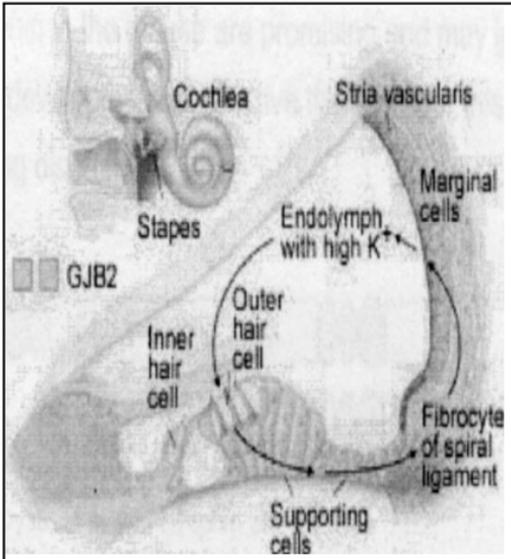


Fig. 10.8: Connexin 26 (GJB2) is one of the main proteins involved in potassium ( $K^+$ ) homeostasis in the cochlea of the inner ear. It is found in the supporting cells, fibrocytes of the spiral ligament and in cells of the spiral limbus. [Adapted from Steel, K.P. (1999) *Science* 285: 1363-1364, with permission]

### 10.2.8 DEAFNESS DISEASE

Hearing impairment is extremely common among human beings and can present itself at any time from infancy to old age. About one out of 1000 infants has profound hearing impairment and half of it is thought to be of genetic origin. Many types of deafness genes exist, but the most common cause of hearing loss in American and European populations is a mutation in the connexin 26 (cx26) gene. Cx26 has a carrier rate of 3 per cent, similar to that of cystic fibrosis, and it causes

about 20 per cent of childhood deafness. It has been proposed that mutations in cx26 may disrupt potassium circulation and result in deafness. The discovery that c x 26 mutations are a cause of congenital hearing loss can help in the early diagnosis of hearing impairment. Early identification and management of deafness is important for the development of language and social skills.<sup>3</sup>(see fig. 10.8)

### 10.2.9 EPILEPSY DISEASE

Epilepsy affects approximately 1 per cent of the population, making it one of the most common neurological diseases. Epilepsy

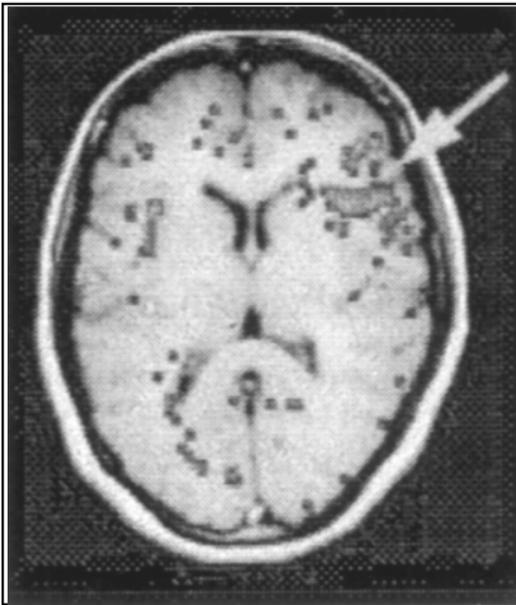


Fig. 10.9: Brain scan of a person with frontal lobe epilepsy. Arrow points to the focus of seizure activity. [Image reproduced with permission from Seeck et al (1998) *Electroenceph. Clin. Neurophys.* 106. 508-512.

can strike at any time of life—from infancy to old age. While epilepsy varies widely in type and all forms of this disorder are characterized by recurring seizures resulting from abnormal cell firing in the brain. In approximately 30 per cent of cases, epilepsy is caused by such events as head trauma, tumour, stroke or infection. In those cases, for which there is no known cause, recent evidence suggests that there may be genetic predisposition for developing the disease. (see fig. 10.9)

It is an autosomal recessive disorder that has been linked to mutation of the gene EFM2A found on chromosome 6. Much progress has been made in narrowing down regions of chromosomes associated with different forms of epilepsy. With this effort, scientists continue to expand the list of genes involved in seizure disorders. Animal models of epilepsy also contribute to our understanding of electrical brain disturbances. By focusing on the genetic basis for epilepsy, scientists hope to develop more effective anticonvulsive treatments and, possibly, gene replacement therapies for seizure disorders such as Lafora disease.

### 10.2.10 ESSENTIAL TREMOR DISEASE

Tremor, or uncontrollable shaking, is a common symptom of neurological disorders such as Parkinson's disease, head

trauma and stroke. However, many people with tremor have what is called idiopathic or essential tremor which may involve other parts of the body; the head and hands are most often affected.

In more than half of the cases, essential tremor is inherited as an autosomal dominant trait, which means that the children of an affected individual also will have at least 50 per cent chance of developing the disorder. In 1997, the ETM1 gene (also called FET1) was mapped for chromosome 3 in a study of Icelandic families, while another gene, called ETM2, was mapped to chromosome 2 in a large American family of Czech descent. The two genes for essential tremor have been found on two different chromosomes, demonstrating that mutation in a variety of genes may lead to essential tremor.

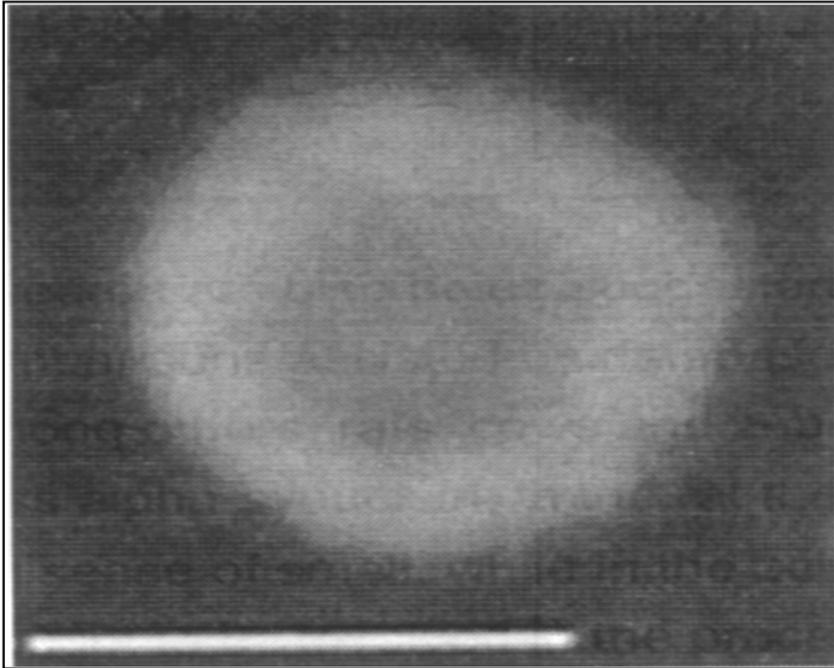
While the mainstays of treatment are drugs such as propranolol and premidon, alternative drugs and surgical treatments are also available. Further understanding of the molecular mechanism behind the disease awaits the discovery and cloning of an essential tremor gene.<sup>4</sup>

#### 10.2.11 PARKINSON'S DISEASE

Parkinsons disease, first described by James Parkinson in 1817, is a growing national problem, with more than half a million Americans affected at one time. Most people are over 50 years old when the disease appears, although it can occur in younger people. It is a neuro-degenerative disease that manifests as a tremor, muscular stiffness and difficulty with balance and walking. A classic pathological feature of the disease is the presence of an inclusion body, called the Levy body, in many regions of the brain. (see fig 10.10)

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4 Website: [www.otherbooks.ncbi](http://www.otherbooks.ncbi).



**Fig. 10.10:** An overlapping immunofluorescent stain showing lapha-synuclein localization in Lewy bodies of Parkinson's disease brain. The Lewy body is stained green (with antibody against ubiquitin), while alpha-synuclein is stained red. Where both ubiquitin and alpha-synuclein are found, the stain appears yellow/orange. With thanks to M. Polymeropoulos for supplying the picture.

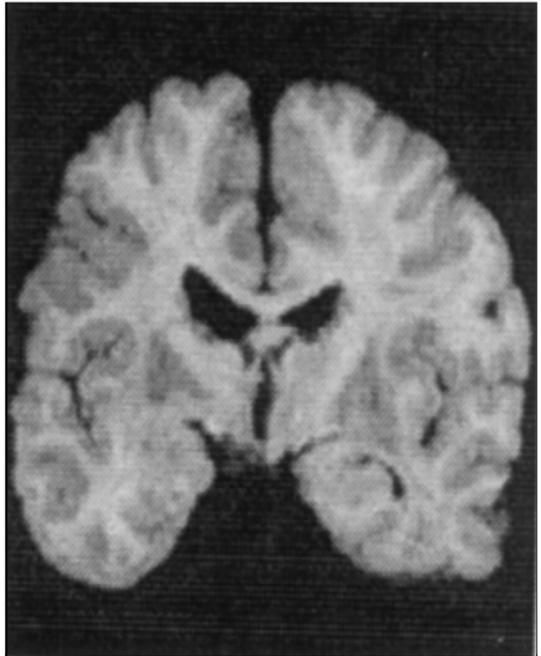
Parkinson's disease was thought not to be heritable, and research was primarily focused on environmental risk factors such as viral infections or neurotoxins. However, a positive family history was gradually perceived to be a risk factor, a view that was confirmed last year which a candidate gene for some cases of Parkinson's disease was mapped to chromosome 4. Mutation in this genes has now been linked to several Parkinson disease families. The product of this gene, a protein called alpha—synuclein, is a familier culprit, a fragment of it is a known constituent of Alzheimer disease plaques.

### 10.2.12 WILSON'S DISEASE

Wilson's disease is a rare autosomal recessive disorder of copper transport, resulting in copper accumulation and toxicity in the liver and the brain. Liver disease is the most common symptom in children while neurological disease is the most common in adults. The cornea of the eye can also be affected, the Kayser Feischer ring is a deep copper-coloured ring at the periphery of the cornea and is thought to represent copper deposits.

The gene for Wilson's disease (ATP7B) was mapped to chromosome 13. The gene sequence was found to be similar to sections of the gene defective in Menkes disease, another disease caused by defects in copper transport. The similar sequences code for copper binding regions, which are part of a transmembrane bronk pump called a P-type ATPase that is very similar to Menkes disease protein. (see fig. 10.11)

A homology to the human ATP7B gene has been mapped to mouse chromosome 8, and an authentic model of the human disease in rat is also available (called the long Evans Cinnamon (LEC). These systems will be useful for studying copper transport and liver pathophysiology, and should help in the development of a therapy for Wilson's disease.



**Fig.10.11:** In Wilson's disease, toxic level of copper accumulate and damage many tissues and organs, including the basal ganglia of the brain [Image credit : Kevin Roth and Robert Schmidt, Washington University, St. Louis, MO, USA.]

### 10.2.13 CANCER DISEASE

Cancer is caused in all or almost all instances by mutation or abnormal activation of cellular genes that control cell growth and cell mitosis. The abnormal genes are called oncogenes.

Only a minute fraction of the cells that mutate in the body ever lead to cancer. There are following reasons for this:

- a. Most mutated cells have less survival capability than normal cells and, therefore, simply die.
- b. Only a few of the mutated cells that do survive does the normal feedback controls that prevents excessive growth.
- c. Those cells that are potentially cancerous are often, if not usually, destroyed by the body's immune system before they grow into cancer. This occurs in the following way—

Most mutated cells form abnormal proteins within their cell bodies because of their altered genes and those proteins then stimulate the body's immune system, causing it to form antibodies or sensitized lymphocytes against the cancerous cells and in this way destroying them. In support of this is the fact that in persons, whose immune system has been suppressed, such as those who are taking immuno-suppressant drugs following transplantation of a kidney or a heart, the probability of developing a cancer is multiplied several fold.

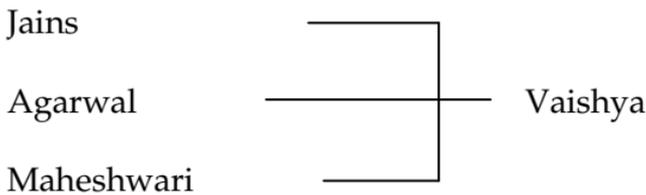
But what is it that causes the altered genes, when one realizes that many trillions of new cells are formed each year in the human being, this question should probably better be asked in the following form: Why is it that we do not develop literally millions or billions of mutant cancerous cells? The answer is the incredible precision with which DNA chromosomal strands are replicated in each cell before mitosis takes place and also because the "proof reading process" cuts and repair any abnormal DNA strand before the mitotic process is allowed to proceed. Yet

despite all these precautions, probably one newly formed cell in every few millions still has significant mutant characteristics.

(i) **Why do cancer cells kill?**—The answer to this question is very simple. Cancer tissues compete with normal tissues for nutrients. Because cancer cells continue to proliferate indefinitely, their number multiplying day-by-day, one can readily understand that the cancer cells will soon demand essentially all the nutrition available to the body. As a result, the normal tissues gradually suffer nutritive death.<sup>5</sup>

#### 10.2.14 INDIAN CASTEWISE DISTRIBUTION OF DISEASES<sup>6</sup>

##### I. Hindus



Most prevailing hereditary diseases in Hindus are as follows:

- Diabetes
- Heart disease
- High blood pressure
- Digestive problem
- Gastric problem
- Overweight
- Knee pain
- Low backache
- Teeth problems

<sup>5</sup> *Medical Physiology*—by Guyton, Prisoem Books Pvt. Ltd., eight edition, 1991.

<sup>6</sup> *Curtesy "Indian Castewise distribution of Disease"*—by Snior Physician—Dr. K.C. Madani, M.D., Jodhpur (Raj.)

## II. Brahamins

In Brahamins, common hereditary diseases are as follows:

- Respiratory infection
- Digestive problem
- Obesity

## III. Rajputs

In Rajputs, common hereditary diseases are:

- Injuries
- Appendicitis
- Color infection

## IV. Mohammedans

In Mohammedans, hereditary diseases are:

- Tuberculosis
- Skin infection
- Cancer

## V. Poverty based castes

The hereditary diseases in poverty based castes are:

- Malnutrition
- Tuberculosis
- Respiratory infections
- Abscesses & boils
- Skin problem

As per the Indian tradition, marriages take place within the caste. So, due to the transfer of genes, common hereditary diseases happen to be in a particular caste as above.

### 10.2.15 BIRTH DEFECTS

About 1,50,000 babies are born each year with birth defects. The parents of one out of every 28 babies receive the frightening news that their baby has a birth defect.

A birth defect is an abnormality of structure, function or metabolism (body chemistry) present at birth that result in physical or mental disability, or is fatal. Thousands of different birth defects

have been identified. Birth defects are the leading causes of death in the first year of life.

A single abnormal gene can cause birth defects. Every human being has 30-35000 genes that determine traits like eye and hair colour, as well as direct the growth and development of every part of our physical and bio-chemical systems. Genes are packaged into each of the 46 chromosomes inside our cells. Each child gets half its genes from each parent.

Abnormality in the number or structure of chromosomes can cause numerous birth defects. Due to an error that occurred when an egg or sperm cell was developing, a baby can be born with too many or few chromosomes, or with one or more chromosomes that are broken or rearranged. Down syndrome, in which a baby is born with an extra chromosome 21, is one of the most common chromosomal abnormalities. Chromosomal abnormalities are due to the *karma* of *jīva* taking birth in that particular womb. Affected children have varying degrees of mental retardation, characteristic facial features and often, heart defects and other problems. Babies born with extra copies of chromosome 18 or 13 have multiple birth defects and usually die in the first month of life. Missing or extra sex chromosome (X and Y) affect sexual development and may cause infertility, growth abnormalities, and behavioural and learning problems. However, most of the affected individuals have essentially normal lives.

#### 10.2.16 CHROMOSOMAL ABNORMALITIES

Sperm and egg cells are different from other cells of the body. These productive cells have only 23 unpaired chromosomes. When sperm and egg cell unite—and pregnancy begins, they form a fertilized egg with 46 chromosomes. But sometimes go wrong before pregnancy begins. In the process of cell division, an error occurs that leaves an egg or sperm cell with too many or few chromosomes. When this cell with the wrong number of chromosomes joins with a normal egg or sperm cell, the resulting embryo has a chromosomal abnormality. A common type of chromosomal abnormality is called

a trisomy. This means that an individual has three copies, instead of two of a specific chromosome. Down Syndrome is an example of trisomy. In most cases, an embryo with the wrong number of chromosomes will not survive. In such cases, the pregnant woman has a miscarriage often without knowing it. Upto 70 per cent of first trimester miscarriages are caused by chromosomal abnormalities.<sup>7</sup>

A person can inherit a genetic disease when one parent (who may or may not have the disease) passes along a single faulty gene. This is called dominant inheritance. Examples include achondroplasia (a form of dwarfism) and Marfan syndrome (a connective tissue disease). Many other genetic diseases are inherited only when both parents (who do not have those diseases) happen to carry the same abnormal gene and pass it on to a child. This is called recessive inheritance. Examples include Tay-sachs disease (a fatal disorder seen mainly in people of European Jewish heritage) and cystic fibrosis (a fatal disorder of lungs and other organs, affecting mainly Caucasians). There is also a form of inheritance (x-linked) where sons can inherit a genetic disease from a mother who carries the gene (usually with no effect on her own health). Examples include hemophilia (a blood clotting disorder) and duchenne muscular dystrophy (progressive muscle weakness).

Birth defects also may result from environmental factors such as drug or alcohol, infections, or exposure to certain medications (such as the acne drug accurate) or other chemicals. Many birth defects appear to be caused by the combination of one or more genes and environmental factors (called multifactorial inheritance). Some examples include cleft lip/palate, clubfoot and some heart diseases.<sup>8</sup>

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7 Website: [www.birthdefects.com](http://www.birthdefects.com).

8 March of Dimes Perinatal Data Centre, and Child Health in the United States, 2001.

Chromosomal abnormalities (numerical or structural alterations) occur from time to time in human beings. They arise in various ways:

**Non-disjunction**—By an error in nuclear division called "non-disjunction," a pair of chromosomes may fail and both are carried to one pole. The resulting daughter cells contain an unequal number of chromosomes 45 to 47. This numerical abnormality, in which the chromosome number is not an exact multiple of the haploid number, is called aneuploidy. If a particular pair of chromosomes has three chromosomes instead of two, it is called trisomy, if there is only one chromosome instead of two in any given pair of chromosome, it is called "monosomy". Non-disjunction may occur during gametogenesis or during mitosis.

**Translocation**—Sometimes, during nuclear division, a portion of one chromosome breaks away and becomes attached to another, which is not homologous to the first. This is called translocation.

**Deletion**—A piece of chromosome may become detached and lost from the karyotype, resulting in the loss of one or more genes. If the loss is severe, it may be incompatible with life birth.

**Duplication**—Some genes may appear twice in the same chromosome. This is called duplication.

**Inversion**—Sometimes a chromosomal segment becomes inverted and then the order of sequence of genes is altered.

**Isochromosomes**—These are special class of structurally abnormal chromosomes, arising because of misdivision i.e. transverse division instead of normal longitudinal division.

**Mosaicism**—The cells of the body are compounded of cells of two or more genetically different chromosomal types. This can result by mutation or non-disjunction either during embryo or later life.

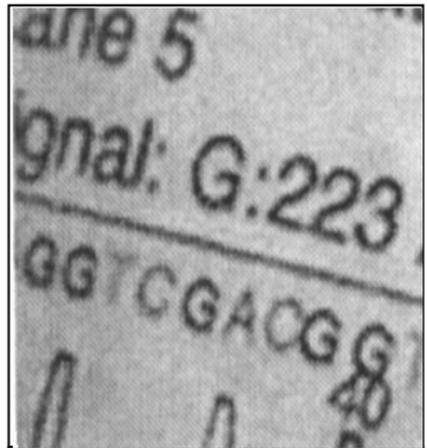
Genes are usually stable, but sometimes normal genes may be converted into abnormal ones, this change is called mutation. Mutation is a regular phenomenon in nature. The natural mutation rate is increased by the exposure of mutagens such as ultraviolet rays, radiation or chemical carcinogens.<sup>9</sup>

### 10.3 Role of faulty genes in chromosome

Cells that make up the human body generally have 23 pairs of chromosomes. Sometimes called the "genome," the full compliment of human chromosomes contains approximately three billion base pairs of DNA or 40,000 genes.

A gene is a functional and physical unit of heredity passed from parents to their child. Genes are pieces of DNA and most genes contain the information for making a specific protein (see fig. 10.12). This explains why traits that relate to physical appearance—such as eye colour, cheek bone structure and hair texture—can be passed from mother to her children. But genes are not limited to effecting physical appearances. Genes play an important role in the health of all parts of the human body. Diseases such as cancer, glaucoma, autism, diabetes, epilepsy, asthma, cystic fibrosis and muscular dystrophy may be caused when genes "malfunction."<sup>10</sup>

The principal role of genes in the chromosomes of human has now been identified. Faulty genes in the chromosomes lead to



**Fig.10.12:** Genetic code sequence in the length of a gene.

9 WHO 1966, Tech. rep. ser. no. 865.

10 Website : [www.genesandhealth.com](http://www.genesandhealth.com).

different diseases as mentioned below:<sup>11</sup>

**Chromosome 1:** Contains record of past lives. Faulty gene for GBA enzyme, which breaks down certain fats, leads to Gaucher's disease.

**Chromosome 2:** It contains the history of journey leading to human life. [It has details of birth in various species we lived before. PAX-2 gene is associated with deafness and colour difference in eyes. This causes wardenburg syndrome.

**Chromosome 3:** It contains evidences for the entire past history in the form of genes. Faulty VHL gene causes abnormal blood vessel formation. This gives non Hippel-Landau disease.

**Chromosome 4:** This contains information about our future. It also carries hints about forthcoming disease and traits. Faulty gene causes dementia. This leads to HD (Huntington's disease).

**Chromosome 5:** This is very sensitive to environment and contains information about our immune system. It helps in the study of genetic diseases like asthma, diabetes etc. Faulty gene causes malformed hands and feet. This leads to DTD (diatrophic dysphasia).

**Chromosome 6:** This is the intelligent chromosome, it is the basis of our intelligence. It has been shown that in some cases, intelligency is hereditary. Faulty SCA1 gene causes clumsiness through withering of the cerebellum. This leads to spino cerebella atrophy.

**Chromosome 7:** It contains those characteristics which determine our behaviour as human being. This is regarded as the most important chromosome. Faulty gene causes fatal building-up of mucus in lungs and pancreas. This leads to cystic fibrosis.

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11 *Brahmāndīya Jaiveka Bhotika and Rasayana Vijñāna*—Acaryaśri Kanaknandji, Publisher Dharamdarśana Vijnana Sodh Saṅsthan, Udaipur, first edition 2004, p. 308-9.

**Chromosome 8:** This contains information about our liking and choices. Our habits and nature are stored and transmitted to the next life. This means that our merits and demerits are also influenced by heredity factors, i.e. genes. Defective gene causes premature aging. This lead to WRN (Werner's syndrome).

**Chromosome 9:** This determines the blood group. It also causes a disease we suffer. Skin cancer is more likely to be in people with faulty CDKN2 tumour repressor gene. This lead to Malignant Melanoma.

**Chromosome 10:** This chromosome contains the gene CYP17, which produces an enzyme that converts cholesterol into hormones called cortisol and testosterone. These hormones produce stress in the body. Defect in MEN2A gene causes tumours of thyroid and adrenal glands. This leads to multiple Endocrine Neoplasia.

**Chromosome 11:** This contains genes which influence our personality. Harvey RAS gene predisposes to common cancers.

**Chromosome 12:** This is self assembled. Defects in PAN gene causes mental retardation by blocking the dygestion of common amino acid in food. This leads to PAH Phenylketounria.

**Chromosome 13:** It stores characteristics of the past lives. Defects in BRCA2 gene raises the risk of breast cancer.

**Chromosome 14:** This is of indestructible nature. Faulty AD3 gene is linked with the development of plaques in the brain. This leads to PS1 (AD3) Alzheimer's disease.

**Chromosome 15:** It determines the gender. Abnormal FBN1 weakens connective tissue potentially by rupturing blood vassels. This leads to marfan's syndrome (position unknown).

- Chromosome 16:** This contains memory. Faulty PKD1 gene causes cysts to form, which trigger kidney failure. This leads to polycystic kidney disease.
- Chromosome 17:** This determines the life span. Mutations in PS3 gene increase vulnerability to cancer. BRCA1 predisposes to breast cancer.
- Chromosome 18:** Helps in recovery from illness. Damage to DPC2 gene accelerates pancreatic cancer.
- Chromosome 19:** This determines fertility. Defective gene for apolipo protein raises blood cholesterol, predisposing to artery blockage. This leads to coronary heart disease.
- Chromosome 20:** Abnormal adenosine de-minase (ADA) gene destroys immunity. This is curable by gene therapy. This leads to severe combined immunodeficiency.
- Chromosome 21:** Wasting disease linked with defective super oxide dismutase (SOD1) gene. This leads to Lou Gehrig's disease.
- Chromosome 22:** This characterizes freedom of thought. Abnormal DGS gene triggers heart defects and facial changes. This leads to DiGeorge Syndrome.
- Chromosome 23:** Abnormal DMD gene triggers muscle degeneration. This leads to Duchenne Muscular Dystrophy.
- Chromosome 24:** Governed by the SRY gene of testis—determining factor. This leads to testicle development.

## 11

## Genetic Engineering

Genetic engineering is the heritable, directed attention of an organism. Altering DNA or adding new DNA allows us to change the characteristic of a cell or cells. Non-germ line alterations are not carried to the next generation. Only half of our genes are given to our offsprings, diluting any germline genetic modifications overtime. DNA carries the instructions as genes, proteins perform the actions. Regulation of gene is as important as gene functions. Foreign DNA may be rejected. While the Human Genome Project may give us the entire sequence of our DNA, scientist must still determine how all the encoded proteins work.

### 11.1 Genetic engineering and its application

Genetic engineering is the method of transferring a gene from the DNA of one species to another species. It gets to the very core of how life works and people are inclined to have very strong feelings about it. Genetic engineering was probably the most important scientific event of the 20<sup>th</sup> century. James Watson and Francis Crick in 1953 discovered the structure of the DNA molecule, which is the basis of heredity. Darwin has shown how species might have changed over eons and slow, random natural processes. Watson and Crick gave us the key to moving evolution much faster, to suit our own purposes.

A DNA molecule is like a string of letters, using a four letter alphabet, easily copied when living cells reproduce. The sequences of letters make sentences, which we call genes. One kind of gene gives a cell the necessary instructions for making

one of the various kinds of protein, used for structures, enzymes, signals and basic mechanisms of life. The other kind of sequence is used as a control mechanism so that a cell can tell when to make which protein and when to do something else.

Scientists learnt the language of protein-making gene sequences. The language is the same for all forms of lives. Gene sequences are control sequences and are like switches that turn other genes on or off. A control sequence could have different results in different organisms. Some control genes are used to turn another gene on, and the others are used to turn another gene off.

For example, a cell needs protein A, but not in much amount. If the genes that tells the cell to make protein A is turned on, eventually, the control gene will sense that there is a lot of protein A available, then it will turn off the protein making gene. Later on, when the supply of protein A is used, the control gene will relent and let the protein making gene turn back.

Each different organism has ten thousand different genes and make a huge number of proteins. Life is enormously complex. However, hundreds of genes are now understood completely. There are many more genes which have been discovered and associated with some functions, but not yet understood very well. There are practical applications of this knowledge. The first practical applications were in medicine, using genetically modified bacteria to make medical drugs such as interferon, human growth hormone and human insuline. The second kind of application was to modify organisms for agricultural purposes.<sup>1</sup>

## 11.2 The Impact of Genetic Engineering

Introduction of new procedures and new products realized through genetic engineering will have a profound effect on public health, agriculture and food industries. Treatment with

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1 *Genetic Engineering and its Application*—by P. Joshi, second edition 2004—Agrobios India, Jodhpur

genetically engineered enzymes that lower cholesterol or saturated fatty acids, can have a great impact on cardio-vascular diseases. Genetic engineering in itself is not a discipline but a powerful tool. Biocompatible pesticides and herbicides can be made through genetic engineering to keep the environment clean. Genetic screening becomes obligatory for employment, life insurance acceptance would have questionable social implications. The development of human and animal proteins will open new vistas for diagnosis and therapy. Vaccines remain one of the best approaches to control infectious diseases. Bacterial, viral, fungal, amoebal and trypanosomes are the major causative agents. A successful experiment has been established by the eradication of small pox globally in 1977.

The recombinant live vaccines are particularly promising in their wide applicability and possibility of combining multiple antigens. The use of manipulated somatic cells in the therapy of genetic diseases is imminent. Beneficial modifications of the germline of domestic animals is a distinct possibility.

#### 11.2.1 DNA FINGERPRINTING

Forensic scientists are able to read the DNA sequences and find differences among species. They reduce base names down to letters "A," "C," "T," "G." Then scientists read the sequences of these letters by looking at one half of the ladder. Although the majority, 99.9 per cent, of the letter sequence on a human DNA strand is identical, there are portions of each strand that differ from individual to individual. Thus, in a DNA strand, three billion letters, one tenth of one per cent difference translates into three million separate spelling difference. These are differences that the scientists examine in the process known as DNA finger printing to determine identity and heritage. Unfortunately, for the purpose of forensic DNA finger printing, scientists do not read all the three billion letters. Instead, to save time and money, they look at very small handful of sites of variation. Along the DNA strand, or genome, there are regions where the base pair sequences repeat

themselves. For instance, one person could have the sequences of T-A-C-T-G repeat three times and another person could have the same sequence repeat twice or appear only once. Thus, these normally biologically insignificant sequences repetitions create spelling difference in particular areas. In general, forensic scientists cut the DNA strands with an enzyme at these point of repetition. Then they record the repetition variations by reducing the data into a bar code type expression. When comparing DNA samples from crime scene evidence to a suspect's DNA sample, scientists will compare the "bar code" information from each site of variation. If "bar code" differs between the evidence and the suspect's DNA at any point, that particular suspect is usually ruled out as a possible source of DNA evidence. However, if the "bar codes" are the same along all points of variation tested, the suspect is considered more likely to have left the evidence.<sup>2</sup>

### 11.2.2 RECOMBINANT DNA TECHNOLOGY

Recombinant DNA technology allows the DNA to be divided into small fragments which can be studied at the nucleotide level and analyzed functionally. The plasmid and foreign DNA are cut by this restriction endonuclease (ECORI in the given below example producing

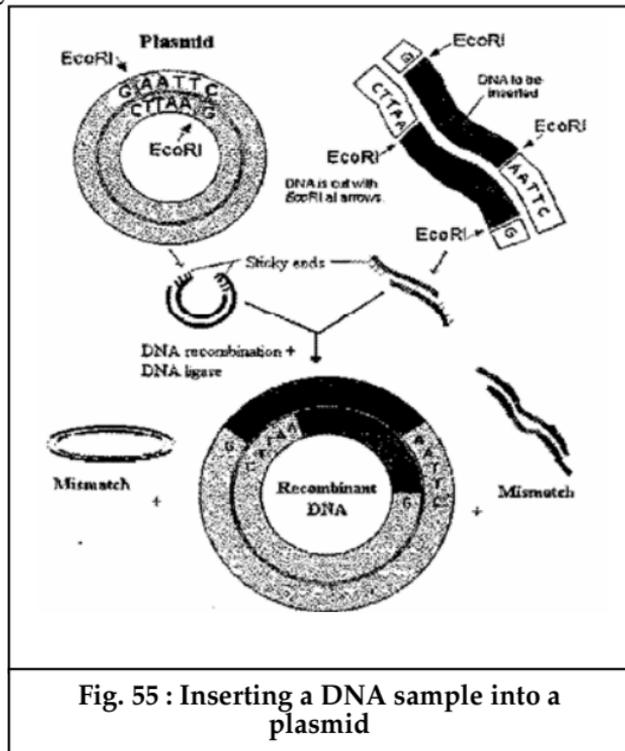


Fig. 55 : Inserting a DNA sample into a plasmid

<sup>2</sup> An international DNA database; "Balancing Hope, Privacy and Scientific Error," Allison Puri.

intermediates with sticky and complimentary ends.) Those two intermediate recombine by base paring are linked by the action of DNA ligase. A new plasmid containing the foreign DNA as an insert is obtained. A few mismatches occur, producing an undesirable recombinant. The term recombinant DNA literally means the joining or recombining of two pieces of DNA from two different species. Recombinant DNA techniques allow an investigator to biologically purify (clone) a gene from one species by inserting it into DNA of other species, where it is replicated along with the host DNA. Actually, the term includes a variety of molecular manoeuvres, including cleaving DNA by microbial enzymes called endonucleases, splicing or recombining fragments of DNA, inserting eucarotic DNA into bacteria so that large quantity of the foreign genetic material can be produced, determining the nucleotide sequence of a segment of DNA, and even chemically synthesizing DNA.<sup>3</sup> (see fig. 11.1)

### 11.2.3 GENERAL APPROACH TO CLONE DNA

The general approach to clone DNA is as follows:

DNA is extracted from cells and cut by the restriction endonuclease enzyme into several segments. Plasmid DNA is also cut by the same enzyme and then the plasmid and cell DNA are mixed together and joined with an enzyme DNA ligase to give recombined DNA. Each of the resulting plasmids contain a piece of DNA from the cell. Under appropriate conditions, the bacteria absorb the recombination plasmids. If the host bacterium is sensitive to the antibiotics tetracycline and ampicilin, it will not grow in their presence. However, the plasmids with its resistance genes allow the bacterium to grow. When a single bacteria divides on an agar plate, each of the millions of daughter cells carries an identical copy of the original plasmid containing the inserted DNA from the cell. By this technique, the total nuclear DNA from a cell may be divided into

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3 WHO 1996, Tech. Rep. S.no. 865.

many clones, each clone having a point of DNA of the cell from which it was extracted. Such a collection of thousands of clones constitute a genomic library.<sup>4</sup>

#### 11.2.4 THE MANIPULATION OF EMBRYOS

The nucleus of the fertilized egg can be removed and a nucleus from white cells of a mother or father can be inserted and if development continues then we have an offspring which is a zerox copy of mother or father. We have to know how to turn these genes on and off. By introducing the gene at the two-celled stage we can expect the desired result. In other words, we have to manipulate embryos in vitro. It is possible to collect embryos from females, culture them in vitro, freeze and store them indefinitely in liquid nitrogen. We can later bring them back to activity, sex them and transfer them back to the reproductive tract of recipient to obtain normal offspring.

Individual embryos can be divided into two, resulting in identical twins or three or four parts making them triplets and quadruplets. These techniques can be used to increase the female reproductive rate analogue to artificial insemination used in male animals. Production of bull calves by embryo transfer is an efficient means of amplifying genes of the best cows through their sons.<sup>5</sup>

#### 11.2.5 CLONES

Clones are individuals that are genetically identical. In theory, it should be possible to produce identical copies of yourself: take one of your body cells, remove the nucleus (which contains the genes) and implant this into a one-celled embryo which has had

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4 *Understanding Genetics*—by O.S. Reddi, Allied Publishers Ltd., New Delhi, p. 125-126.

5 Corey Goodman and Michel J. Bastiani—"How Embryonic Nerve Cells Recognize One Another," 251(6), 58-66, December, 1994.

its own nucleus removed. Then your genes will control the development of a duplicate of your self.

We can, however, produce several genetically identical individuals by splitting up the embryo at an early stage. At the eight-cell stage, for instance, each cell can reform a whole embryo. But these approaches produce only a finite number of clones from the embryo. The cloning of mice is shown below: (see fig. 11.2)

With the development of genetic engineering, biologists have preferred techniques for introducing genes from one organism into another organism. The result—a cow, say carrying a human gene among its own genetic material—is called a transgenic

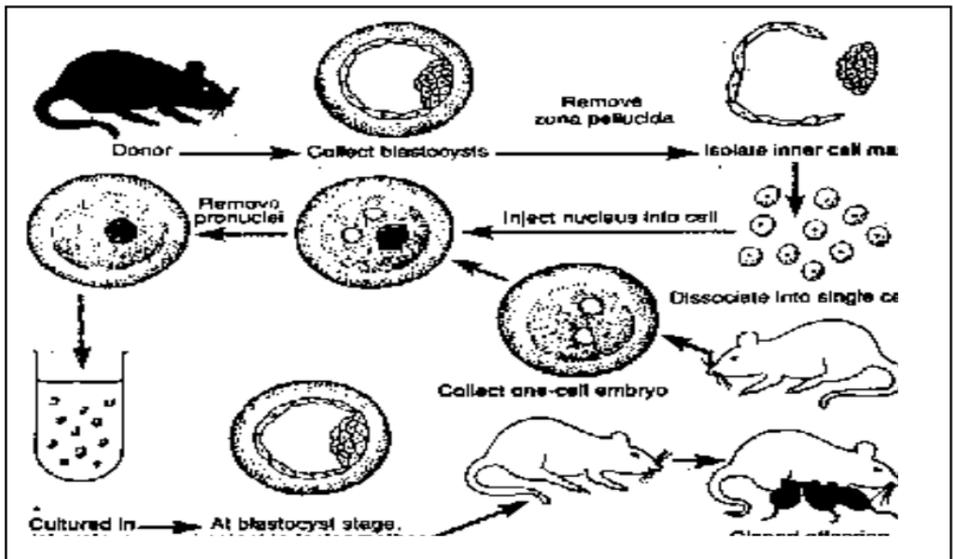
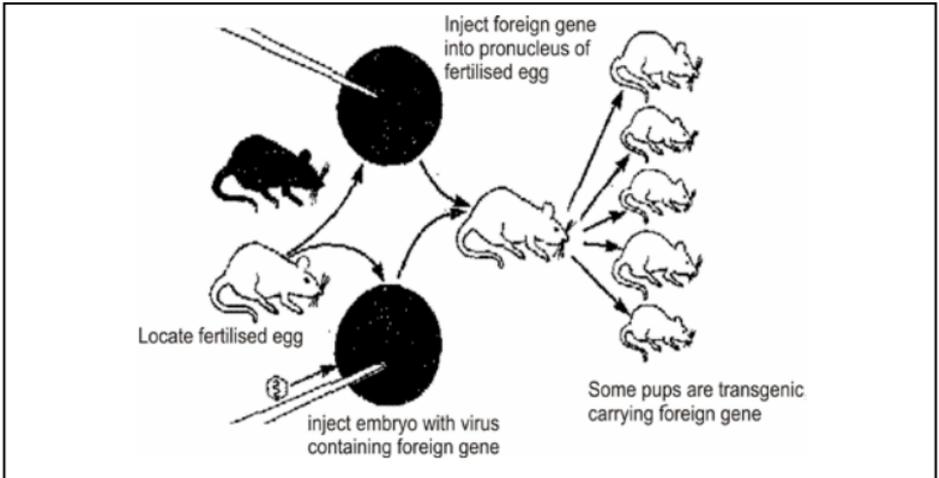


Fig. 56 : Transplant a nucleus from one embryo to another

animal. The most popular way of producing transgenic animals is to inject genes directly into one of the pronuclei in a newly fertilized egg. This delicate task is performed by holding the egg in a suction tube, piercing the egg and pronucleus with a micropipette to inject the foreign gene. Remarkably, this crude procedure works at least for some time. The foreign gene is permanently incorporated into the genetic material of animal.



**Fig. 57 : Supermice Created by Introducing a Gene for Growth Hormone into a Mouse Embryo**

Some may also damage the host's genetic materials creating what are known as insertional mutations.

In spite of these problems, "microinjections have created many transgenic mammals—including mice, rats, pigs and sheep. The first to emerge from the laboratory, in 1981, were mice carrying a gene for growth hormone. These grew upto 50 per cent larger than their counterparts. Another way to create transgenic animals is to take advantage of viruses (retroviruses) that naturally infect cells. These retroviruses insert their own genes into the genetic materials of a cell. The genetic engineers take away the key infecting parts of the retrovirus and add to this foreign gene of their choice. Such a recombinant retrovirus, made from artificially combined bits of genes, can then carry foreign genes into the embryonic cells. The embryo is infected with this engineered virus at four or eight-cell stage. The difficulty is that the virus may not infect all the cells of the embryo. If it infects some of them we get a chimera, that is all cells are not genetically identical. To begin with, this technique is being tried to infect the

stem cells of bone marrow as a therapeutic intervention in certain blood disorders.<sup>6</sup> Figure 11.3 shows the creation of supermice.

#### 11.2.6 GENE THERAPY

Gene therapy is the introduction of a gene sequence into a cell with the aim of modifying the cell's behaviour in a clinically relevant fashion. It may be used in several ways, i.e. to correct a genetic mutation (as for cystic fibrosis), to kill a cell (as for cancer) or to modify susceptibility (as for coronary artery disease). The gene may be introduced using a virus (usually a retrovirus or adenovirus) or by means of lipids or receptor targeting. There is now almost universal agreement that gene delivery to somatic cell to disease is ethical, and that gene therapy should take its place along side other forms of medical treatment.<sup>7</sup>

#### 11.2.7 POPULATION GENETICS (THE GENES IN POPULATIONS)

In the study of heredity, the first question that arises is how the genotype of an individual is formed from the constituents of the genotypes of his parents. This is the genetics of individual or basic genetics. One may also enquire how the genotype in a fertilized egg cell influences the developmental pattern of organisms and thus realizes its potentialities. This is the developmental genetics. An individual, at least an individual of a sexually reproducing species, is not, however, biologically complete in itself. Its biological role is to actualize through its membership in a reproductive community, a Mendelian population. A Mendelian population consists of individuals among whom mating may or do occur. An individual is mortal and temporary; a Mendelian population has a continuity through time. The genetic process in Mendelian populations is the subject matter of population genetics. Population genetics has been defined as the study of the precise genetics composition of

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6 *Understanding Genetics*—by O.S. Reddi—Allied Publishers Ltd., New Delhi.

7 WHO (1996) Tech. rep. ser. no. 865.

population and various factors determining the incidence of inherited traits in them.<sup>8</sup>

Population genetics is founded on a principle enunciated independently by Hardy in England and Weinberg in Germany in 1908. Let us consider the results when a human population consisting of tall (TT), intermediate (Tt) and short (tt) individuals were allowed to mate at random. Even after several generations of interbreeding, it will be found that there will be some individuals who are tall (TT), some intermediate (Tt) and some short (tt). In other words, we cannot produce a race which is pure or uniform in height.

The Hardy-Weinberg law states that "the relative frequencies of each gene allele tends to remain constant from "generation to generation" in the absence of forces that changes the gene frequency. Thus, the study of gene frequencies, and the influences which operate to alter the "gene pool" and their long term consequences is the central theme in population genetics.

#### 11.2.8 FACTORS WHICH INFLUENCE THE GENE FREQUENCIES

The Hardy-Weinberg law assumes that human population is static. But in reality, human population and consequently human gene pool is never static. There are several factors which influence the human "gene pool." The following are some factors:

- (i) **Mutation**—Mutation implies a change in the genetic material of an organism which results in a new inherited variation. Mutation is a rather regular phenomenon in nature. It is now recognized that mutant genes are so widespread in their occurrences that every one of us might be harbouring a few or many of them. According to modern genetics, the entire body structure of man and every other animal and plant cell has been

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<sup>8</sup> Indian Council of Medical Research (1972) "*Genetics and Our Health*" Techn report ser. no. 282.

built through hundreds of millions of years by means of a long succession of mutation.<sup>9</sup> The cause of spontaneous mutation is not yet known. The Jaina doctrine of *karma* says that the cause of mutation is *karma* of individual organism. Accumulated *karma* of living organism direct mutation of genes. All the activities of genes are determined by *karma* of individual organism. But we know that certain external influences such as ionizing radiation and certain chemicals are capable of producing mutations experimentally and there is no reason to believe that man is an exception. Most mutant genes are believed to be harmful. But there are instances where a mutant gene could be beneficial, e.g. sickle cell anaemia. The heterozygotes of sickle cells trait were found to be resistant to *falsiparum* malaria. Some mutant genes remain "neutral" that they do not harm or impair the survival ability of the carriers.

- (ii) **Natural Selection**—Darwin proposed the theory of natural selection or survival of the fittest to explain evolution. Natural selection is the process whereby harmful genes are eliminated from the gene pool and genes favourable to an individual tend to be preserved and passed on to the offspring. When DDT was first used, it was lethal to houseflies. Today, not many houseflies are killed by DDT. This is an example of natural selection in response to DDT, the resistant variety of houseflies have become the usual form. The forces which operate in the animal kingdom do not apply in human populations because man by his superior intelligence has interfered with natural selection in every conceivable way by changing the environmental conditions under which people live by advances in technology, public health and medical care services.
- (iii) **Population Movement**—Because of industrialization, increased facility for earning, ways of living and education, people are moving—sometimes on a large scale from rural to urban areas.

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9 Corwin, E.H.L. (1949) "*Ecology of Health*," The Commonwealth Fund, New York (U.S.A.)

Such migrations will lead to changes in the distribution of genes, affecting both the areas of immigration and emigration. The intermixing of people makes new genetic combinations possible.

- (iv) **Breeding Structure**—If all marriages were to occur in a random fashion, the effect would be the attainment of a genetic equilibrium. In practice, however, mating tends to occur selectively within various subgroups based on religion, economic and educational status and family relationships. In open societies, there is more freedom in mating. For instance, doctors tend to marry doctors or nurses, musicians tend to marry musicians. This type of mating is called "assortative mating," or "birds of the same feather flocking together." The genetic consequences of assortative mating have not been adequately studied.
- (v) **Public Health Measures**—Advances in public health and medical care services do effect the genetic endowment of people as a whole. More lives are now being saved by advances in medical sciences than ever before. For instance, Ramstedt's operation which was introduced in 1912 has saved many children suffering from congenital pyloric stenosis. Individuals with genetically conditioned retinoblastma may be saved by timely surgery. The provision of insulin has saved the lives of diabetics. The carriers of hereditary diseases, malformations and constitutional weaknesses are able to survive and pass their genes to their progeny. Public health measures are thus decreasing the selection rates and increasing the genetic burden. This has led some scientists to the prophesy, "Medicine will harm in the long run by helping them in the short run".<sup>10</sup>

### 11.3 Preventive and Social Measures

The basic principles of genetics were laid down by Mendel and Galton towards the close of 19<sup>th</sup> century. But it is only during the

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10 WHO (1964) Techn. rep. ser. no. 282

past few years, the science of genetics including human genetics has made rapid progress. The discovery of the biological role of nucleic acid, the uncovering of the structure of genetic information and its role in regulating life processes and discoveries, the importance of which can hardly be over estimated, with increasing control of communicable diseases and infant mortality, abnormalities are assuming a proportionately greater importance in medical practice. Over 2300 hereditary diseases have been identified and more are added to the list every year. According to many authors, genetically conditioned diseases with a clear genetic component account for 25-40 per cent of all cases treated by the health services.<sup>11</sup>

Human genetics is much more than the study of mere hereditary diseases and inborn abnormalities. It has emerged as a basic biological science for understanding the endogenous factors in health and disease and the complex interaction between nature and nurture. Owing to rapid specialization, several branches in genetics have come into being, for example cytogenetics, biochemical genetics, clinical genetics, pharmaco genetics, immune genetics, microbial genetics, population genetics and so on. Achievements in these fields have created a basis for effective medical and preventive intervention in many diseases, and also the possibility of "genetic engineering," i.e. of controlling the traits of an individual.

### 11.3.1 HEALTH AND PROMOTIONAL MEASURES

- (a) **Eugenics**—Galton proposed the term eugenics for the science, which aims to improve the genetic endowment of human population. Eugenics has both negative and positive aspects.
- (i) **Negative Eugenics**—Hitler sought to improve the German race by killing the weak and defective; this was negative

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11 Wald I (1976) in "*Health, Medicine and Society*" proceedings of the international conference on the Sociology of Medicine, D. Reidel Publ. Co. Boston

eugenics. Nobody in the civilized world would approve of such a measure to improve the human race.

On the other hand, if people who are suffering from serious hereditary diseases are sterilized or otherwise debarred from producing children, there should be serious objection to marriage. The aim of negative eugenics is to reduce the frequency of hereditary diseases and disability in the community to the least possible degree. However, the question one would ask is how far negative eugenic measures would be helpful in eliminating genetic defect. The simple answer is that in spite of eugenic sterilization, new cases of hereditary diseases will continue to arise in the population partly because of fresh mutations, and partly because of marital alliances between hidden carriers (heterozygotes) of recessive defects. Nevertheless, it may be hoped that if eugenic measures should be applied, hereditary diseases would become less frequent.<sup>12</sup>

**(ii) Positive Eugenics**—This is a more ambitious programme than negative eugenics. It seeks to improve the genetic composition of the population by encouraging the carriers of desirable genotypes to assume the burden of parenthood. At present, positive eugenics has very little application. Its realization is difficult for two reasons:

**(a)** The majority of socially valuable traits—let us say intelligence and positive character features, though partially determined biologically are not inherited in such a simple way as blood groups. These traits have a complex, multifactorial determination, both genetical and environmental. It would be difficult to expect, therefore, that positive eugenic measures will yield direct results.<sup>13</sup>

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12 WHO (1964) Techn. rep. ser. no. 282.

13 Corwin E.H.L. (1949) "*Ecology of Health*," the Commonwealth Fund, New York, U.S.A..

- (b) **Euthenics**—Mere improvement of the genotype is of no use unless the improved genotype is given access to a suitable environment, an environment, which will enable the genes to express themselves readily. Throughout the course of history, man has been adopting environment to his genes more than adopting his genes to the environment. Studies with mentally retarded (mild) children indicated that exposure to environmental stimulation improved their IQ. Thus, the solution of improving the human race does not lie in contrasting heredity and environment, but rather in mutual interaction of heredity and environmental factors. This environmental manipulation is called euthenics and has considerable broader prospects for success.
- (c) **Genetic Counselling**— The most immediate and practical service that genetics can render in medicine and surgery is genetic counselling.<sup>14</sup> Genetic counselling may be prospective or retrospective.<sup>15</sup>

Most genetic counselling is at present retrospective, i.e. the hereditary disorder has already occurred within the family. A survey carried out by the WHO showed that genetic advice was chiefly sought in connection with congenital abnormalities, mental retardation, psychiatric problems and inborn errors of metabolism and only a few sought premarital advice. The WHO recommends the establishment of genetic counselling centres in sufficient numbers in regions where infectious disease and nutritional disorders have been brought under control and in areas where genetic disorders have always constituted as a serious public health problem (i.e. sickle cell anaemia and thalassemia).<sup>16</sup>

The methods which could be suggested under retrospective genetic counselling are:

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14 WHO (1964) Techn. Rep. Ser. No. 282.

15 *Ibid*, Ser. 49.

16 *Ibid*, Ser. no. 282

- (i) Contraception,
- (ii) Pregnancy termination, and
- (iii) Sterilization depending upon the attitudes and cultural environment of the couples involved.<sup>17</sup>

### 11.3.2 SPECIFIC PROTECTION

Attention is now being paid for the protection of individuals and the whole community against mutagenes such as x-rays and other ionizing radiations and also chemical mutagenes. Patients undergoing x-ray examination should be protected against unnecessary exposure of gonads to radiation. X-ray examination of the pregnant uterus to determine the presence of twins or the position of the foetus is to be strongly deprecated. Rh haemolytic disease of the new born, which is a genetically determined immunological disorder, is now preventable by immunization of anti D globulin.

### 11.3.3 EARLY DIGNOSIS AND TREATMENT

- (i) **Prenatal Diagnosis**—Amniocentesis in early pregnancy (about 14-16 weeks) has now made it possible for prenatal diagnosis of conditions associated with chromosomal anomalies (e.g. Down syndrome); many inborn errors of metabolism (e.g. Tay-sach disease, galactosemia, Maple syrup urine disease, Alpha thalassaemia and neural tube defects). The indications for prenatal diagnosis are listed in the following table:

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<sup>17</sup> *Ibid*, Ser. no. 49.

**Indications for prenatal diagnosis<sup>18</sup>**

S. No.	Indications	
a.	Advanced maternal age, previous child with chromosome aberration, intrauterine	Cytogenetics (amniocentesis, chorionic villus sampling)
b.	Biochemical disorders	Protein essay, DNA diagnosis
c.	Congenital anomaly	Sonography, Foetoscopy
d.	Screening for neural tube defects and trisomy	Maternal serum alpha-fetoprotein, and chorionic gonadotropin

**(ii) Amniocentesis**—The examination of a sample of amniotic fluid makes possible the prenatal diagnosis of chromosomal anomalies and certain metabolic defects. The procedure can be used before the 14<sup>th</sup> week of pregnancy, when abortion of the affected foetus is still feasible. The diagnosis of chromosomal anomalies is made by culture and karyotyping of fetal cells from the amniotic fluid, and of metabolic defects by biochemical analysis of fluid.

**(iii) Screening of Newborn Infants**—Today, we have long list of screening tests for the early diagnosis of genetic abnormalities—sex chromosome abnormalities, congenital dislocation of hip, PKU, congenital hypothyroidism, sickle cell disease, cystic fibrosis, Duchenne muscular dystrophy, congenital adrenal hyperplasia, G6PD deficiency, etc.

Neonates should be routinely examined for congenital abnormalities, particularly dislocation of the hip, which can be simply corrected at this stage. Bio-chemical screening of newborn infants was first used for PKU in 1966. Heel-prick blood samples are usually collected from 5-10 days after birth, several drops of blood

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18 *Current Medical Diagnosis and Treatment*—Ed. by Lawrence in tierney. Jr. Stephen J. McPhee and Maxine A, Papadakis, 34<sup>th</sup> edition (1995) A LANGE Medical Book.

are collected on a filter paper (the Guthrie card) which is sent to screening laboratory.

Screening of new borns for congenital hypothyroidism is carried out in most developed countries. Sickle cell disease can be detected cheaply and reliably by haemoglobin electrophoresis using Guthrie blood spots. Neonatal screening for cystic fibrosis is based on the measurement of immunoreactive trypsin in Guthrie blood spots.

**(iv) Recognizing Preclinical Cases**—Today, we have pretty long list of screening tests for the early diagnosis of hereditary diseases. For example, heterozygotes of phenylketonuria can be detected by a phenylalanine tolerance test. A simple urine examination for sugar after morning breakfast is good enough to detect diabetics. Examination of sibs and close relatives of diabetics by a glucose tolerance test will often reveal preclinical case of acholuric jaundice. A raised serum uric acid should arouse suspicion of gout. Sickle cell trait can be uncovered by subjecting the red cells to reduce oxygen tension. Thalassaemia minor can be detected by studying the blood sample.

Genetic counselling can have the greatest impact when individuals or couples at genetic risk are identified prospectively, i.e. before they have developed symptoms or produced their first affected child. Prospective counselling is technically possible only when carriers can be accurately identified. To some extent, the established genetic population screening services may serve as models for the development of future genetic screening programmes.<sup>19</sup>

Once diagnosed, some of the genetic conditions can be treated with complete or partial success by medical and surgical measures. For example, diets low in phenylalanine are now prescribed as treatment for PKU children. Persons suffering from haemophilia can be greatly helped by administering antihemolytic globulin, which

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19 WHO (1996) Tech. rep. ser. no. 865.

promotes the clotting of blood. Modern surgical techniques have brought great improvements in dealing with cases of spinabifida.

**(v) Rehabilitation**—Finally, rehabilitation, with many genetic or partially genetic conditions, causing physical or mental disability, much can be done for the patient and for his family in helping him to lead a better and more useful life.

**(vi) Transplantation Organ and Tissues**—It is a common misconception that genetic diseases are, by their nature, untreatable. This stems from a lack of understanding of the modifying effects of the environment on expression of the genotype. As in all medical therapy, the treatment of genetic disease depends upon modifying the environment so that any harmful expression of the mutant gene can be counteracted. Thus, in the disease phenylketonuria, the expression of mutant gene is counteracted by putting the affected person on a low diet in phenylalanine. Similar dietary manipulations can effectively control many other inborn errors of metabolism. As a result of the developments in somatic cell and molecular genetics, researchers have elucidated the precise molecular defect in many genetic disorders, often making it possible to neutralize the defect by the application of appropriate drugs or dietary changes. On occasions, surgeons can counteract the consequences of a mutant gene by using bone marrow, kidney or even liver transplants. The increased understanding of immune mechanisms involved in organ rejection has greatly increased the ability to transplant these tissues and organs. In other cases, surgical repair of physical defects can be extremely effective treatment.<sup>20</sup>

**(vi) Immuno-Genetics**—Immunity is the ability of an individual to recognize the "self" molecules that make up one's own body and to distinguish them from such "non-self" molecules as those found in infectious micro-organisms and toxins. This process

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<sup>20</sup> *Britanica Encyclopaedia*, deluxe edition 2005.

has a prominent genetic component. Knowledge of the genetic and molecular basis of the mammalian immune system has increased in parallel with the explosive advances made in somatic cell and molecular genetics.

There are two major components of the immune system, both originating from the same precursor "stem" cells. The bursa component provides B lymphocytes—a class of white blood cells, when appropriately stimulated, differentiate into plasma cells. These latter cells produce circulating soluble proteins called antibodies or immunoglobulins. Antibodies are produced in response to substances called antigens, most of which are foreign proteins or polysaccharides. An antibody molecule can recognize a specific antigen, combine with it, and initiate its destruction. This so-called humoral immunity is accomplished through a complicated series of interactions with other molecules and cells. Some of these interactions are mediated by another group of lymphocytes, the T lymphocytes, which are derived from the thymus gland, once a B lymphocyte has been exposed to a specific antigen, it "remembers" the contact so that future exposure will cause an accelerated and magnified immune reaction. This is a manifestation of what has been called immunological memory.

The thymus component of the immune system centres on the thymus, derived T lymphocytes. In addition to regulating the B cells in producing humoral immunity, the T cells also directly attack cells that display foreign antigens. This process, called cellular immunity, is of great importance in protecting the body against a variety of viruses as well as cancer cells. Cellular immunity is also the chief cause of the rejection of organ transplant. The T lymphocytes provide a complex network consisting of a series of helper cells (which are antigen specific), amplifier cells, suppressor cells and cytotoxic (killer) cells, all of which are important in immune regulation.<sup>21</sup>

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21 H. Hugh Funderberg et al; "*Basic Immuno Genetics*," 3<sup>rd</sup> edition (1984), a comprehensive technical discussion.

**(viii) The Genetics of Antibody Formation**—One of the central problems in understanding the genetics of the immune system has been in explaining the genetic regulation of antibody production. Immunobiologists have demonstrated that the system can produce over 1,00,000 specific antibodies, each corresponding to a particular antigen. It would be difficult to envisage that each antibody is encoded by a separate gene—such an arrangement would require a disproportionate share of the entire human genome. Recombinant DNA analysis has illustrated the mechanisms by which a limited number of immunoglobulin genes can encode this vast number of antibodies.<sup>22</sup>

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22 Charles J. Epstein, et al Risk, (eds) "Communication and Decision Making in Genetic Counselling" (1979).

## Part-III: Comparison of *Karma* and *Genes*

## 12

## Comparative Study of *Karma* and the Science of Genetics

### 12.1 Correlation between *karma* and *genes*

In psychology, the difference between the living organism (*jīva*) and life is very specific. The study of *karma* theory makes the difference quite clear. Heredity is related to life, in the same way *karma* is related to *jīva*, in which all the *karmas* and reactions of so many pre-births are accumulated in the form of *karma śarīra*.<sup>1</sup> So the individual's ability and extraordinary talent based not only on present life, it can be traced out beyond it in the accumulated *karmas* bonded with *jīva* i.e. *karma śarīra*.<sup>2</sup>

Biology believes that the important component of the body is gene. It is the characteristic formula, it is very subtle. Its subtleness is merely a hypothesis. Where does our consciousness reside? Whether it is present in chromosomes or genes? That is why, so much difference is there from man to man. Everyone's self-exertion and consciousness are not the same. As per the doctrine of *karma*, the cause of this dissimilarity is due to "*karma*."<sup>3</sup>

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1 "Karmavāda," *Uvācārya sṛī Mahāprajña* (presently *Ācāryasṛī*), p. 237.

2 *Jo tullasāhaṇaṇī fale viśeṣe ṇa so viṇā heuṇī. Kajjatanāo Goyamā! Ghadotva heuṇya so kamma—viśeṣavāsyaka Bhāṣya.*

3 *Karmavāda*, p. 136.

Once Gandhara Gautama asked Lord Mahāvira:<sup>4</sup> *kammonan bhante jīve no akkammaō vibhakti bhavan pariṇamaī*. There appears dissimilarity in whole world, some possess less knowledge and the other possess more. What is the reason for this?

Mahāvira replied, "*Karma* is the cause of this dissimilarity."

If a biologist of today is asked this question, he will reply that the root cause of all dissimilarity is "gene." The characteristics of genes and chromosomes determine the human personality. His temperament and behaviour becomes the same as the genes are. This gene is responsible for all dissimilarities.<sup>5</sup> As per biology, every gene contains sixty lakhs orders in it. As per the doctrine of *karma*, on every *karma* particle written infinite instructions.<sup>6</sup>

Now science has reached only upto the genes. It is the component of physical body, but *karma* is the component of subtle body. Inside this physical body lies astral body—the electric body which is subtle and *karma śarīra* which is subtler than that; it is the subtlest. It's every part has infinite inscriptions. All records of our self-exertion, of goodness, of bad works, of limitations and of specialties are inscribed in the *karma* body. Man behave according to vibrations received from *karma śarīra*. The theory of *karma* is very subtle. It is the theory beyond the subtle intellect. Science of the genetics has helped us in understanding this theory of *karma*.

Genes are the transporters of heredity characteristics.<sup>7</sup> The difference, perceptible in every man, is due to the *genes*. For every special characteristic, a special type of gene exists. These laws of heredity are the messenger laws of *karmavāda*.<sup>8</sup>

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4 *Bhagavatī sūtra* 12/5.

5 *Karmavāda*, p. 137.

6 *Bhagavatī Sūtra*.

7 *Manovijñāna aura śikṣā*, 1960, p. 161.

8 *Karmavāda*, p. 164.

The travel from the physical body to the subtle body is very important in itself. This body is physical, and it is made of subtle biological cells. There are about 100 trillion cells in human body. If these cells are understood, according to the Jaina Philosophy, that at the point of a needle, infinite *nigoda jīvas* be accommodated there.<sup>9</sup> Nigoda is one of the species of vegetation. It is a subtle thing. But the present science also postulates many subtle concepts. There exist trillions of cells in our body, and they contain the chromosomes, and every chromosome is made of one-two thousand genes. There are 46 chromosomes in one cell in our body which are made of genes. Genes are very subtle.

If a comparative study is made—the heredity, genes and all the chemical changes all three are the doctrine of *karma*. Gene is the component of our physical body, and the *karma* is the component of our subtler body (*karma śarīra*). Both are related to the body. *Ācārya Mahāprajña* says that genes not only transport the traits of parents, but they also represent our bonded *karmas*.<sup>10</sup>

### 21.1.1 Parapsychology

The parapsychology comes closer to find the answer as to what is behind genes. They claim that we have an unconscious mind and a subconscious mind. As per Jainism, the unconscious mind is *karma śarīra* and the sub-conscious mind is *taijasa śarīra* (*leśya* and *bhāva* are produced by *taijasa śarīra*). They talk about things that are controlled by other than the senses. They talk about ESP (Extra Sensory Perception), telepathy (sending thoughts/feelings from one person to another), Clairvoyance (awakening of objects or things without the use of senses), pre-recognition (knowledge of future events) and psychokinesis (the power of mind over matter). *Avadhi jñāna* (knowledge limited by area, time and feelings), *manahparyava jñāna* (knowledge of other's thoughts) and *kevala jñāna* (perfect

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<sup>9</sup> *Bhagavatī Sūtra*.

<sup>10</sup> *Karmavāda*, p. 165.

knowledge), these three knowledges are not dependant on our senses and mind. *Karma śarīra* and its effect on our soul are behind every thing. Similarly, *karma śarīra* is behind genes also.<sup>11</sup>

Thirty-five years ago when the science of genetics was still in its infancy, in the West, my "God gene" (read spiritual hunger) became active and I found myself in India sitting at the feet of a great scholar (*Mahātmā*). His view of spiritual practice as a preparation for enlightenment was based on the idea of burning out or exhausting the traces of *karma* (read soul genes) that has accumulated in the causal body (read DNA). I don't know where the first references to the God gene appear in *Vedic* literature but the idea is, certainly, many thousand years old. The DNA that the West has been investigating and is meant to contain the "God gene" among others, is known as the *karma śarīra* or the causal body in *Vedantic* literature. It is called causal because, like the DNA, it is the cause of the psyche and the motivating force behind action. The genes themselves are referred to as *vāsanās* or *sanskāras*. The way the causal body manages the *vāsanās* is similar to the way the DNA is thought to manage the genes. The *Vāsanās* explain how psychic material passes through time, survives then death of the physical and comes to generate new life. The *Vāsanās* are responsible for psychological as well as physical traits. In fact, the search for the ultimate building blocks of life is a search for its cause. The *Vāsanās* are the genes for genes; they are the linke between non-material unmanifest consciousness (spirit or God in the West) called the source of life, and its subtlest manifestation, the DNA which contains the *genes*. Although it has discovered the DNA and its genetic material the Western science will discover the *vāsanās*, except by inference because its epistemology is ultimately based on sense data; the *vasanas* are much subtler than the senses.<sup>12</sup>

India's reputation as the world's super power is well deserved. Long before the 'West,' as we know it, embarked on the enquiry into

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11 Website : [www.Jainism.com](http://www.Jainism.com)—doctrine of *karma*, p. 82.

12 The "God-gene" article from "Time Magazine" November, 2004, p. 2.

the nature of the material world, that is the modern science, the Vedic seers had developed a method called "yoga" that allowed them to transcend the mind and, therefore, observed extremely subtle phenomena that the senses cannot record. As a result, they were able to understand the DNA and the genes. In spite of its success in understanding the material world, the Western science is burdened with an undeserved proud regarding its achievements. It would not take kindly to the idea that another civilization on it regards as primitive owing to its lack of water seal toilets and other material amenities could have understood something as subtle and important as genetics, not to mention the science of God, long before it even existed.<sup>13</sup>

The limitations of the experimental scientific approach to God are evident in geneticist Dr. Hamer's statement, "I think we follow the basic law of nature, that we are a bunch of chemical reactions running around in a bag. Perhaps, but the real question is: What or who is the chemist? Because chemicals are insentient, they do not react on their own..... although they appear to do so. A conscious agent is required to make life. The very scientists who are investigating the DNA among other things are conscious beings and no instrument can validate their existence..... because it is self evident that human beings are conscious, it does not make a mirror to know that we have eyes eventhough the eyes cannot see themselves. And it is quite clear from simple observations that the creation too is conscious."<sup>14</sup>

The article considered other relevant research on the relationship between the functions of the brain and spiritual state (combination of soul and *karma śarīra*)—The deeper the people descend into meditation or prayer, the more active the frontal lobe and the limbic system become. The frontal lobe is the seat of concentration and attention: the limbic system is where powerful

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13 *Time magazine*, Nov., 2004, p. 6.

14 *Ibid*, p. 8.

feelings, including raptures, are processed. This is being done by specific genes. More revealing is the fact that at the same time these regions flash to life, another important region, the parietal lobe at the back of the brain—goes dim. It is this lobe that orients the individual in time and space. Take it offline and let the boundaries of the self fall away, creating the feeling of being at one with the universe. Combine that with what is going on in the other two lobes and you can put together a profound religious experience. The most interesting idea in this statement is the idea of taking a portion of brain offline. This is done by specific genes. All that is needed is to substitute the word mind or brain and this is fundamentally the same idea as that of a great 2<sup>nd</sup> century BCE Indian yogi Pātañjali "Yoga is the removal of the thoughts in the mind." He says it is taking the brain off line. "When you clear the mind," Pātañjali says, "the seer shines in all its glory." In other words, you have a profound religious experience. You can also have a profound religious experience without taking anything offline or removing the thoughts in mind. If consciousness is everywhere, informing everything in every second how unreasonable is it to assume that revelation (*Ākāśavāṇī*) is a daily and universal phenomenon.<sup>15</sup>

#### 12.1.2 THE HUMAN GENOME AND THE DOCTRINE OF KARMA

Scientists decoding the human genome may persuade us to re-examine our belief in fate, predestination, free will and the law of *karma*. Some genes, we are told, determine our mood swing. Some predispose us to diseases, some determine how faithful we are to our companions, while others the intensity of our spirituality. If genes predetermine our behaviour, if *karmic* destiny is encoded in our genes, do we have a choice?

What about free will? Are we to drift as a sailor on a stream without ever being able to change the course of our life? Dean Hamer, who is working on the 'spirituality gene', says that by

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<sup>15</sup> *Ibid*, p. 9.

exercising our free will, we could change the nature or quality of our genes. Through our effort, dormant genes could get activated. For example, creativity gene can lie dormant till a person is passed her middle age. At a later stage, one might have found time and suitable circumstances to activate her dormant creativity genes.

Similarly, the spirituality gene (VMAT2 or God gene) gets activated when a person feels inner need for God and devotes himself\herself whole heartedly to spiritual pursuits. When young Vivekananda requested Ramakrishna to pursued Goddess Kali to give him wealth, the sage advised him to ask the goddess directly. Facing the goddess, Vivekananda asked for wisdom and enlightenment instead. What could have promoted the young man to desire enlightenment and not wealth? In the light of genomic findings, we may see that he was promoted to do so by the spirituality gene.<sup>16</sup>

### 12.1.3 KARMA PLAYS ROLE THROUGH GENES

The scripture talks about the place of storage of *karmic* molecules too, and that place is incidentally not this physical body. The *jīva* comes to a mother's womb with its own bag and baggage, this alone can explain the existence of abnormally different indignations of child and parents. So no physical manipulation can really alter the inclinations (*karma*) of any *jīva*. Yes, the health of people can certainly be altered, and so far so good. Moreover, these genes themselves are a later manifestation in the beautiful process of creation, and they are basically meant to facilitate bringing about the ideal conditions of the *karmas* of a *jīva* to express and exhaust. Physical features and same such gross things are provided by the parents to the child, but the *jīva* comes in the womb with its own *karmas*. That alone is the reason why a *śūdrā* couple too can possibly have a child with the inclination of

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16 *The Times of India*—editorial article.

a *brāhmaṇa* or even a *kṣatriya*. If what was provided by parents alone draw the line within which this *jīva* lives and operates then such things could never have happened.<sup>17</sup>

Is there a possibility that the psycho-somatic effect of committing a sin or crime can cause an epigenetic change in a person and whatever the consequence of that change will get transmitted to his or her offspring? So far no scientific evidence can be provided for that possibility. Perhaps "*karma*" will prevail over dogma.<sup>18</sup> Such misperception of genetics sounds—strange as this might seem at first—like the common use of the Sanskrit term "*karma*" often defined as the "law of cause and effect." Both *karma* and genetics are frequently used to refer to something predestined fate. "But *karma* provides the situation, not the response to the situation," according to Śambhālā dictionary of Buddhism and Zen. Further under the title "*Karma*" in another book by the same publisher says; "Future conditions depend on what we do in the present, substitute "genetics" for "karma".<sup>19</sup>

#### 12.1.4 GENES ARE BECAUSE OF YOU AND NOT VICE-VERSA

The fundamental difference between the materialism and spirituality is that while the former believes that "matter" is the important thing and it controls our lives and its joys, the latter brings about a paradigm shift in our priorities and perceptions by passing the back of importance to an all pervasive, non-material conscious principle—the subjective essence of all. When the scriptures talk about this, the entire cosmos coming out of a spiritual essence. Which is your trueself, they in fact are saying that you are the creators of these very genes. Genes may be

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17 Vedānta article—"Mapping of Human Genome and the Possible Dangers of Karmic Manipulations"—by Swami Ātmānanda, *Vedānta Mission*, p. 1.

18 Dr. Sethuramaṇa Subramanian, subramaniansethu@hotmail.com published on 18-11-2003.

19 Website—www.scattletimes.com, escaping your genetics.

chemically made up of DNA molecules etc.—but are in this context clubbed under one genetic term, the "matter." They are comparable to seeds. They are the first perceptible manifestations in this beautiful process of the grossification of the great yet highly subtle, creative, self revealing, blissful existence which is continuously infolding itself—in a highly intelligent and orderly way. This is so called because the "spirit," or more approximately—the consciousness, is not a product of any chemistry, but it is the basic element of what they are. This consciousness is called a *Brahmana* by the *Upaniṣadas*, because from this alone everything has come, and into this alone goes back. That alone is the truth and the rest is an illusion, a mere continuum of time and space.<sup>20</sup>

The extract of Jaina Philosophy, in the form of formulas, has been given in "*Tattvārtha Sūtra*." If these formulas are analyzed in the light of cell, nucleus structure, *genes* and genetic codes provide us a new vision, and it clearly appears that *karma*, in one or the other way, is certainly attached to these controller units—the *genes*. Every cell has a nucleus, the nucleus possesses the chromosomes which are made of DNA.

The structure and function of body of every living being is according to their chromosomes. In conducting life, at every stage, protein of one or other type is necessarily required and its formation is only done by some specialized *genes*.<sup>21</sup> These *genes* are ever changing and this change is called "mutation." According to mutation, the changes happen in the characteristics of every living organism. In this way, all the activities of a creature, its destinies, its forms, according to the "Jaina Doctrine of karma," are decided by karmic particles (*karma*) and according

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20 *Vedānta article*—by Swami Atmananda.

21 Acārya Kakanandī—*Svatantratā ke Sūtra (Tattvārtha Sūtra with its annotation)*—*Dharma Darśana Sodha prakāśana*, Badota, 1992.

to biology, are decided by genes. According to this research work, *karmas* are the cause and genes are their effect (fruits). *Karmas* direct, instruct and motivate genetic codes and *genes* to function and mutate accordingly.

Every creature gets the different types of body according to its bonded *karmas*. It is only due to the consequences of *karmas*, one is born blind, sans intellect, some remains dwarf (short structured) and other is quite tall, some is born with fair and the other with dark complexion, and these are all done by the *genes*. Only due to the *genes*, the structure of the body of creature takes place and certain *genes* also decide the gender of a living being like man, woman or eunuch. The fundamental compounds of genetic code—glucose, phosphate and alkalines finally having in alliance with elements like nitrogen, carbon, hydrogen, oxygen, etc. and make the genetic codes. These elements pervade in our environment. This research work brings the possibilities that the invisible *Pudgalas* (*karmic* particles), i.e. the *karmas*, create the genes.<sup>22</sup>

## 12.2 Effect of *karma* over genes

### 12.2.1 PHYSICS AND KARMA

When the living organism performs the various activities, it attracts the *karmic* particles all around it. According to one theory of physics, all inert matters, due to their present heat, radiate the electromagnetic rays. When any creature (*jīva*) is attracted towards anything living (animate) or inert (inanimate) the living being (*jīva*) according to the intensity of his/her passions and yoga, adjusts clock frequency equal to the frequency of that thing, such condition is called the stage of attraction. In this state of intense attraction, the creature (*jīva*) and the matter (*pudgala*)

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22 Acārya Kānakanand ī—*Svatantratā ke Sūtra*.

exchange the highest form of power. When the waves having two different frequencies pass through any matter, its effect is marked in holograph form in that matter. Similarly, due to its attachment and aversion, the holograph is imprinted on the soul of creature (*jīva*) in positive or negative charge.<sup>23</sup>

Even the modern scientists have begun to believe the presence of invisible fine matter particles around human body. Those particles are *karmic* particles, i.e. *karma vargana*, which ultimately become *karma* when attracted by *jīva* due to its activities.<sup>24</sup> The way in which radioactive elements keep on radiating the rays for millions or billions of years very slowly. Similarly, the *karma* particles radiate special types of rays. It should be understood here that the changes in living beings (*jīva*) occur mainly due to these radiating rays.

#### 12.2.2 KARMA AND GENE

All the characteristics of every living organism are carried by its chromosomes in the form of genes. These chromosomes are packed in the cells and the body is formed by many cells put together. So in every cell similar type of genes exist, but at the same time it is necessary that some genes should remain inert and some active during a certain time. This process is very complex.<sup>25</sup> It is believed that in developed complex creatures (*jīvas*), during a certain time only, upto 2-15 per cent genes remain active.<sup>26</sup> How the various creatures (*jīvas*) function under whose control? This research work supposes that the creature's active or inactive state, the *karma* particles (*karma*) are the only cause for it.

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23 Jaina Jineswaradāsa—*Arhata Vacana* research magazine, p. 57-58.

24 Gangawāla mānika Candra *Arhata Vacana* research magazine, p. 61.

25 *Molecular Biology*—by P.K. Gupta, p. 50.

26 *Ibid*, p. 50.

Keeping the genes active or inactive is done by hormones, vitamins, minerals, chemicals and immune system.<sup>27</sup> It is believed that the genes are controlled by the environment around it, cell nutrition wrapped around the genes, and the temperature of the light.<sup>28</sup> Thus, genes are the deciding factors for the various characteristics of a living organism (*jīva*) and genes are controlled by some known or unknown causes and these causes are certainly the karmas of an individual.

### 12.2.3 CHANGE OF MODES, RE-BIRTH AND GENETIC CODES

The nucleus of cells and the existing chromosomes and the genes thereon (which are formed by meeting of genetic codes) control the various activities of the organism (*jīva*) and on these genes and genetic codes, the *karma* waves exercise its definite control and regulate the life. There is an interesting fact here that all big or small subtle creatures or plants contain the same genetic codes.<sup>29</sup> Thus, right from amoeba to man, the life deciding fundamental genetic codes are the same. So the theory of rebirth gets force from this principle of same genetic codes.

Perhaps the *karma* particles controlling the genetic codes regulate them for the next birth/modes and give them such a serial system that the soul migrate in search of further body, having left its own body. According to the *karma* reward, genetic codes and fate, soul reaches such a body and place and further develop it. This can be interpreted that *karma śarīra* of that nature is formed which can easily fit in such created genetic codes and the soul begins a new life in the new body. Again, having the genetic codes of a living being—a cow, a lion, an insect, a bird, or any form of creature can be created. So on the basis of the study

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<sup>27</sup> *Biology* XII (1), p. 857.

<sup>28</sup> *Ibid*, p. 260.

<sup>29</sup> *Ibid*, p. 69.

of biology, it appears that every control on the life of every creature is conducted by the genes and the genetic codes.

It is this *karma*-body, which perhaps controls the genes and gives favourable or unfavourable results and decides the forthcoming body. If this hypothesis is tested in a laboratory, it will be found that man's thoughts and actions attract such atoms around him which further give him happy or tragic results. Telepathy and Reiki therapies have given such results. Through these therapies, one man's thoughts are conveyed to the other man and affect the other man to a great extent. Research done in this direction will be able to prove this biological hypothesis. This theory will help us lead a happy, contented and balanced life and a new happy contented society will come into existence.<sup>30</sup>

One germplasm contains many chromosomes. These chromosomes have genes. In fact, only the genes are the messengers of virtues and vices, they are the cause of virtues and vices. According to genetics, every embryo contains 23 chromosomes of father and 23 chromosomes of mother.<sup>31</sup> The biologists guess that due to the meeting of these all chromosomes-16, 77, 216 kinds of various similarities are expected.<sup>32</sup> Till now the science of genetics has reached only upto genes. It is one of the component units of this gross body, on the other hand, karma is one of the component of our subtle body. Inside this gross body (sthūla śarīra) resides the astral body (taijasa śarīra). The more subtle is the karma body, and it is the most subtle body.<sup>33</sup> At every limb of this most subtle body is written the account of our self-exertion of our virtues and vices, of our limitations and of our reactions. The human starts behaving according to the vibrations coming from karma śarīra. Ācārya

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30 *Jaina Karma Theory of Biological Hypothesis*—by Ajit Jain "Jalaj"—*Arhata Vacana Research Magazine*, July, 99, p. 17-22.

31 *Ibid*, p. 161.

32 *Ibid*, p. 161.

33 *Karmavāda, Ācārya Mahāprajña*, p. 137.

Mahāprajña writes, "the genes not only bears the genetic traits of its parents, but these also represent the karmas performed by the individual."<sup>34</sup>

One scholar tells us that the controlling elements of our body have been found out and it seems to be a great achievement. Today, through the genetic mapping, all the genes have been found out which control the various states of our traits. We have also discovered all the sequences of genes set up, and everyday new researches in this field are revealing new knowledge about the genes. A group of researches led by Paul Thomasan of the University of California of Los Angles has given clear evidence that intelligence is largely determined before birth.<sup>35</sup> Still the whole puzzle, regarding all the traits of human beings, has not been fully solved. But the Jaina *karma* theory—describes elaborately about the *karma* particles—and these *karma* particles determine not only the characteristics of the body of *jīva* but also its happiness, sorrow, perception, age and *gotra* are also decided.<sup>36</sup>

Thus, the genes and genetic codes to which the scientists are considering supreme of all are the only particles functioning under the *karma vargaṇās*. It requires a great research because while science has stopped only on body characteristics, on the other hand, the doctrine of *karma* has gone far ahead of it. Genetic science states that they have found out only those atoms which determine our characteristics, but the doctrine of *karma* goes upto the *kārmaṇa* body and describes many more characteristics. The doctrine of *karma* also describes how *āśrava*

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34 *Jaina karma siddhanta and manovijñāna*—Ratanlāla Jaina—*Arhata Vacana Sodha Patrika*, July, 1997, p. 35-45.

35 *Invention of Intelligence*—Sept. Oct., 2002, N.R.D.C. 20-22, Kailasa Colony Extension, New Delhi.

36 *Addho jñāna-darśanavarṇa vedanīya mohanīya yurnāma gotrantarāyan*—*Tattvārtha Sūtra* Tika, Acārya Kakanandī (1992) *Dharma Darśana Bodha Prakāśanaḥ*, Badota (meerut), p. 476.

*karma* sticks to soul and how *āsṛava* can be detached from soul. It also says that the unwholesome *karmas* can be removed by austerities and the state of joy can be achieved.<sup>37</sup>

It is sure that mental as well as intellectual merits of genes are necessarily affected by a man's prebirth internal state, i.e. nature, and also by the after-birth, outer environment such as air, temperature, light, moisture, nutrition, etc., i.e. nurture.<sup>38</sup> If two identical twins are kept separately in the outer environmental conditions, their body structure, their personality and mental characteristics will greatly differ from each other. Whereas both have the same genome structure and similar development of the embryo. These two identical twins, in spite of having similar internal and outer environment, their original form will differ. These factors clearly indicate towards *karma*—the controlling factors and existence of soul. After a thorough research of Jaina Theory of *Karma*, the described consequences may be achieved.<sup>39</sup>

#### 12.2.4 THE SCIENTIFIC COMMUNISTIC THOUGHT OF JAINISM

According to the modern anatomy, all creatures have the same genetic codes—fundamental building blocks of life.<sup>40</sup> It is only due to the mutation of the genetic codes, different types of species of creatures—right from amiba to man, take birth. Thus, the doctrine of Jaina *karma* believes that all the *jīvas* are possessed with similar soul and similar capacities but their different *karmas* provide them different bodies.<sup>41</sup>

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37 *Ādhunika Vijñāna ka Sāpekṣa Karmavāda*—Ajit Kumar Jain "Jalaj"—*Arhata Vacana*, Jan.-March, 2005, p. 59-64.

38 *Srivastava, Nirupamā*—A Blind Rush of Human Cloning—*Vijñāna Pragati*, March 2004, C.S.I.R., Dr. K.R. Krishna Marg, New Delhi, p. 13-12.

39 *Srivastava, Nirupamā*—as above.

40 *Cytology Genetics and Plants Breeding*—molecular biology, p. 69.

41 Ajit Jain 'Jalaj', *Jīvana kā Vikasa tathā Jaina Siddhanta*, *Arhata Vacana*, p. 3.

First of all, it should be made clear that every incident does not occur only due to *karma*. *Karmas* are not all in all. If we believe that whatever happens is subject to *karmas* only, it will be such an explanation that the thiest (believer in God) says that every thing happens only due to the command of God or all that happens is subject to fate (fate or pre-destined), we cannot introduce any change. If *karma* is believed to be all in all, there will be no room for self-exertion to eliminate them nor there will be any possibility for achieving salvation (*mokṣa*), because—as the *karmas* are done, so do they rise and reward the doer, and he or she will act according to them and bear further bondage of *karmas*. If it is so, then the thought of self-exertion and salvation will prove wrong. Thus, it is proved that *karmas* are not all in all.

*Karma* is not an autocratic dominion. It has also a check on it. Changes can be made in *karmas*. Lord Mahāvīra says, "performed *karma* will give its fruits," is a general principle, but there is an exception to it. In *karmas*, *Udīrṇā* (to attract premature *karma*), *Udvartana* (lengthening of *karma* period), *Apavartana* (shortening of *karma* period) and *sankramaṇa* (changing nature of *karma*) all these stages are possible, and changes can be introduced in the *karmas*. Thus, we can say that due to self-exertion eradication of *karmas* can be done even before their maturity. Their duration and intensity can be minimized or maximized and one nature of *karma* can be changed with other subgroup of the same nature. The *karma* which has come in rising, their reward can be subsided for a time, they can be made incapable for a certain period in their reward. This process is called "*upaśama*."

According to Ācārya Mahāprajña "The theory of *sankramaṇa*," is the theory of mutation of gene. One important thing worth paying attention is that the rise of *karma* takes place according to substance, area, time, mode and state of living being. This rise depend upon medium and rewards accordingly. Let the pain-causing *karma* rise at the same time in two different persons, and one person listens to

the religious sermons and devotional songs, the other one is kept in a closed room doing nothing. The pain causing *karma* will cause more pain to the second person in comparison to the first person who spends his time in listening to the religious sermons and devotional songs. There is a psychological reason of it also.<sup>42</sup>

Thus, we reach the conclusion considering all the above facts that in building personality, *karma* is not all in all, but heredity, environment, geographical location and ecological conditions all effect nature and behaviour of man. *Nāma karmas* are not all in all. In facial and body formation of man, effect of the place and time can easily be perceptible on human physique. If two children are born to a mother—the one in some cold country and the other in some hot country, the child born in a cold country can comparatively be more fair than the other child. If some person begins to live in a cold country, his complexion will change. According to Ācārya Mahāprajña, the change of genes and the chemical changes bring change in human personality.

*Āyusya karma* is also a *karma*. But the outer mediums like poison etc. can minimize life span of a creature. Similarly, if some change is made in chromosomes and genes, a person's physique can be changed. Thus *nāma karma* alone does not decide human physique but environmental conditions can bring change in human physique. If we produce carbon copy of donor parent (i.e. clone) by changing nucleus of the cell by a special scientific method, the theory of *karma* is not violated because *Sankramaṇa* is possible in *karmas*.<sup>43</sup>

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42 *Karmavāda—Yuvācārya Mahāprajña* (presently Ācārya Mahāprajña), *Ādarśa sahitya saṅgha, Chūrū* (Raj.) second edition, p. 102.

43 *Cloning and Karma Theory*—by Dr. Anil kumar Jain, *Arhata Vacana*, July, 99, p. 9-15.

### 12.3 Spirituality (combination of spirit and *karma śarīra*) and genes

The advantage we have today is that our understanding of genes is growing so quickly. Understanding of genes does not mean resigning ourselves to some programmed fate. This is a tool for liberation, a scientific window into the soul. Yes, we are born with a certain genetic make up. No, that does not mean we have no control over our lives. Neither scientists, nor observant parents, really believe we are born as completely blank states to be filled in by our upbringing. The key is the interplay between the hardware we are born with and the software we add. It is not nature or nurture. It is both nature and nurture. In fact, it is part of our nature to respond to nurture.<sup>44</sup>

The essence of spirituality, which can include a belief in God or higher power or a divine order of the universe, is looking inward, searching for meaning and purpose, and seeking to understand what truly matters. People turn away from materialism in search of inner peace, through identification with God or with the cosmos. Is spirituality simply an adaptive response, a self deception to deal with old age, infirmity and death? Or is it wisdom, a gradual realization of the real truth about the universe? A scientist might wonder whether spirituality was not written into our genetic codes. Perhaps, as the body begins to expire, the brain wires a new set of neuronal connections in the cerebral cortex that allows us to accept the end with grace, dignity and even hope. On the other hand, this may be a lot of mumbo jumbo, a far too clinical explanation for what we know as the soul with subtle body (*karma śarīra*).

Prominent geneticist, Cloninger found another thing that seems to increase with aging: spirituality. Not only that, but spiritual people are relatively more likely to express warmth,

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44 Rose, Richard J. "Genes and Human Behaviour" *Annual Review of Psychology*, 46, 625- 54, 1995.

altruism, positive emotions and openness to feelings. They are relatively more intimate and friendly, they are generous, and concerned with the welfare of others. They also tend to be more optimistic about life and more likely to experience positive emotions such as love and happiness. Above all, spiritual people are open to their own inner feelings and emotions. They experience happiness and joy—as well as pain and suffering—with heightened intensity.<sup>45</sup>

### 12.3.1 THE GOD GENE THEORY

Why is spirituality such a powerful and universal force? Why do so many people believe in things they cannot see, smell, taste, hear or touch? Why do people from all walks of life, around the globe, regardless of their religious backgrounds or the particular God they worship, value spirituality as much as, or more than pleasure, power or wealth? It is argued that the answer is hardwired into our genes. Spirituality is one of our basic human inheritances. It is, in fact, an instinct.

The reason a sparrow sings the song of a sparrow, and not of a robin or a lark, is that it has the genes and brain of sparrow, not that it was raised by sparrow. Moreover, there is a dedicated brain circuit for song. In the God gene, it is proposed that spirituality has a biological mechanism akin to bird song, albeit a far more complex and nuanced one: that we have a genetic predisposition for spiritual belief that is expressed in response to, and shaped by, personal experience and the cultural environment. These genes act by influencing the brain's capability for various types and forms of consciousness, which become the basis for spiritual experiences.

The first task for any scientist attempting to link genetics to spirituality is to show that spirituality can be defined and

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45 Pomm R., J.R. Nesselrode, "Genetic influence on Life Events During the Last half of the Life span." *Psychology and Aging* 5, 25-30, 1990.

quantified. This is essential for any scientific analysis, regardless of the topic. Scientists measure things. If we cannot measure it, we cannot test a hypothesis about it, and if we cannot test a hypothesis about it, it cannot be proved. Our major new finding revealed in "The God *gene*" is our discovery of a scientific individual gene associated with the self transcendence scale of spirituality. This "God *gene*" codes for a monoamine transporter—a protein that controls the amount of crucial brain signaling chemicals. Interestingly, those same brain chemicals can be triggered by certain drugs that can bring about mystical like experiences.

The specific gene (God gene) identified the entire story behind spirituality. It plays only a small, if key, role; many other *genes* and environmental factors also are involved. Nevertheless, the gene is important because it points out the mechanism by which spirituality is manifested in the brain. One of the important roles that God genes play in natural selection is to provide human beings with an innate sense of optimism. At the psychological level, optimism is the will to keep on living and procreating, despite the fact that death is ultimately inevitable. At the physical level, studies show that optimism seems to promote better health and quicker recovery from disease, advantages that it would help us live long enough to have and raise children and pass on our genetic heritage.<sup>46</sup>

### 12.3.2 SELF TRANSCENDENCE AND GENES

Of course statics alone cannot tell us what that common root is. It could be the result of a gene. But it could equally well be the result of an environment or culture. Self transcendence is, so far, the simplest way we have to measure spirituality. One reason for confirming the validity of the self-transcendence scale was that we wanted to measure individual differences in spirituality and correlate them with genes. It was also important, however, to know

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46 "The God *Gene*"—by Dean Hamer—Anchor Books—A division of Random House, Inc., New York (U.S.A.), first edition September, 2005, p. 6-12.

if there were any group differences in the scale, because these would complicate and possibly compromise the genetic analysis. Our data base of 1388 subjects allowed us to examine the relationship between self transcendence and three potentially important demographic variances—race, age and gender.

A statical analysis showed that the higher scores of women could not be accounted for any of the other personality factors we measured. It might be something to do with the fact that women are more willing to express their feelings than men or perhaps there is something about our society that brings out the spirituality in women. Or it might have something to do with their genes, a possibility we would later have a chance to test experimentally. Although statistics cannot tell us what spirituality is or is not, or where it comes from, it can help measure spirituality in individual and conform its uniqueness. In a study of the connection between genes and spirituality, that is a good place to start.<sup>47</sup>

Unlike most young children, Jane and Rose loved going to church, not just on Sunday but during the week as well. They both decided as teenagers to devote their lives to the church and took their vows together. Sister Jane Frances and Sister Rose Marie are nuns at the same convent in Akron, Ohio. In addition to their mutual interest in God and spirituality, Jane and Rose have another important similarity: their DNA. They are identical twins—the product of the same fertilized egg. Twins, especially identical ones like Jane and Rose are fascinating. There is something mysterious and alluring about people who look and sound identical. But identical twins are more than curiosities. Because they share identical DNA, for scientists they offer a way to dissect the role of genes and environment in complex human characteristics like spirituality.

The main use of twins in behaviour genetics research is to determine heritability, which is defined as the percentage of

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47 Maslow A.H., "The Core Religious or Transcendent Experience—the Highest State of Cconsciousness," Garden City N.V. Anchor, 1972.

variation in a behaviour that is due to genetic differences. Heritability can most directly be measured by comparing identical twins who were separated at birth and raised apart. Because such twins have the same genes but are raised in different environments, the extent to which they are similar to each other is a direct approximation of heritability. The degree of similarity can be calculated as a correlation.

The result of their study were consistent, for every scale examined, genes seemed to play an important part. The calculated heritabilities were all between 41 and 52 per cent, meaning that genes were responsible for roughly half of the variation in religious belief from one twin to next. In other words, the study seemed to suggest that at least part of the reason people believe that religion can help answer life's questions in their DNA.<sup>48</sup> In other words, nearly half of the reason that the twins felt religion helped them, spent time privately praying and head a sense of God's presence was inherited. Since these twins were raised by different parents, in different neighbourhoods, and sometimes even in different religions, their similarities seemed to be the result of their DNA rather than their environment. Something in their genes helped push them towards religion.

How did the researchers conduct their studies? First they evaluated the data, using a modelling technique that took into account three main sources of variation in self transcendence: genetic influences and shared environmental influences. The first two factors make twins alike, the third makes them different. The analysis indicated that genes are responsible for 48 per cent of the variation in self transcendence in twins, both male and female. The remaining 52 per cent of variance was due to environmental factors for females. Age also had an effect, in

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48 Kirk, K.M., N.C. martin—"Self Transcendence as a Measure of Spirituality in a Sample of Twins," *Twin Research* 2, 81-87, 1999.

males it accounted for four per cent of variance (environmental factors accounted for the other 48 per cent). The researchers also examined the data by a statistical technique called "multivariate modelling." Once again, they found that genes played an important role in self-transcendence.

Using this analysis, the estimated heritabilities were 37 per cent for men and 41 per cent for women, which are similar to the numbers obtained in the first analysis. The take home lesson from the Martin and Evas study was clear: genes are a major factor in self transcendence. In other words, spirituality is in good measure an inherited trait. This was a surprising result. The implication is that spirituality, at least as measured by self transcendence, does not result from outside influences. Contrary to what many people might believe, children don't learn to be spiritual from their parents, teachers, priests, imams, ministers or rabbis, nor from their culture or society. All of these influences are equally shared by identical and fraternal twins who are raised together, and yet the two types of twins are strikingly dissimilar in the extent to which they correlate for self transcendence. In other words, William James was right: spirituality comes from within. The kernel must be there from the start. It must be part of their genes.<sup>49</sup>

Maslow, Cloninger and many others before them and since have argued that spirituality and religiousness are fundamentally different. The twins studies, by looking quantitatively at both qualities in a single population, strongly support and distinction. More important, they tell us something about why they differ. Religiousness as measured by church attendance is learned in the classical sense—from parents, teachers, religious leaders and seers. People go to the Church or mosque or temple because that is what they were told to do?

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49 Wright, L. *Twins and What They Tell us About Who We are?* New York John Wiley and Sons Inc. 1997.

Spirituality, as measured by self transcendence, is more innate. It comes from within, not from without. Of course, spirituality has to be developed, just like any other talent. But the evidence suggests the predisposition is there from the beginning.

What makes some siblings, like Tenkai and his brother, so spirituality dissimilar despite their common upbringing? And what makes others, like Gloria and Louise, so similar despite their very different life trajectories? Could it be something in their genes? There was only one way to find out.<sup>50</sup>

The first gene on the list of candidates was D4DR, which codes for a receptor that senses the presence of dopamine, one of the monoamines in the brain. It was a prime suspect for several reasons. In Comings' study, dopamine was the neurochemical most strongly associated with self transcendence of all those examined. Comings speculated that this was because the D4DR gene contains an extremely variable repeated DNA sequence that changes the number of amino acids in the protein, which in turn alters the way it works in the brain. Some people have only three copies of this odd sequence: others have as many as eleven copies. D4DR's high association with self transcendence might also be because it is expressed both in the limbic system of the brain—the seat of emotions—and the prefrontal region of cortex—the thinking part of the brain. Moreover, this gene has previously been linked to novelty seeking, a personality trait that is slightly correlated with self transcendence.

There was a clear association between the VMAT2 (on chromosome 10) polymorphism and self transcendence. Individuals with A and C in their DNA—on either of the chromosome or both scored significantly higher than those with an A. The effect was greatest on the overall self-transcendence scale and was also significant for the self-forgetfulness subscale.

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50 Waller, N.G., A—Tellegen—"A study of twins reared apart and together" *A psycho social*, 138-42, 1990.

With transpersonal identification and mysticism, the effect was in the same direction but just short of statistical significance. Somehow, this single base change was effecting every facet of self-transcendence, from loving nature to loving God, from feeling at one with the universe to being willing to sacrifice for its improvement. To delve further into the biology of spirituality, we need to understand more about how monoamines work normally in the brain to produce the greatest hat-trick of biology—consciousness.<sup>51</sup>

### 12.3.3 CONSCIOUSNESS AND GENES

Our brains are bombarded with information every second of every minute of the day, day in and day out. There is the data we receive from the outside world through our senses: sights, sounds, smells, tastes and touches. And then there is the news that one part of the brain receives from other parts of the brain: memories, feelings, thoughts and dreams. This is the consciousness or awareness of our surroundings and ourselves. It is at once both the common place and the most mysterious of all life processes.

Our aspect of consciousness has puzzled philosophers, theologians, metaphysicists, psychologists and biologists for centuries and probably will continue to do so for many years. Sometimes called the mind-body problem, it boils down to this: Can consciousness (soul or spirit) be explained scientifically? Rene Descartes, "I think therefore I am"—who believed that the mind and the body are distinct substances that communicate through the pineal gland, which he believed was the seat of the soul. By a scientific explanation i.e. one that can be expressed in terms of the basic principles of chemistry and physics, proponents of this view are often called "materialists" because they believed that all mental processes can ultimately be

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51 Joseph, R. "The Transmitter to God, The Limbic System, the Soul and Spirituality" San Jose, CA, University Press California, 2001.

accounted for a few basic physical laws. Most scientists are materialists.

Other thinkers simply proclaim that the origin of consciousness is too difficult to be solved with our present knowledge. So far so good for scientist Edelman's theory: Consciousness links the physical senses to the emotions through widely distributed brain networks. But that still leaves the critical question of how those emotions are generated, what is that actually makes us feel happy, sad, excited or anxious? This is where the monoamines and the VMAT2 gene comes to the fore. The monoamines are the biochemical mediators of emotions and values. They are what make us feel. But monoamines are not freely available to the brain, like a gift, they first need to be wrapped up and unwrapped. That is where the VMAT2 gene plays a critical role.

Wrapping up the monoamines is a hard work. This is where the vesicular monoamine transporter encoded by VMAT2 enters the picture. The VMAT2 transporter is a long, snakelike molecule that weaves in and out of the vesicular membrane. The head and tail of VMAT2 are both securely tucked inside the vesicle. The body crosses the membrane twelve times to form six coils running from inside to outside and vice versa. At each juncture with the membrane there is a trans-membrane helix, a tight spiral of amino acids that fits perfectly into its slippery, greasy oil, once the monoamines are packed into the vesicle, they sit there, completely shielded by the vesicular membrane, waiting for something to happen.

Like Ari, Tomas is under the influence of monoaminergic drug, in this case cocaine. Cocaine releases dopamine, the brain's reward chemicals. Although dopamine and serotonin are chemically similar, there are big differences in what they do. Dopamine makes people feel good rather than bad, sociable rather than hostile. If serotonin is the brain's stick, dopamine is its carrot. How could such a temporary change in brain

chemistry have such long lasting consequences? It is because the psilocybin made Young question the one thing that he, like all of us, depends on most in life: his consciousness. Without consciousness, there would be no life as we know it. We would not know who we are or where we are going? Yet we take our consciousness for granted. It is automatic and effortless like breathing. Only when it suddenly stops working and goes haywire do we realize what an incredible gift it is!

The integration between primary and higher consciousness allows us to remember the present. And this is where VMAT2 enters the picture. VMAT2 controls the flow of monoamines within the brain.<sup>52</sup> As the Buddhist meditate, they consciously attempt to clear their minds of thoughts and emotions. To do so, they send signals through the thalamus to the cortex, the seat of will. As more and more of the brain's energy is directed towards this area, output to other region is decreased through the process that the neurobiologists call deaf fermentation. It would be like simultaneously turning on all the air conditioners in a house; the flow of power to the other appliances would be decreased.

Based on this experiment and other lines of evidence, Persinger believes that the biological basis of all spiritual and mystical experience is due to the spontaneous firing of the temporo-parietal region—highly focal microseizures, without any obvious motor effects. He calls such episodes transient and theorizes that they occur in everybody to some extent. Exactly, how often and how strongly is determined by a mix of genes, environment and experience. The main effect of such transients is to increase communication between the right and left temporoparietal areas, leading to a confusion between the sense of self and the sense of others. The outcome, he says, is a sense of presence that people interpret as a God, spirit or other mystical

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52 Kaori, G.R. Uhi—"Heterozy go us VMAT2 Knockout Mice Display Prolonged QT Intervals"—*Mol brain Res.* 71, 354-57, 1999.

being. That is why, feelings of spirituality are a matter of emotions rather than intellect. No book or sermon can teach one person to use a different monoamine transporter or another to ignore the signals emanating from his limbic system. It is our genetic make up that helps determine how spiritual we are. We don't know God, we feel Him.

Where did "God gene" come from? At first that might seem like a question of faith or philosophy rather than science. But the actual answer is quite obvious. They came from our parents. Who inherited them from their ancestors. Those ancestors received them from their predecessors, and so on down the evolutionary line to the very beginnings of life on earth, over the ages, of course, the genes evolved. At every step, the genes that helped their owners survive and reproduce were most likely to be passed on to the next generation. Genes that do not successfully accomplish this do not survive in succeeding generations. If the organism, in which such genes resided, did not have offsprings, the genes would soon be lost from the population, discarded in the dustbin of failed evolutionary experiments. Only the genes that promoted our post survival and reproduction are still with us today.<sup>53</sup>

The scientific method, of course, is based on observation, experimentation and replication—methods that exclude most religious phenomena from consideration. There is no way for objectively test, for example, whether the consciousness continues after death or whether God listens to our prayers there is no MRI or CAT scan for the human soul. It is, therefore, not surprising that many scientists regard religion with suspicion. First, it is essential to realize that there is nothing intrinsically theistic or atheistic about postulating a specific genetic and biochemical mechanism for spirituality. If God does exist, he

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53 Alper, M. "The "God" Part of the Brain, A Scientific Interpretation of Human Spirituality and God." Brooklyn, New York, Rouge Press 2000.

would need a way for us to recognize his presence. Indeed, many religious believers have interpreted the brain scan experiments of Persinger. Ramchandran and Newberg supporting the existence of deity ask, "Why else would we have a 'God module' prewired in the brain?" Science can tell us whether there are God genes but not there is a God. Spiritual experiences, like all experiences, must at some level be interpreted by biologically constructed brains.

The experiment implies that it is possible to strengthen one's sense of spirituality by practising it—an idea that has been stressed by every great spiritual leader from Buddha to Gandhi from Muhammad to Martin Lutherea King Jr., from Jesus to Bishop Ruisa. We have no say over the exact group of genes that we inherit; whether we have A, C or an A at the critical position in VMAT2 (God gene), the genes of a Tenkai or of a Hainnibal Lecter is purely a matter of chance. What we do with our spiritual genes, however, is very much upto us. Spirituality is based on consciousness, religion in cognition. Spirituality is universal, where, as cultures have their own forms of religion. It is argued that the most important contrast is that spirituality is genetic while religion is based on culture, traditions, beliefs and ideas. It is, in other words, mimetic. This is one reason why spirituality and religion have such differing impacts on individual life and society.

The idea that spirituality is inherited is not new. A Tungus Shaman cited in Joseph Campbell's *The Masks of God* says, "A person cannot become a sharman if there have been no sharmans in his sib." As we have seen from twin studies, self-transcendence, a quantifiable measure of spirituality, is partially inherited. At least one of the **God gene VMAT2**, appears to code for a protein that controls the ebb and flow of monoamines, brain chemicals that play a key role in emotions and consciousness.

The fact that spirituality has a genetic component implies that evolved for a purpose. No matter how selfish a gene is, it still needs a human being as a carrier to perpetuate itself. There is now reasonable evidence that spirituality is, in fact, beneficial to our physical as well as mental health. Faith may not only make people feel better, it may actually make them better people. Are we condemned to endlessly repeat the said mistakes of the past? It is believed that understanding the difference between spirituality and religion gives us another tool in offering hope for the future. For, while our spirituality may be engraved to a degree in our DNA, we can change, reinterpret and reconsider the impressions written on the scrolls of our religious history.<sup>54</sup>

## 12.4 Life and genes

Where there is soul and *karma śarīra*, life will take birth. Every living organism is built of a number of cells. Where there is cell, means life is there. A cell is made up of genes. That means, where there are genes, life is there. Soul generates life with the help of *karma śarīra*. *Karma śarīra* plays its role in the gross body of a living organism with the help of genes only. Thus, we can say life is a composite building up of soul, *karma* and genes. Without the soul, *karma* and genes cannot survive more in gross body of living beings and vice-versa. Thus, life cannot be survived without the common efforts of *karma* and genes. So we should compare life with genes, i.e. to compare *karma* with genes.

### 12.4.1 THINKING (INHERITING INTELLIGENCE) AND GENES

The brain begins with genes. Genes, from both parents, combine to design and create the lump of gray flesh in the head, plus the rest of the body, which operates and is operated by the brain. The slightest disruption in the physical development of brain can

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54 Polkinghorne, J. "Belief in God in an Age of Science" New Haven, Yale University Press, 1998.

have a devastating effect on future intelligence. A single glitch in the DNA code can limit mental development or cause severe retardation. On the other hand, "good" genes make the birth of genius possible. There is no single factor more important in an adult's IQ score than genes. However, parents also pass along the environment in which the genes are expressed. What we think about, the language we think in, and how we apply our intelligence, are all products of the environment; how we will think depends very much on that original set of blue prints from the genes. Just like a person who hops into a car decides where to go and how to get there, the car sets limit on how fast and how successfully.

Short term memory is similar to the random access memory (RAM) on a computer; it controls the information needed to run at any given moment. Long term memory is like the hard drive, a repository for all the information needed to operate. Just a computer needs both the RAM and a hard drive, so both short term and long term memory are essential for intelligence. For example, adding the numbers 349 and 217 requires long term memory to remember the rules of addition, and short term memory to execute the specific problem. Memory itself is so in control to the thinking process that memory is one of the best predictors of human intelligence as measured by IQ tests.

There are two basic types of memory: short term and long term. Short term memory, also known as working memory, operates over seconds where as long term memory lasts for minutes to an entire life. If you hear a random telephone number 441-9620, you might remember it until the end of the sentence, probably not until the end of the paragraph. Your own telephone number, however, is securely stored and easily remembered. The reason is that the random telephone number went into short term memory only, because there was no reason to save it, while your own number is stored in a personal long term vault.

How is information in short-term memory converted into long term memory? It must be a selective process. Otherwise, long term memory would soon be swamped with useless information such as restaurant menus, road signs and old TV guides. It would be like the hard drive of a computer that stores every revision of every document, or a radio that records every song. The machinery would soon be filled up with useless, disorganized information, somehow the brain must have a filter to sieve out what needs to be remembered from what can be discarded.

The filter is a physical structure built by genes. It was discovered by studying a simple invertebrate, the sea slug *Aplysia*. Sea slugs hardly have a brain, and they probably could not pass the bar exam, but they do have a nervous system and are able to 'remember' simple stimuli and respond accordingly, one of the best studied responses is the gill withdrawal reflex. When the gill of a sea slug is touched, the body withdraws into its shell; presumably the touch is a warning that a predator may be nearby. But if the gill is touched repeatedly, the withdrawal response slows down or disappears, as if the sea slug knows that it has nothing to fear. To the extent that intelligence is the ability to adopt behaviour to the environment, the sea slug shows a primitive form of intelligence.

Scientist Eric Kandel wanted to know how the sea slug adopts its response. The first step was to recreate the reflex without the sea slug, using isolated nerve cells grown in a petri plate. By recording the electrical signals between nerve cells, Kandel found that after a single stimulus there is a strong electrical signal at the synapse between nerve cells, but as the stimulus is repeated, the strength of synaptic connection decreases. The nerve cells are "remembering" their past, Kandel showed that the nerve cell 'remembers' by synthesizing a burst of proteins and that the key activator of this explosion of gene expression is a protein called CREB. Kandel proved that the nerve cells could be fooled into

thinking they had been stimulated simply by adjusting the amount of active CREB protein.

Geneticist Tully established three things: flies, just like humans, have two forms of memory, short term and long term; short term memory is required to learn the difference between odors, where as long term memory is required to remember the difference and behave accordingly: and that converting short term memory into long term memory requires new gene expression. But what genes were turning on? Taking a clue from Kandel's work on sea slugs, Tully decided to look at the CREB mechanism. The part of the brain responsible is the hippo campus which makes a mental map in minutes and stores it for weeks. Later, if it is an important map, the information is transferred to the cerebral cortex for long term storage. A damaged hippocampus, as can occur from injury or stoke, would prevent a person from finding his way out of a new room, even though he could remember the layout of a place he had lived long before.

Even though the loss of single gene can prevent a mouse from finding its way, the thought process depends upon more than just genes. A simple experiment showed that experience is important too. Some mice were raised either in a sparse, unfurnished cage with only a water bottle and food tray, while others grew up in a special "play ground" equipped with plastic tubes, a tunnel with multiple openings, and an exercise wheel. After three months the mice brought up in the more stimulating enviroment showed a 15 per cent increase in the number of cells in the hippocampus. The more the mice used their brains to remember the complex topography of the play ground, the better their brain becomes. Even for this simple type of intelligence, environment makes a difference.

What do different people, even when they are brought up the same way in the same environment, get different scores on IQ tests? Although there is no single answer to this question, the results of decades worth of study on tens of thousands of subjects

have been remarkably consistent in showing that the single most important factor is genes. The "environment" includes many factors that influence intelligence, such as prenatal care, nutrition, child care, schooling, etc. Together they are a powerful force, but not one of those environmental factors alone has a great impact than genes.<sup>55</sup>

#### 12.4.2 BODY WEIGHT AND GENES

Nothing could be further from the truth. Eating is one of the most ancient and evolutionarily conserved of our behaviours. If we did not eat enough to replenish the calories we burn, we could not survive. So naturally, we have inherited genes that make our bodies conserve calories instead of burn them. Unfortunately, even though our genes have not changed in the last several hundred thousand years, our culture has dramatically. Now most people recognize that body weight responds both to the biology and society, to genes and emotions. The most recent experiments show that genes are the single most important contributor to body weight, than any other factor or combination of things.

The bottom line is that the genes are very important, but still depend on the environment. A person who might balloon to obscene fatness in one setting could stay relatively thin in another. To understand how genes and behaviour work together to control body weight, it is necessary to understand what the genes are doing. The scientists chose ten Pimas suffering from both obesity and diabetes and screened the DNA for the B-30 adrenergic receptor gene. The researchers were astounded to find the five out of the ten had the same gene mutations.<sup>56</sup>

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55 Tully, T. "Regulation of Gene Expression and its Role in Long-term Memory and Synaptic Plasticity"—Proceeding of National Academy of Science, USA, 94, 4239-41, 1997.

56 Arner, Peter, "*The B-3 Adrenergic—Receptor—a Cause and Cure of Obesity*"—The New England Journal of Medicine 333, 382-3, 1995.

When you think about genes of your personality, you are asking who am I? The simple answer is "you are who your brain thinks you are." And who your brain thinks, you are the result of an intricate, one of a kind interaction of genes and life experiences. So what about free will? It is alive and well, and probably genetic. Free will means taking control of your life. This is only possible when you understand who you are. As humans, we are born with instinct to survive, to love and to produce. As individual we are born unique, each of us a variation on the human theme. Genes play an essential role in the overall theme and the individual variations: genes make us human and they make us unique. People cannot be mass produced even if we tried. Every individual has too many choices and possibilities to ever predict the future. You are born with a pen and paper in hand, but you have to write your own story.<sup>57</sup>

#### 12.4.3 RELATIONSHIP AND GENES

On the other hand, genes made Paul a man and Madeleine a woman, thus making possible their sexual attraction. They met at the age of maximum reproductive potential, a time when biology throws young people at each other with enough force to tilt the earth. Both had genes that made them attracted to the opposite sex; perhaps a simple variation could have made Paul sexually attracted to Madelein's brother. Genes might have also influenced how the relationship developed. Was Madeleine a genetically driven thrill seeker? Did she pursue the ship's captain because she craved a new high? Or, was it harm avoidance that caused Paul to flee at the first sign of trouble instead of sticking with Madeleine, when she was confused? We are the products of our genes, so it is natural that our relationship, too, will fall under the sway of DNA.<sup>58</sup>

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57 Kitcher, Philip—"The Lives to Come, The Genetic Revolution and Human Possibilities," New York (U.S.A.), Simon and Schuster, 1996.

58 Bailey, J.M. and R.C. Billard, "A Genetic Study of Male Sexual Orientation" *Achieves of General Psychiatry* 48, 1089-96, 1991.

One afternoon, at the HIV clinic, after I had finished an interview, the subject asked me why I was so interested in his family history. When I explained that we were trying to see whether sexual orientation was influenced by genes. He made an interesting suggestion: "You should look at the sex chromosomes. That is what makes men different from women." In fact, I was interested in the sex chromosomes not so much because of their role in making men and women different as because of their distinct pattern of inheritance. Specifically, fathers transmit their single Y chromosome to each of their sons and their single X chromosome to each of their daughters. This generates unique family trees and makes the sex chromosomes easy to track.<sup>59</sup>

It was a prominent scientist, Botstein, who had, in 1980, proposed that it might be possible to map the entire human genome by using random bits of variable DNA called markers. The second principle that influences linkage is that genes found close to one another on a chromosome usually are inherited together. Because of simple chemistry, two genes that are "close together" are by definition found on the same DNA molecule. DNA is tough and wiry: only rarely do its long strands break in two. As a result, genes that are located on the same piece of DNA almost always travel together into the germ cells that make up the fertilized egg.

To understand how genes help shape who we are, rather than just what we suffer from, it helps start with something simple and move to more complex areas of behaviour. The first example is something which most people take for granted. Genes make us all alike. When people hear a trait is influenced by a gene, they sometimes assume that it only comes in two opposite

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59 Meyer—Bahlburg, H.F.L. 1982, "*Psychoendocrine Research on Sexual Orientation*"—*Progress in Brain Research* 61: 375-98.

varieties: smart or stupid, mean or kind, passive or aggressive. We know that physical characteristic such as height, weight and skin colour don't come in just two varieties, so we must assume that the variations of personality are equally vast. Just look in the mirror. Facial features are largely determined by genes but there is nobody else in the world (unless you have an identical twin) who looks quite like you. Given the wonderful diversity with which genes sculpt the human face, they must be equally dexterous and imaginative when it comes to shaping the nooks and crannies of human brain. Such breath taking detail on the outside of the human form suggests an equal, or even more elaborate, construction on inside.<sup>60</sup>

## 12.5 Classification of *karma* and genes

(i) *Jñānavarṇa karma genes*—No matter in which country, in which historical time period, in what age group, or with what type of test, the result is always the same: no other single factor is more important than genes in determining cognitive ability. What would be remarkable at this point would be scientific study in which heredity was not important for IQ.<sup>61</sup> This is comparable with *jñānāvaraṇa kṣayopāśama karma*. Glutamate receptor gene is both critical and specific for both the types of thinking involved in making a mental map.<sup>62</sup> This can be compared with *jñānāvaraṇa kṣayopāśama karma*.

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60 Ott, J. "Analysis of Human Genetic Linkage," 1991, Baltimore: John Hopkins University Press.

61 Capron C and M Dyme "Assessment of Effects of Socio-economic Status on IQ in a Fullcross Fostering Study," *Nature* 340, 552-3, 1989.

62 Bouchard, T.J. Jr. and M. Mc Gue, "Familial Studies of Intelligence" A Review, *Science* 212, 1055-9, 1981.

In many ways, we live in the past. Our thoughts are dominated by memories of what we have seen, heard and experienced. Without the ability to remember, we would not know where we live or what we do. Nor could we understand this sentence. According to Eric Kandel, a neurobiologist at Columbia University's College of Physicians and Surgeons, "Memory is who we are." Kandel is a pioneer in understanding the molecular biology of memory: his work has led to the surprising conclusion that memory works the same way in the simplest animals as it does in the most complex mammals like ourselves. More surprisingly, memory in the lowly sea slug and the highly developed mammals comes from exactly the same genes.<sup>63</sup> This can be compared with *jñānavarṇa kṣayopāśama karma*.

(ii) ***Darśanāvārṇa karma gene***—The evidence is strong that IQ is largely determined by genes.<sup>64</sup> This can be compared with *darśanāvārṇa kṣayopāśama karma*. In other words, serotonin affects consciousness in many ways that are connected to self transcendence and spirituality. It alters perceptions, one concept of mystical experience. It increases socio-ability, an aspect of transpersonal identification. It elevates mood, an aspect of the perception of sacredness. All of this can be influenced by a simple monoamine.<sup>65</sup> This is compared with both *darśanāvārṇa karma* and *darśanāvārṇa kṣayopāśama*.

(iii) ***Vedanīya karma genes***—Dopamine chemical is an activator of happiness in behaviour. The breakthrough came from an unexpected quarter. A small research team in Israel led by scientist Richard Ebstein, the laboratory director at the S.

63 Bailey, C.H.D., Bartsch and E.R. Kandel "Towards a Molecular Definition of Long term Memory Storage," U.S.A. 93, 1996.

64 Scarl. S. and R.A. Weinberg "IQ Test Performance of Black Children Adopted by White Families," *American Psychologist*, 1976.

65 Fabre V, M.P. Martres "Altered Expression and Functions of Serotonin 5-HT/1A and 5-HT/1B," *Eur J Neurosci* 12, 2000.

Herzog Memorial Hospital in Jerusalem, and Robert Belmater, an Israeli psychiatrist interested in Schizophrenia, who thought to involve several dopamine disruptions. Looking at one after another of the dopamine related genes potentially involved in schizophrenia, they noticed one gene that seemed peculiar. It was the gene that makes the DR dopamine receptor called D4DR, a gene of happiness.<sup>66</sup> This can be compared with *śatāvedanīya karma*.

The interpretation is that the diabetes gene makes the leptin receptor: a brain protein that senses the presence of the fat hormone. If the receptor detects peptin, it tells the body to stop eating and start burning fat. When the leptin receptor gene was isolated, first from mice and then from humans, it was found to be located primarily in the hypothalamus, the brain's eating centre. When fat cells are well-fed and plump, they produce leptin which goes to the brain and binds to the receptor, which in turn decreases food intake and increases metabolism. Thus, the leptin receptor must send signals both within the brain to decrease hunger and the body to increase metabolism.<sup>67</sup> This can be compared with *śatāvedanīya karma*.

Around the time, a research group in Texas claimed to have found a specific gene coding for the dopamine D2 receptor, associated with alcoholism. It was not known what to make of the study, but it was encouraged because it was another potential connection between genes and behaviour. The mention of this specific gene was intriguing because dopamine is a chemical in the brain thought to play a key role in rewarding dependence and pleasure. We could easily imagine how changes in these

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66 Menza, Matthew, A, Lawrence, I, Golbe Ronald A, Cody and Nancy E. Forman "Dopamine Related Personality Traits in Parkinson's Disease" *Neurology* 43.

67 Lee, Gwo-Hwa, R. Proenca "Abnormal Splicing of the Leptin Receptor in Diabetic Mice," *Nature*, 379, 1996.

pathways might make a person dependent on alcohol.<sup>68</sup> This can be compared as *śatāvedanīya karma*.

Started in 1990, the scientific community and the U.S. government initiated a fifteen year \$ 3 billion plan called the Human Genome Project. The goal is to precisely map all the three billion base pairs, a bit of information, that makes up the human genome, which is the complete compliment of genetic information in a single person. The first step was developing genetic markers, which are signposts that indicate the exact position of a piece of DNA in a chromosome. Scientists also were developing ingenious ways to use these markers to map the genes even when it was not known what the gene did or whether it was located on the genetic make up. They already had used these methods to map genes for several important diseases, such as cystic fibrosis, Huntington's chorea, and one type of colon cancer.<sup>69</sup> This is comparable to *Asātāvedanīya karma*.

**(iv) Mohanīya karma genes**—Serotonin receptor is called 5HTIB.

Low serotonin causes aggression. Since the genes have a role in serotonin levels and how it is used, then genes must be causing aggression,<sup>70</sup> comparable with *Krodha mohanīya karma*. If this is happening in society at large, it does not take much imagination to realize that a person who is born in poverty, who lives in a slump, who does not have a good education, who has the "Wrong skin colour, religion or language might expect to have low status. With that comes low serotonin, and with low serotonin comes aggressiveness,

68 Blum, K, E.P. noble, P.J., Sheridan 1990, "Allelic Association of Human Dopamine D2 Receptor Gene in Alcoholism." *Journal of American Medical Association*, 263.

69 *The Science of Desire*—by Dean Hamer and Peter Copeland, publisher Simon and Schuster, New York (U.S.A.).

70 Cases O, Isabelle Self, Joseph Grimsby "Aggressive Behaviour and Altered Amounts of Brain Serotonin in Mice," *Science*, 268, 1995.

hostility and violence which, of course, can only lead to more of the same. Obviously, this tendency to violence occurs only to a small minority, even in the worst environments, so other factors are at work<sup>71</sup> This is comparable with *krodha mohanīya karma*.

The question of whether genes play a role in aggression and crime is tremendously controversial. Yet, even the most vocal critics who convinced that only bad environment produces bad people, cannot deny one simple biological fact. The most important single factor, whether a person is violent or aggressive is determined by just one chromosome, the Y which assigns gender.<sup>72</sup> This is comparable with *Krodha mohanīya karma*.

If the only difference between man and woman is the single Y chromosome, is it directly involved in aggression? Experiment with mice suggested that it does have an important role, since changing the structure of the Y chromosome can alter the level of aggressive behaviour. The theory was perfect that Y chromosome is the difference between men and women, and men are violent, so there must be something on the Y chromosome that is involved in violence. The problem was finding a way to test the theory on humans<sup>73</sup> This can be compared with hatred *mohanīya karma*.

Probably, the most important role of the Y chromosome in aggression is manufacturing testosterone, the hormones that makes half the population male.<sup>74</sup> This can be compared with hatred *mohanīya karma*). The discovery of "crime gene" generated headlines around the world and prompted criticism from

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71 *Ibid.*

72 *Living with Our Genes*—by Dean Hamer and Peter Copeland, Anchor Books, a division of Random House, New York (U.S.A.), 1999, p. 107.

73 *Ibid*, p. 108.

74 *Ibid*, p. 110.

scientists who refused to believe that something so simple—even simpler than the mechanism that determines blue eyes or brown eyes—could turn man into monsters (*rākṣaṣa*). Doubters said that the mutation alone could not cause such a personality change, that other genes must be involved or it was something in their childhood.<sup>75</sup> This can be compared with hatred *mohanīya karma*.

The three judges who heard Filiaggis' neurobiology defense did not buy it. He was sentenced to death. But lawyers are persistent, and they will probably keep trying. As they do, judges and juries will lead to listen closely to one of the main theme of this chapter: predisposition is not predestination. Genes neurotransmitters and hormones may tip the scales, but people are not robots programmed by genes. There is plenty of room for free will and conscience in how we behave and how we judge the behaviour of others. Remember that simply having Y chromosome makes a person already genetically predisposed to crimes. Should we then pardon a murderer simply because he is male?<sup>76</sup> This can be compared hatred *mohanīya karma*.

5HT1B receptor is used to test the idea that serotonin is involved in aggression.<sup>77</sup> (Comparable with *krodha mohanīya karma*). The master gene is called TDF, which is named for the protein it codes for, the test is the determining factor. It is located not surprisingly on the Y chromosomes, the only chromosome that men have but women do not. At the beginning of life, for an embryo, there is no difference between a male and female, except for a mere streak that will become genitals. If the foetus is male, the TDF gene is turned on about eight weeks after conception, and differences begin to appear. To carry out its male mission, the TDF gene activates another gene that makes muellerian-

75 Hen, Rene "Mean Genes," *Neuron*, 16, 1996

76 Soudou, F., D.A. Amara, A. Dierich "Enhanced Aggressive Behaviour in Mice Lacking *5H-T1B* receptor," *Science*, 265, 1994.

77 *Ibid.*

inhibiting hormone, which keeps internal female organs from overlapping. The gene's second job is to activate a group of cells that synthesize testosterone, the male sex hormone, that leads to the formation of the male genital track. TDF works like a switch at a railroad yard, when it is absent the train process along the female track; when present, it switches development over to the male track.<sup>78</sup> This is comparable with *puruṣaveda nokaṣāya mohaniya karma*.

The next gene on the list was serotonin transporter, which modulates the brain's supply of another important monoamine. Although Comings found only a weak line between this gene and self-transcendence, it was of interest because of the important role serotonin plays in emotions—especially negative emotions like depression, anxiety and hostility. Scientists still don't know whether it is high or low levels of serotonin that are associated with negative emotions, because what they measure is the amount of serotonin circulating at one time, not the total amount of serotonin in the brain. What they do know, however, is that variation in serotonin levels are associated with negative emotions. But once again we found no association. It did not make any difference whether people had the form of the serotonin transporter gene associated with feeling good or bad—the self transcendence scores of the individuals in our study were the same.<sup>79</sup> This is comparable to hatred *mohanīya karma*.

Richard Dawkins, another pioneering evolutionary biologist best known for popularizing the concept of the "selfish gene," but he does not think that genes have anything to do with spiritual beliefs.<sup>80</sup> Comparable with *Lobha mohanīya karma*. Testosterone, the

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78 Bailey, J.M. and R.C. Pillard "A Genetic Study of Male Sexual Orientation, *Archives of General Psychiatry*" 48, 1991.

79 *The God Gene*—by Dean Hamer—Anchor Books, A division of Random House, Inc, New York (U.S.A.), p. 72.

80 *Ibid*, p. 142.

male sex hormone, made over years perk up, because several early researchers had speculated that testosterone and other sex hormones played a role in sexual orientation.<sup>81</sup> This is comparable to *Veda nokaṣāya mohanīya karma*. More precisely, our mapping showed the "gay gene" is most likely somewhere between the markers GABRA3 and DXYS154 which span a distance of about five million base pairs. This represents less than 0.2 per cent of the three billion base pairs in the human genome, but because the genome includes somewhere around 1,00,000 different genes, such a small area has enough room for upto 200 or so different genes.<sup>82</sup> Comparable with *veda nokaṣāya mohanīya karma*.

The dopamine D2 receptor gene, which had been correlated to alcoholism in some studies.<sup>83</sup> This is comparable with *mohanīya karma*. Some of the most intriguing evidence for the role of genes in human personality comes from the studies of opposite traits: shyness and aggression.<sup>84</sup> This is comparable with hatred *mohanīya karma*. Other research has suggested that people with low levels of the chemical serotonin are prone to both impulsive, violent acts and to depression and suicide although this might seem contradictory, psychologists have long postulated that aggression and depression are linked, one is anger directed without, the other is anger directed within. Low serotonin by itself is probably not hazardous but when combined with stress, alcohol or abnormal levels of nor adrenaline, it might lead to impulsive reactions as extreme as murder.<sup>85</sup> This is comparable with hatred *mohanīya karma*.

81 Bailey J.M., and R.C. Pillard 1991 "A Genetic Study of Male Sexual Orientation. Archives of General Psychiatry," 48; 1889-96.

82 The Science of Desire, p. 147.

83 Blum K., E.P. Noble, P.J. Sheridan 1990. "Allelic Association of Human Dopamine D2 Receptor Gene in Alcoholism," *Journal of American Medical Association*, p. 263.

84 Science of Desire, p. 200.

85 *Ibid*, p. 202.

(v) *Āyusya karma gene*—The recent discovery of several key genes related to aging suggests that the car analogy is a good one, but not for any obvious reason. The body does not wear out from use as much as it is designed to last only a short time. The reason why car companies stay in business is that car needs to be replaced every few years; they are built with planned obsolescence. The human body is built the same way, our parts wear out not by simple use but by design. We die from planned obsolescence. Our genetic blue print comes with fine print that reads: warranty valid only for limited time.<sup>86</sup> This is compared with *Āyusya karma*.

Mistakes are alterations accumulated in the DNA, especially the mitochondrial DNA, and death follows. The first life extending mutation was found in a gene dubbed "age 1."<sup>87</sup> This is compared with *Āyusya karma*.

(vi) *Nāma karma gene*—There is a growing evidence that genes play an important role in language.<sup>88</sup> This can be compared with body *nāma karma*. One due is the large number of genes that have been identified for mental retardation.<sup>89</sup> This can be compared with body *nāma karma*. Body weight depends upon a simple, unaltered balance: caloric intake verses energy expenditure, how much is eaten verses how much is burned. If you eat more than you need to live, you gain weight; eat fewer calories than you burn, and weight drops.

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86 Costa, P.T. Jr. and R.R. McCrae, "Still Stable after all these Years' Personality as a Key to Some Issues in Adulthood and Old Age," edited by P.B. Baltes, New York, 1980.

87 Corral-Debrinski, M., T. Horton, "Mitochondrial DNA Deletions in Human Brains: Regional Variability and Increase with Advanced Age," *Natural Genetics*, 2, 1992.

88 *Living with our Genes*, p. 231.

89 Whatstrom, J., "Gene Map of Mental Retardation," *Journal of Mental Deficiency Research*, 34, 1990.

Genes play an important role in every part of the process: what makes us start eating? How we stop and how calories are burned?<sup>90</sup> This is compared with body *nāma karma*. This was the clear proof that leptin was a key player in human weight control, just as in mice.<sup>91</sup> This can be compared with body *nāma karma*. A gene called myostatin control muscle growth.<sup>92</sup> This can be compared with body *nāma karma*.

There are various theories about why being left handed is not more easily inherited, such as blaming it on early brain injury, but an alternative explanation is that there is a single "handedness gene" that only affects people. According to this model, advocated by the English scientist, I. Chris Memanus, individuals with two copies of the "sinistral gene" and one copy of the "dextral gene" have a 25 per cent chance of being left handed, and people with two copies of the "dextral gene" are almost always right handed. This model remains to be tested, but it should not be hard to find several hundred pairs of left handed siblings. Finding such a gene could offer new insights into one of the most fundamental and uniquely human aspects of how brains are organized.<sup>93</sup> This is comparable with body *nāma karma*.

## 12.6 Functions of genes on all 24 chromosomes

The principal role of genes in all the 24 chromosomes of human has now been identified.

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90 Fabsitz, R.R., P. Shilinsky "Genetics Influence on Adult Weight Gain and Maximum Body Mass Index in Male Twins," *American Journal of Epidemiology*, 140, 1994.

91 Lee, Gwo-Hwa, R. Proenca. "Abnormal Splicing of the Leptin Receptor in Diabetic Mice," *Nature*, 379, 1996.

92 *Living with our Genes*, p. 308.

93 McCormick C.M., S.F. Witelson and E. Kingstone, 1990. "Left Handedness, Homosexual Men and Women:" Neuroendocrine Implications, *Psychoneuroendocrinology* 15 : 69-76.

**Chromosome 1:** *Genes* in chromosome one contains the record of past lives. This can be compared with *Kārmaṇa śarīra nāma karma*.

**Chromosome 2:** *Genes* in chromosome two contains the history of journey leading to human life. It has details of birth in various species we lived before. It is comparable with *gati nāma karma*.

**Chromosome 3:** Contains evidences for the entire past history in the form of genes. This is comparable with *Āyusya karma*.

**Chromosome 4:** Genes on chromosome 4 contain information about our future. This is also comparable with *Āyusya karma*.

**Chromosome 5:** Genes on chromosome 5 are very sensitive to environment and contain information about our immune system. This is comparable with body *nāma karma*.

**Chromosome 6:** This is the intelligent chromosome. Genes over this chromosome are the basis of our intelligence. It has been shown that in some cases intelligence is hereditary. This is comparable with *jñānāvārṇa kṣyopaśama* state of soul.

**Chromosome 7:** Genes over chromosome 7 contain those characteristics which determine our behaviour as human being. This is comparable with *gotra nāma karma*. (*Uccagotra* and *nīcagotra*)

**Chromosome 8:** Genes over this chromosome contain information about our liking and choices. Our habits and natures are stored and transmitted to next life. This means that our merit and demerits are also influenced by hereditary factors i.e. genes. This is comparable with *sātā* and *asātā vedanīya karma*.

**Chromosome 9:** The genes of chromosome 9 determine the blood group. This can be compared with body *nāma karma*.

**Chromosome 10:** This chromosome contains the gene CYP17, which produces an enzyme that converts cholesterol into hormones called cortisol and testosterone. These hormones

produce stress in the body. This is comparable with *asātā vedanīya karma*.

**Chromosome 11:** This contains genes, which influence our personality. This is comparable *gotra nāma karma*.

**Chromosome 12:** Genes of chromosome 12 are self assembled. This is responsible for mental retardation. This can be compared with *jñānavarṇa* and *asātā vedanīya karma*.

**Chromosome 13:** Genes of this chromosome store characteristics of past lives. This is comparable with *Āyusya karma*.

**Chromosome 14:** The genes of chromosome 14 are of indestructable nature and are responsible for brain diseases. This can be compared with *asātā vedanīya karma*.

**Chromosome 15:** The genes of chromosome 15 determine male and female gender. This can be compared with *puruṣaveda* and *strīveda nokaṣāya mohanīya karma*.

**Chromosome 16:** The genes of this chromosome contains memory. This is comparable with *darśanāvarṇa karma kṣyopaśama* state of soul.

**Chromosome 17:** Genes of this chromosome decide the life span. This is comparable with *Āyusya karma*.

**Chromosome 18:** The genes of chromosome 18 help in recovery from illness. This can be compared with *Sātā vedanīya karma*.

**Chromosome 19:** This chromosome decides fertility. This can be compared with *puruṣa* and *Strīveda nokaṣāya mohanīya karma*.

**Chromosome 20:** The genes of chromosome 20 destroys immunity. This can be compared with *asātā vedanīya karma* and body *nāma karma*.

**Chromosome 21:** Genes of this chromosomes produce diseases in body. This can be compared with *asātā vedanīya* and body *nāma karma*.

**Chromosome 22:** Genes of chromosome 22 characterize freedom of thoughts. This is comparable with *jñānāvarṇa karma*, as well as *kṣayopaśama* of the soul.

**Chromosome 23:** The genes of chromosome 23 produce muscle degeneration. This is compared with body *nāma karma*.

**Chromosome 24:** This chromosome is governed by the SRY gene of testis—determining factor. This leads to testicle development. This can be compared with *puruṣaveda nokaṣāya mohanīya karma*.<sup>94</sup>

### 12.7 Role of genes in behavioural responses/personality

Individual differences in temperament are produced in the past by biology, just like the shape of a nose or the colour of skin. The instruction for human development, including aspects of temperament are carried in genes passed from parents to children. Although there are important non-genetic factors, such as parenting style and schooling, no single influence is more profound than genetic make-up. That is why, temperamental traits are expressed only by pursuit throughout life. We die with the same genes we are born with. But the genes themselves don't make a baby cry or giggle, or make the difference between a gregarious car salesman and a shy data processor. Rather the gene controls certain aspects of brain chemistry, which in turn influence how we perceive the world and react to that information.<sup>95</sup>

But why are some babies shy and other outgoing? The shy baby and outgoing baby are responding to the same new faces, but why does the first baby's brain react negatively to a stranger, while the second baby react positively? The root of these responses is in the genetically determined chemistry of the brain,

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94 *Brahmandīya Jewika Bhotika* and *Rasāyana Vijñāna* by AcāryaśrīKanakanandiji—Publisher Dharmadarśana Vijñāna Bodha Sansthāna, Udaipur, first edition 2001, p. 308-309.

95 Rose, Rechar J. "Genes and Human Behavior" *Annual Review of Psychology*, 46, 1995.

especially the primitive part of the brain called the limbic system. The limbic system is responsible for emotional behaviour—the way people feel and by generating gut reactions they can feel beyond the control of consciousness. Deep in the limbic system are the roots of fear, aggression, lust and pleasure.

If everybody had the same genes that built the same limbic system and then had the same life experiences, all the personalities would be the same. But limbic systems are different because genes are different. Experiences are different, because we live in a world with so many possibilities. No two people, even identical twins raised in the same home, can share the exact same experiences, which is part of the reason for the unlimited variety of the personality character.<sup>96</sup> The theory is not only stupid but cruel, people are different because they have different genes that created different brains that formed different personalities. The real breakthroughs in understanding personality are not occurring on leather couches but in laboratories, some of these new findings from labs around the world are explained here for the first time. The lessons can be applied to our own life and to the lives of our children.<sup>97</sup>

The serotonergic is the most wide spread neurotransmitter system in brain. The cell bodies of the serotonin nerve cells are clumped together in the raphe nucleic deep in the mid brain, and the axons branch out like veins throughout the brain. They spread extensively into the limbic system, the "heart" of emotional responses. They wind into the cerebral cortex. Which is involved in cognition and sensory perception, and into the frontal lobes, which are involved in impulse control, empathy and social awareness. Other branches reach the hippocampus,

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96 Shultz, Duane and Sydney Ellen Schultz. *"Theories of Personality"* 5<sup>th</sup> ed. Cole Publishing, 1994.

97 Zuckerman, Marvin, "Good and Bad Humors: Biochemical Bases of Personality and its Disorders," *Psychological Science*, 6, 1995.

the site of memory and learning and the hypothalamus and pituitary gland, which are involved in appetite and sex. All these organs function with the help of different genes.<sup>98</sup>

The power of love is simple. The way humans pass on their genes is through sexual production. People with genes that somehow made them incapable or disinterested in having sex, never had children and therefore did not pass on those genes. They may have been wonderful, even extraordinary people. All their other genes may have been great—genes that made them kind or generous or strong or brilliant or beautiful—but if they did not have sex, those genes were lost forever. People with genes that inspired sex and attracted a partner had children. The children had children of their own and go on down to us. Their other genes might have been rotten, they might have made them mean or selfish or stupid—but it did not make any difference, their genes were passed on to the next generation.<sup>99</sup>

To guarantee their survival, the genes found a clever trick. Instead of appealing to our higher sense of thinking to continue the human race, the genes made sex feel good, real good. Genes code for millions of touch receptor in the genitals and for the nerves that connect them to the brain, the most important sex organ. In the somatosensory cortex, the part of the brain, linked to the genital area is larger than any other, that is why the genitals are so delightfully, exquisitely sensitive to the touch. Other genes code for the flood of hormones that are released during pregnancy and at child birth, infusing the mother with warm feelings towards her child. Still other genes, presumably in the primitive limbic part of the brain, help us make receptive to the social interactions and signs of mutual attraction that we feel

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98 Kagan Jerome, "*Galen's Prophecy, Temperament in Human Nature*," New York, Basic Book, 1994.

99 Bailey, J.M. and R.C. Pillard "A Genetic Study of Male Sexual Orientation," *Archives of general psychiatry*, 48, 1991.

instinctively that is called love.<sup>100</sup> Even if a woman has no conscious desire to have children, her genes are telling her to choose a man with the resources to raise them.<sup>101</sup> We had found a pattern of maternal transmission, we thought the X chromosome would be a good place to start searching. There was no way a father could pass his X chromosome to his son.<sup>102</sup>

There are many different serotonin receptors, each of which is produced by its own distinct gene. Already more than a dozen distinct serotonin receptors have been identified and their genes have been cloned. This diversity of receptors, along with the widespread geographic distribution of the serotonin nerve cells, is why serotonin effects so many different brain functions. But there is only one serotonin transporter, which comes from just one gene. So anything that effects the serotonin transporter will affect all the psychological traits controlled by serotonin.<sup>103</sup>

Fortunately, there are two scientists working on the serotonin transporter gene who are not so fickle: Dennis Murphy, a senior NIMH researcher who has been studying serotonin for more than 20 years and Peter Lesch, a former postdoctoral fellow with Murphy who now heads his own laboratory at the University of Wurzburg in Germany. They were particularly interested in how the gene was turned on and off by signals from the body such as hormones and stress. They went beyond the gene itself to look at bits of DNA upstream that promote the activation of the

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100 Fisher, Helen E. "Anatomy of Love, The Natural History of Monogamy Adultery and Divorce," New York, w.w. norton, 1992.

101 Bailey, J.M., R.C. Pillard, "Heritable Factors Influence Sexual Orientation in Woman," 1993.

102 Hus, S, A.M.L., Patatucci "Linkage between Sexual Orientation and Chromosome Xq28 in Male but not in Females," *Nature Genetics* 11, 1995.

103 Lesch, Klaus—Peter, Dean H. Hamer—"Association of Anxiety Related Traits with a Polymorphism in the Serotonin Transporter Gene Regulatory Region," *Science*, 274, 1527-31, 1996.

transporter gene. There was one region of the gene that was especially intriguing because it has an unusual composition and structure. Also, when this bit of DNA was removed, the activation or expression of the gene increased. That meant the region was designed to slow down the process of turning on the gene. Intriguingly, the region contained 16 imperfect repetitions of the same sequence of 21 to 22 bases. It was like a piece of music repeated 16 times with slight variations. Less suspected that this repeated structure might be important because such sequences were often different from one person to the next.<sup>104</sup>

If this is happening in the society at large, it does not take much imagination to realize that a person who is born in poverty, who lives in a slump, who does not have a good education, who has the "wrong" skin colour, religion or language might expect to have low social status. With that comes low serotonin: and with low serotonin comes aggressiveness, hostility and violence which, of course, can only lead to more of the same. Obviously, this tendency to violence occurs only to a small minority, even in the worst environments, so other factors are at work.<sup>105</sup> This can be compared with *karma vipāka* of individual.

The first signs of Parkinson's disease are stable. An author notices that certain keys on his computer keyboard are hard to press. A seamstress has difficulty in threading her needle. Slowly but surely, the symptoms worsen. The slight weakness in our finger spreads to the entire hand, then to the arm and leg. The minor tremble becomes a constant palsy that can explode into spastic fits. One's gait becomes hesitant, then slows to a shuffle. Speech become slurred, and the face becomes frozen and expressionless. Towards the end, even simple daily functions like getting dressed and eating become impossible.

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104 Kramer, Peter D. "Listening to Prozac," New York, Viking, 1993.

105 Cases, O. Isabelle Seif, Edward D. Maeyer—"Aggressive Behaviour and Altered Amounts of Brain Serotonin"—*Science*, 268, 1763-6, 1995.

These symptoms are due to the loss of a single brain chemical: dopamine—a monoamine involved both in motor functions and in reward pathways. As the disease progresses, the cells producing dopamine in the striatum and *substantia nigra* gradually die off. By the time, the symptoms are severe enough to warrant a visit to a doctor, only 10 to 20 per cent of the normal number are left. The underlying causes of the disease are due to inclusion of faulty genes, internal or external toxins, and viral infections. The first treatment of Parkinson's disease was a drug called levodopa, a precursor of dopamine. In some patients, it brought about a miraculous cure—but it also led to debilitating side effects, including nausea, dizziness and confusion. An improved version that is less rapidly metabolized and thus requires lower doses is now available but it is still a toxic medicine that can cause as many problems as it solves.<sup>106</sup> This is a good example of *karma vipāka*.

There are examples of mental disorder that have been properly mapped. One of them, Huntington's Chorea, is an incurable disease that slowly destroys the brain is caused by a single, dominant gene on chromosome.

Alzheimer's disease is not caused by a single gene. There are many examples of identical twins who do not share the disease but research has found a substantial genetic component involving at least three genes. The first gene is involved in the rare cases, where the disease strikes during middle age. Analysis of the brain plaques in these patients implicated a protein called beta-amyloid, which is produced by a gene on chromosome 21, the same chromosome involved in Down syndrome. In several

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106 Strawbridge, G.A.—Kaplan, "Religious Attendance Increases Survival by Improving and Maintaining Good Health and Relationship," Soc behav Med. 23, 68-74, 2001.

families, all the younger victims of Alzhemeir's had a mutation in the middle of the beta-amyloid gene.<sup>107</sup>

Genes not only help determine how we look, but also how we act, feel and experience life. In case, after case discovered by researchers' nature won over our nurture.<sup>108</sup> This is not to say that shyness is not biological, but a better way to search for biology's role is to look directly at genes.<sup>109</sup> With the mutation of genes disease take place.

**Emotional instinct**—The dictionary definition of personality is "the sum total of the mental, emotional, social and physical characteristics of an individual." It is personality that determines the way you react to others, the way you communicate, the way you think and express emotions. These are the outward manifestations of the basic traits that characterize a personality throughout life. Your thoughts, fears, hopes, reactions, behaviours and dreams all come from this core personality.

Personality determines not just by being but by behaving. It influences how much you eat, drink, smoke and sleep. Personality determines whether you are aggressive or shy, active or passive, who you are attracted to, and what you want to do with them if they will let you. It influences the amount of stress in your life, your physical health or whether you live in pain or pleasure or in a sleepy haze. Personality is so complex that even though millions of people have walked the earth, no two have ever been the same. Just as the physical body has a seemingly unlimited variety, so does the personality that makes the body get up and go. Personality is what makes each person unique.

107 R.C. Pillard "Sexual Orientation and Mental Disorder"—*Psychiatric Annals* 18 (1988): 52-56.

108 Wingerson, Lois—"Mapping our Genes: The Genome Project and the Future of Medicine," New York, 1991.

109 Kagan, J.J.S. Reznick—"Biological Bases of Childhood Shyness," *Science*, 240, 167-71, 1988.

The latest research in genetics, molecular biology, and neuroscience shows that many core personality traits are inherited at birth, and that many of the difference between individual personality styles are the results of difference in genes. When you are conceived by two people, you are created from their genes. You are the product of generations of evolution, countless bits of information collected over millions of years, focused, narrowed and refined until you were pushed out of the birth canal into the world. You look like the people in your family—and in some respects you feel and act like them, too. You have about as much choice in some aspects of your personality as you do in the shape of your nose or the size of your feet. Psychologists call this biology, in born dimension of personality "temperament."<sup>110</sup>

Genes can influence not just whether a person uses a drug but also how the drug affects the person.<sup>111</sup> Thus, with the variation (mutation) of genes different diseases happen to the individual.

**Gene pool**—one hundred years ago, or 1000 years ago, we were the same people genetically; what is changed is the way we live and govern our behaviour. Crime is not an individual problem, but a social problem. The way to predict which individuals are going to be violent today cannot be done by testing their blood. The best way to predict who is going to be violent is to see where and how they live. Today's criminal violence is not about brain chemicals but about poverty, the gulf between rich and poor, racial polarization, urban squalor, lack of responsibility, family breakdown and the deterioration of civil society.

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110 Bouchard, Thomas, J., Jr. "Genes, Environment and Personality," *Science*, 264, 1700-1, 1994.

111 Zuckerman Marvin, "*Sensation Seeking*," The initial motive for drug abuse, 1983.

However, social and environmental factors alone are not enough to explain violence and crime. If that simple minded view were true, then everybody born in the ghetto (hardship) would be a criminal, and everybody born in plenty would be a model citizen. The truth is more complex. All the researches show that anger and hostility are their visible outcomes such as crime and violence, are caused neither solely by the environment nor by biology. Neither do genes make criminals nor does "gangsta" rap. The mix is what is deadly; the combination of genes and environment, temperament and character. There are individuals who are violent because of what is going on in their heads, and there are societies in which violence flourishes. In no other domain of human behaviour are both nature and nurture so thoroughly intertwined.<sup>112</sup>

Men are proof that DNA is not necessarily destiny and that character traits can override genetic predisposition. In the case of Daniel, his strong character worked to overcome what could have been a genetic problem. Eventhough Russell did not have a disadvantage at birth, he still was miserable. Just as a person can be tall and not play basketball, you can have happy genes and feel terrible. If you feel your own level of harm avoidance is too high, there are plenty of ways to improve your outlook on life, such as working on a positive attitude, changing jobs, losing a few ponds, taking a vacation, exercising or even indulging in an occasional hot fudge Sunday.<sup>113</sup>

The pattern of brainwaves fits with what is known about the role of the right and left frontal areas in the control of emotional expression. The right side seems to be more involved in controlling negative emotions, whereas the left side plays more

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112 Bock, G.R. and J.A. Goode, *"Genetics of Criminal and Antisocial Behaviour,"* Chichester, U.K., Wiley, 1995.

113 Segal, Nancy L, and Alec Roy *"Personality and Individual Differences"* 19, 937-40, 1995.

of a role in positive emotions. The anxiety felt by Valerie may be because the more dominant side of her brain, which is the right side, is sending out more negative controlling signals than the left side, which send out the positive controlling signals.<sup>114</sup>

Violence and aggression also have genetic roots. Some people are born with shorter fuses and are more likely to lash out at others. Numerous studies show that altering the levels of a single brain chemical can completely change an animal's level of aggression. A simple manipulation of a single gene can turn a meek and mild rat into a crazer killer. The same brain chemicals are found in humans, and certain people are driven to violence by a force within them. Their lifelong struggle will be to consciously override what they are programmed to do.

How we think is also a product of genes. The evidence that IQ is largely inherited is overwhelming. Some genes determine how quickly the brain can process information. Others may control particular circuits, such as those for mathematical calculation or perfect pitch. What we have always called "God given talents" are known in laboratories as genetically endowed traits. The encouraging news is that genes do not always play their strongest role until adulthood.<sup>115</sup>

The news are shocking to Maria and her parents. Who never suspected she was anything but a healthy young woman. Further test revealed she had a rare condition present in about one out of 20,000 (XY) births called androgen insensitivity syndrome. There was a crippling mutation in the gene for the androgen receptor—the protein that senses the presence of male sex hormones. Maria was born with a normal Y chromosome and TDF gene. Her development train should have been directed in the male direction.

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114 "A Biological Theory of Sensation Seeking"—In *Biological Bases of Sensation Seeking, Inpusivity and Anxiety*, edited by Marvin Zuckerman, Hillsdale, NJ, Erlbaum, 1983.

115 Cloninger, C. Robert, Rolf Adolfsson and Nenad M. Svrakie, "Mapping Genes for Human Personality," *Nature Genetics*, 12, 3-4, 1996.

But because there was no receptor to sense the androgen, it was a circular track. No external male features were formed, and the train was routed back to the female track. That is why her external genitalia and secondary sex characteristic were those of woman. The only difference between Maria and any other woman was that Maria had internal tests and an incompletely developed Vagina, which would seem irrelevant to her ability to leap over hurdles.

Maria is an example of how a little knowledge of genetics can be dangerous. The officials thought that XY must mean male, but in fact, many other genes, most of them on other chromosomes, are necessary to distinguish a man from woman. And since Maria was a woman under any definition, except in the vocabulary of their particular gene, other genes must play a role in the behaviour that we consider to be female or male.<sup>116</sup>

“I think therefore I am” (Rene Decartes). Native talents and native intelligence—innate and inborn are derived from the constitution of mind, as seem to being derived from experience all due to Genes.<sup>117</sup>

As individuals, there is no doubt we want to live longer, or at least look younger, we have a strong instinct to survive jointly with an acute sense of morality, which has pushed us to improve living conditions that prolong life. Not to mention the power of human vanity, we still fantasize about discovering a "fountain of youth" but now search for longevity has turned inward to look at our genetic code. By discovering the genes that control aging, perhaps we will be able to prevent or at least slow the process. More likely, we will be able to prevent some of the diseases, disability and discomfort that accompany aging. Perhaps, the most important result of discovering the genetics of aging will be

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116 Bailey J.M., R.C. Pillard, M.C. Neale and Y. Agyei, "*Heritable Factors Influence Sexual Orientation in Woman*," *Archives of General Psychiatry* 50, 217-23, 1993.

117 Bouchard, T.J. Jr. and M. McGue, "Familial Studies of Intelligence," *Review, Science*, 212, 1055-9, 1981.

to understand what can be changed. These are some aspects of mental and physical decline that cannot be avoided, but enjoyment of our final years certainly can be increased through medical advances, healthy living and positive thinking.<sup>118</sup>

By the first decade of the twenty-first century, we will know the entire sequence of the human genome, every one of more than three billion nucleotides that make up the 1,00,000 genes that constitute our genetic patrimony. Deciphering the meaning and function of those genes will be slower but success is inevitable. Already an entire new field has emerged "Functional genomic" dedicated to figuring out what genes do. At the sametime, new technologies are emerging to exploit this information with drugs and by manipulating the genetic information itself. So far the manipulations are being performed only on animals, Dolly, the sheep, being the first well known example, but humans are just a few steps away.<sup>119</sup>

Supporters of International Human Genome Project argue convincingly that mapping the entire genome will help produce new drugs, reduce birth defects and allow us to live longer and healthier lives. The focus of attention so far has been on discoveries of genes for cancer and other physical illness.<sup>120</sup>

Families sought to marry their offspring with people of high rank and stature. People from particular religions or races sought their own kind. The highest social classes, the blue bloods, sought to preserve the purity of their lines.

The difference is that in the near future science will give us the power to do it more quickly, more accurately and more decisively,

118 Lokowski B, and S. Hekimi "Determination of Lifespan in Caenorhabditis Elegans by Four Clock Genes" *Science*, 272, 1010-3, 1996.

119 Cook Deegan, Robert, *The Gene Wars: Science Politics and the Human Genome*, New York: w.w. norton, 1994.

120 *Ibid.*

we will select mates not because of some superficial trait like a prominent family: but because we will be able to read their DNA as easily as an x-ray. Nor will we settle for the randomness of sexual blending of sperm and egg. With all its billions of possible combination when we can build desired combination to the letter.<sup>121</sup>

In future, a person who complains of depression or anxiety could have a DNA test to check the serotonin genes. People with compulsive behaviour such as gambling, drinking, drugs or promiscuous sex, would be checked for dopamine genes. Eating disorder or obesity? Look at the genes for leptin, the leptin receptor and its largest. A new technology called DNA chips, already under development by a biotech firm called Afymatrix, will make the entire DNA blueprint as easy to read as supermarket bar code.

Doctors will not be the only ones to read this information, but insurance companies, which profit by charging based on risk factors such as smoking would be very interested in genetic predispositions towards addiction or mental disorders. The military, which today rejects people who took medication as teenagers to control attention deficit disorder, might want to know about genes for rebellious temperament. Employers might be interested in genes for loyalty. Religious orders would be wise to discourage high novelty seekers, while the maker of sport cars would want to forget them with ads. Dating services should have revealing new ways to match people, imagine how excited certain school administrators would be to track students who are bright, troubled or aggressive.

We all will have new ways to understand people and label them, discriminate against them or help them. The technology is coming, how to use it is upto us.<sup>122</sup>

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121 Geller, Lisa N, Marvin R. Notowicz "Individual, Family and Societal Dimensions of Genetics Discrimination. A case study analysis," *Science and Engineering Ethics*, 2, 71-88, 1996.

122 Kitcher, Philip, *The Lives to Come, the Genetic Revolution and Human Possibilities*, New York: Simon and Schuster, 1996.

Rather problems with this kind of "gene therapy" on brain cells would arise because it usually would be used to clean up damage rather than prevent it, and it is good for only one generation. The best way to fix a gene before it is passed on to the next generation is to go into the germ cells in the sperms and eggs, an approach to this germline therapy has already been developed, at least in mice. Now DNA is introduced into the cells that are grown in a culture, then mixed together with natural cells from an early embryo. Some of the resulting babies will have the engineered genes in their germ cells and can pass them on to the next generation.<sup>123</sup>

Andrew married a woman he met in college, and they had two beautiful children. Andrew and his wife were thoroughly modern and dutiful parents, reading to their babies and playing classical music in the nursery. Before the children were conceived, Andrew and his wife had gone to their geneticist for routine counselling. The doctor has offered to run their DNA through the scanner and discuss any modification they might want to consider. Andrew, of course, was opposed to genetic engineering, but they were a little concerned because Andrew's wife had a brother who was paranoid schizophrenic, a condition with strong genetic roots. The doctor assured them that routine screening would weed out such obvious flaws in the DNA. Several mental conditions, obesity, extreme hyper activity, socially limiting shyness (SLS) and criminal aggression all had been virtually eliminated through routine genetic screening before conception. People no longer aborted babies with obvious problems: such babies were no longer conceived.<sup>124</sup>

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123 Lyon, Jeff and peter Gorner, *"Altered Fates: Gene Therapy and the Retooling of Human Life,"* New York, w.w. norton, 1995.

124 Wilmut I A.E. Schnieke, and K.H.S. Campbell "Viable Offspring Derived from Fetal and Adult Mammalian Cells," *Nature*, 385, 810-3, 1997.

An example of this experimental switching of genders was shown with two rats, known as Mork and Mindy and recorded on video. Mindy was genetically female and dosed with deprived testosterone and injected with female hormones. The X rated video of their first encounter, made of UCLA researcher Roger Gorski, has a simple and decidedly unromantic plot: Mindi meets Mork, Mindi mounts Mork, Mindi leaves Mork.<sup>125</sup>

Adaption studies suggest that in these cases most of the similarity between relative is due to genes rather than specific family environments. For example, the correlation between biological parents and child is about 15 per cent compared to less than one per cent for an adoptive parents and child. Webster's defines personality as the sum total of the physical, mental, emotional and social characteristics of an individual. Since the 1920s hundreds of family, twin and adoptee studies of IQ, have been reported in the scientific literature. The main conclusion is that roughly half of the variation in IQ scores is caused by genetic differences.<sup>126</sup>

It is now technically feasible to take a gene from one species and make it part of the genome (genetic 'blue print') of another species. A toxin producing gene from a bacterium can be added to make it pest-resistant. The gene that makes a firefly glow at night can be added to a plant's DNA to make the leaves lightup when the crop is ripe. A cow can be engineered to produce a drug in its milk. Human genes can be added to a pig's genome so that it grows organs for transplantation to mass without being rejected by the patients.<sup>127</sup>

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125 Dohler, K.D., and R.A. Gorski 1984, "Influence of Testosterone on Nucleus of the Preoptic Area in Male and Female Rats," *Brain research* 302 : 291-95.

126 Pillard R.C. and J.D. Weinrich 1986, "*Evidence of Familial Nature of Male Homosexuality*," *Archieves of General Psychiatry*, 43 : 808-12.

127 See Science for the 21<sup>st</sup> century—A new commitment "*The Possible and Acceptable*"—ethics in science UNESCO's O.P.I..

The advances in genetic science raise multiple legal issues that emphasize the need to educate and train legal minds to comprehend and cope with the challenging task that would arise in the legal field. Acquiring knowledge of genetic science in the context of law and law enforcement should be tempered with concern for social and cultural effects of the new genetics, so that a human being doesn't come to be viewed as a bundle of mere gene cells. The genetic science instantly brings into sharp focus that in a human body, besides the human cells that compose its totality, there lies a separate and independent entity, which cannot be seen or analyzed in terms of cells and that entity will alone be concerned with scientific, legal and ethical norms which should be devised to regulate and control the progress of genetic science for the betterment of all human beings and the vast biodiversity that surrounds it. If there be detected genetic component to various traits relating to individual's behaviour, personality including intelligence, anger, aggressiveness and social conduct, anxiety and addiction, let there be devised a gene therapy that prompts the mankind towards world peace and economic prosperity. The term trait is meant, in its broadest sense, to include physical attributes, mental or physical abilities, dispositions and capabilities. Most discussed enhancement technology is one in which a person's genome is altered.<sup>128</sup>

Jaina *karma* theory helps us understand the complexities of personality traits of human beings. Jaina approach for modifying human behaviour through the practice of right faith, right knowledge and right conduct is also psychological in nature. Compared to modern psychological approach through the application of principles of repression, inhibition, redirection and sublimation, Jaina approach is rather an attempt to overhaul the

wholeness of an individual. It involves only psychological approach, a short non-drug theory.<sup>129</sup>

### 12.8 Karma and Genes

Jaina *karma* theory seems to be so sophisticated that it appears to have shown the seed of modern genetic engineering. Jaina principle of "*sankārmaṇa*"—ingression, propounds the theory that *karma paramāṇua* can be modified through some variation by following the principles of Jaina *karma* theory. This clearly indicates towards the possibility of changes in the genes in modern times. Jaina *karma* theory had, thus, paved the way for such transformation in human beings, the ideas of which have led to the development of modern genetic engineering.<sup>130</sup>

Every worldly soul happens to be confined (not free). The imprisonment is due to the bondage of *karma* (*bandha*). Inflow of *karma* is due to *āśrava*, the stoppage of inflow is due to *sanvara* and the eradication of *karma* is due to *Nirjarā*. *Jīva* can shed the *karmas* and purify his soul with the help of austerities. The six types of *Sanvara*—*samiti*, *guṇti*, *yatidharma*, *bhavanās*, *parīṣaha* and *cāritra*, will be helpful in eradicating *karma* only if they are carried out with a firm faith in the commands of *Jīna*. The special efforts to destroy *karma* is done through *Tapas* or austerities. Austerity means restraint, which is done willingly by giving away some of the bodily comforts to discipline our mind from passions and pleasures. Austerities are performed at various occasions and in various different ways. All austerities have their own uniqueness.

To achieve *mokṣa*, we need the "right knowledge, high faith and right conduct" known as the "three jewels" of Jainism. Regarding right conduct, we must achieve control over our inner

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129 Jaina Karma Theory and Psychology—by S.S. Lishk, *Arhata Vacana Magazine* from Indore July 94, p. 55.

130 *Ibid.*

desires and reach a single stage where there is no attachment or hatred. Although different people take different vows and despite the outer difference in the observance of these vows, the goal of all is to attain right conduct. As we find in the scriptures, there are different vows for monks and nuns and for male and female householders.

Every cell of a multi-cellular organism contains same blue print of organism but in different type of cells, i.e. skin cell, nerve cell, bone marrow cell, genes operate in different way according to body requirement. These genes are directed by the rising *karmas* to operate according to body requirement, nature, duration, intensity and quantity of *karmas* in rise. With the processes of genetic engineering, we can switch on and off the desired working of genes.

### **12.9 Karma and genetic engineering**

In a short but interesting article, "Religion, Genetics and Embryo" by Sophie Boukhari, Unesco Courier Journalist, an array of responses to the bioethical questions posed by genetic technologies, by Catholics, Protestants, Buddhists, Muslims and Jews are referred. "Although religious practice may be declining," says French geneticist and Member of Parliament Jean Francois Mattei, "the metaphysical issue is still at the core of the question raised about genetic engineering, either by tradition, culture or duty." Should a person has recourse to prenatal screening and consider having an abortion if a serious genetic defect is discovered? Should search on embryos, gene therapy and cloning be allowed? All the "religions of book" (Christianity, Judaism and Islam) believe that the answers to these questions largely depend on the status of embryo. The frontier between "good" and "bad" genetic engineering depends on whether or not the embryo is considered to be "animate." "If the embryo has a soul, then it is endowed with a human (with *karma śarīra*) as well as biological life and any attack on its integrity is seen as a crime," says French geneticist, Hene Frydman. That is to say that even geneticists and

religious books both believe in *karmas* by playing role through genes in this gross body.<sup>131</sup>

Concept of *karma* resembles the concept of gene in all its functions. Rather the concept of *karma* goes one step ahead in the sense that apart from transporting the hereditary influences over the twenty four generations of both the parents, it also takes into account the effect of individual performances in the previous births. Probably, further studies in the field of Genetic Engineering may break upon a new era in the field of transmigration of soul striving for ultimate state of liberation.

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131 *The Gene Age*—A legal prospective by justice R.K. Abichandani, p. 32.

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