

Notes on the Human Cell

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Introduction

I am not a scientist, merely a writer interested in many things. My recent studies of genetics and evolution, doing research for a Telicom article (*On the Denial of Intelligent Design*, May-June 2008) inspired me to investigate aspects of the human cell that those studies only touched on. This article is a space-limited summary of what I found. Its purpose is to describe in readable language the very complicated human cell and its functions. Presenting the entire cell story (which must include its powers of replication) meant that I could not delve deeply into any single area and even had to omit some of the less interesting facts. While I have checked everything as best I could, do not look for scientific exactitude and please consider all numbers approximate.

Cell Types and Numbers

Cells are the structural and functional units of all life forms except viruses (which may not deserve the label of “life”). They are the smallest living biological structure. The word *cell* comes from the Latin *cellula*, meaning a small room. In a 1665 book (*Micrographia*) Robert Hooke used this name for cork cells that he saw through his microscope, because they reminded him of the small rooms of monks in a monastery.

There are three types of cell life on earth:

- Archaea, bacteria-like and possibly the ancestor of all cells, are survivable in extreme environments like those of the earth’s early history. Once thought to be a primitive type of bacteria, it is now known that they are as different from bacteria as bacteria are from humans.
- Bacteria. They go back some 3.5 to 4 billion years. Generally single-celled, there are multi-cellular types (e.g., cyanobacteria, also known as blue-green algae). At one time they were lumped together with archaea as merely different forms of “prokaryotes.” While they are still both prokaryotes, which merely means “before the nucleus,” that term now seems superfluous.
- Eukaryotes, which unlike the other two types have a nucleus within the cell. Usually multi-celled, they include animals, plants, fungi, and protists. Like those of all animals, human cells are eukaryotic. Confusingly, there is evidence of descent from both archaea and bacteria! Estimates of their age range from 1.2 to 2.7 billion years, about half that of bacteria.

The human body comprises 10 to 100 trillion cells (not counting bacterial residents), depending on whom you believe. The number varies greatly from person to person. A typical cell is 10 millionths of a meter in size, with a mass of one billionth of a gram. Some 50 million of the cells in your body will have died and been replaced while you have been reading this sentence. Humans shed and regrow all outer skin cells about every four weeks, replacing a half-million per hour, resulting in almost 1,000 new skins in a typical lifetime. Intestinal cells last just a few days, urinary cells two months, red blood cells four months, and some brain cells, years.

There are at least 210 distinct subtypes of human cell, each with its own structure and function. Some,

like white blood cells, are independent of other cells and move freely. Others, like muscle cells, are tightly joined. Some produce chemical substances such as hormones and enzymes. Others produce milk, insulin, mucus, saliva, etc. The main job of muscle cells is not to produce, but to contract. Nerve cells generate and conduct electrical impulses that enable the entire body to communicate with the brain and spinal cord.

Example of a Specialized Cell - Photoreceptors

Describing every subtype of human cell in detail would take many volumes, so let's take just one as an example. The gross anatomy of the human eye: lens, retina, iris, etc., is familiar to all of us, but the emphasis here is on cells. Of course all of the eye is made of cells, but let's stick to those that detect light (photons). The detectors, lodged in the retina, are photoreceptor cells, both rods and cones, of which there are 126+ million in each eye.

The 120 million rods see light only as shades of gray, black to white. They can detect a single photon, while the best photography media require 25 photons to detect a point of light. The rods provide 5,000 times the resolution of a high-quality magazine photograph. The 6 to 7 million cones, tightly packed in the center area (macula) where there are no rods, can distinguish colors but are much less sensitive than rods. That's why we don't see color in a dark room.

Three pigments, each consisting of protein complexed with a light-absorbing compound derived from vitamin A, sit in the membranes of cone cells. When a pigment absorbs light, it triggers a cascade of molecular events that leads to the excitation of the cell. Almost two-thirds of the cones are more sensitive to red, almost one-third to green, and the rest to blue. Those numbers do not reflect the relative strengths of the perceived colors, which are roughly equal among the three because of overlapping and varying sensitivities. The "blue" cones have the highest sensitivity, helped by some sort of "boosting" mechanism. The overall equality of color sensitivity lets us see a fairly pure white when looking at light that has equal amounts of the three primary colors. The detailed process by which this equality is achieved is not known.

A mere three million ganglion cells preprocess information from the photoreceptors into "digitized" nerve spikes. These are relayed to the brain's 12 visual centers (and a few other places) by a million ganglion cell axons (long slender projections) bundled in the optic nerve. Out of the equivalent of 10 billion bits per second arriving at the retina, just 6 billion bits per second leave the retina through the output ganglion cells, but only 10,000 bits per second make it to the visual cortex, traveling at speed of 270 mph. After further processing, visual information feeds into the brain regions responsible for forming conscious perception. By that time the amount of information making up that conscious perception is less than 100 bits per second, but the brain has intrinsic processing power to make sense of what is being seen.

Inside the Cell

The typical human cell is surrounded by a two-layer phospholipid membrane that controls what can pass in or out. Each cell has tens of thousands of phospholipids, whose hydrophilic heads and hydrophobic tails (each layer's heads pointing outward, tails inward) link with proteins to form the cell membrane. Lipids, another name for fat molecules, do more than just store energy. Some act as messengers between and within cells. Inside the cell is cytoplasm, comprising a gel-like substance called cytosol and organelles ("little organs"), which are specialized organs within the cell. A network of microtubules

made up of protein molecules acts as the “skeleton” of the cell and as “tracks” along which the cell can transport organelles and vesicles. They also play a part in cell division. An included nucleus, the “brain” of the cell, is separated from the rest of the cytoplasm by a membrane similar to the one that encloses the cell. The nucleus contains genetic information and the nucleolus, which manufactures ribosomes. The nuclear envelope is perforated by thousands of nuclear pore complexes that control the passage of molecules in and out. Other organelles have various functions that keep the cell healthy and help it do its job. These include ribosomes, which synthesize proteins, which in turn perform their allotted tasks. Proteins, also called polypeptides, are polymers (chains) of numerous amino acids. Ribosomes may be free-floating or attached to an organelle called the endoplasmic reticulum.

The Endoplasmic Reticulum (ER)

The function of the ER is to support the work of ribosomes and pass on the results. It provides a large surface area for the organization of chemical reactions and synthesis tasks. One milliliter of liver tissue contains about 11 square meters of ER. There are two versions, rough ER and smooth ER. The former is coated with ribosomes. The latter is where the vesicles carrying newly synthesized proteins (from the rough ER) are budded off. Besides packaging the proteins for their next destination, the smooth ER synthesizes phospholipids to maintain membranes of the nucleus, the Golgi Apparatus, lysosomes, vacuoles, and the entire cell. Most of the phospholipids go to maintenance of the ER membranes themselves! The smooth ER has many other functions, such as the release of calcium, detoxification of many drugs, and facilitation of contraction in muscle cells.

The Golgi Apparatus (GA), Lysosomes, and Vacuoles

The GA is the distribution and shipping department for the cell's chemical products. It modifies proteins and lipids that have been built in the ER and prepares them for export outside the cell or transport within the cell. The GA also forms lysosomes, which carry digestive enzymes that pre-process food coming into the cell and also dispose of bacteria, viruses, and cell garbage. Vacuoles are small fluid-filled membrane-bound sacs that temporarily store this material. Lysosomes fuse with the vacuoles and inject their enzymes into them, digesting their contents.

Centrioles, Cilia, and Flagella

Cells include two centrioles aligned at right angles, each consisting of nine groups of three short microtubules, arranged in a circle to form a cylinder. During cell division they move to opposite sides of the cell and support the division process. Cilia and flagella are projections from the cell. They are made up of motile microtubules designed to either move the cell itself or move substances such as fluid, mucus, or other cells, over or around the cell. They have the same internal structure, with the main difference their length, as cilia are much shorter than flagella. One example of cilia are those lining the trachea and bronchial tubes, moving bad stuff upward and out. The best known flagellum is that of the male's sperm cell, which moves the cell toward the female's egg cell, seeking to fertilize it.

Mitochondria

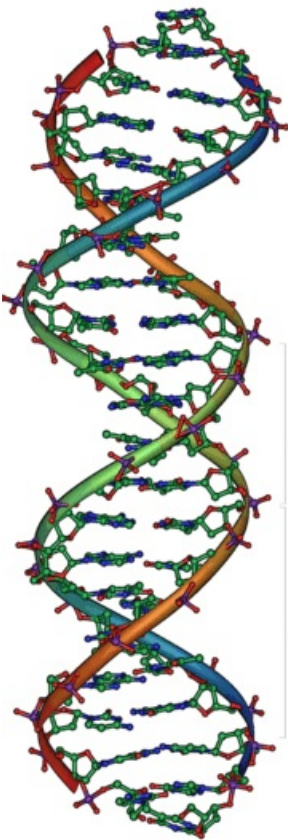
Mitochondria, free-floating in the cytosol, are powerful little producers of the form of energy (adenosine triphosphate, ATP) used in all living cells. Each one is a chemical factory processing more than 700 different chemical substances in long, interweaving assembly lines along the surface of its intricately folded membranes. Many fuel sources are utilized in the production of ATP, which powers almost every activity of the cell and organism. ATP is used to build complex molecules, contract

muscles, and generate electric pulses in nerve cells, among a host of other tasks. Some amino acids are metabolized also, all but one of which are put to work in the mitochondrial matrices. ATP has another important role as a signaling molecule that allows cells and tissues throughout the body to communicate with one another. Thus the universal fuel serves as a common language as well.

Energy is usually liberated from the ATP molecule by a reaction that removes one of its three phosphate-oxygen groups, leaving adenosine *diphosphate* (ADP), whereupon the ATP is said to be "spent." Then the ADP is recycled in the mitochondria, where it is recharged using protons derived from such raw materials as glucose that has undergone several steps of processing, and comes out again as ATP. The enormous amount of activity that goes on is shown by the fact that at any instant each cell contains about a billion ATP molecules. This amount satisfies the cell's needs for only a few minutes, so each ADP molecule is recycled three times a minute.

Each cell type contains mitochondria according to its particular needs. Some cells have very few, photoreceptor cells have several thousand, and red blood cells have none. Lynn Margulis, the first wife of the late Carl Sagan, argued for the now well-accepted theory that mitochondria are descendants of bacteria that invaded early eukaryotic cells and stayed on in a symbiotic relationship. No longer capable of living outside the cell, mitochondria produce energy much more efficiently than the cell could previously, so it's win-win.

Mitochondria are independent in that they have their own genetic makeup, unrelated to that of the cell, and their own ribosomes. They therefore reproduce on their own (and know when to do so). Surprisingly, mitochondrial DNA has few genes that encode for its energy-making function. Most, 95 percent, appear to be involved in less well-defined duties, telling the cell how to build, use, break down, and recycle proteins, the workhorses of life. They also are involved in other processes, such as signaling, cellular differentiation, and control of the cell's life cycle.



Chromosomes and the Genetic Code

The cell nucleus contains billions of bits of genetic information that govern the minute chemical processes that constitute life. It encloses the 46 chromosomes of the human cell, each a single large molecule of deoxyribonucleic acid (DNA), usually spiraled around histone protein cores. The combination, together with strings of ribonucleic acid (RNA) and other proteins, is called chromatin. Squeezing the 46 chromosomes, totaling over two meters in length, into a nucleus that may be only 10 micrometers across requires extensive folding and compaction into packing units called nucleosomes.

Nucleotides and the Double Helix

Nucleotides are the building blocks of DNA. They comprise a deoxyribose sugar, a phosphate group, and one of four nitrogen bases—adenine (A), thymine (T), guanine (G), and cytosine (C), the “letters” of the DNA alphabet. A always pairs with T, and G with C. James D. Watson and Francis Crick, helped immensely by the X-ray crystallography work of Rosalind Franklin, determined that the pieces fit together in the shape of a twisted ladder, a clockwise-spiraling double helix (see illustration). The “rungs” of the ladder are formed by complementary pairs of nitrogen bases—AT,

TA, CG, or GC—joined lightly by hydrogen bonds. The number of pairs ranges from 51 million on the shortest chromosome to 245 million on the longest. The “rails” supporting the bases consist of alternating deoxyribose and phosphate molecules joined by ester bonds (oxygen-carbon linkage). The two complementary strands of DNA are anti-parallel, running in opposite directions. The total constitutes a chromosome. The story is told in Watson’s 1968 book, *The Double Helix*.

The most important feature of the double helix layout is that all the information in it is redundant. This is the basis of one-strand DNA repair. In this process a damaged or missing base is replaced using the information on the opposite strand. Also, when separated, each strand can serve as a template for making the other strand, since each nucleotide’s partner is known.

The chromosomes are usually in a relaxed state that looks like a stringy tangle, not the beautiful double helix pictured here. They are organized as 23 pairs. One pair determines the sex of the individual. Dubbed X and Y chromosomes, the sex-determining pairs are XX in a female (one from each parent) and XY in a male (X from the mother and Y from the father). The other 22 pairs are “twins” called autosomes. Chromosome pairs are not always close to each other, but can be made to form up neatly (e.g., for cell division) by some process that is not understood.

The Genetic Code

The genetic code is the set of rules by which information encoded in DNA specifies the sequence of amino acids that define a protein. Because the vast majority of genetic information is encoded using the same code, it is called the canonical or standard genetic code, or simply the genetic code, even though it is not universal. Mitochondria have a genetic code that varies somewhat from the canonical code. Specifically, the code defines a mapping between tri-nucleotide sequences called codons and amino acids, with codon triplets each specifying a single amino acid.

The DNA code must designate the 20 different amino acids used to create all the proteins a cell needs, plus a stop codon (all-purpose punctuation mark). The code is read along one side of the ladder, each half-rung providing a nucleotide “letter.” A single half-rung provides just one of four codes (A, C, G, or T); two half-rungs give 16 possible codes (AA, GC, TA, etc); and a triplet of half-rungs has 64 possible codes (AAA, CGG, TCA, etc.). Since only 21 are needed, the 64 codes result in considerable degeneracy (redundancy). All of them have a known function, with 61 coding for amino acids and the other three serving as a stop or termination signal for DNA “sentences.” There are multiple codons for most amino acids, with only methionine and tryptophan having a single codon. The degeneracy of the genetic code makes it more fault-tolerant for point mutations (base errors). Even so, single-point mutations can still cause dysfunctional proteins. One such causes sickle-cell disease.

Not all DNA genetic information is stored as the genetic code. DNA contains regulatory sequences, intergenic segments, and chromosomal structural areas, which can contribute greatly to phenotype (resultant effect) but operate using a distinct sets of rules which may or may not be as straightforward as the well-defined codon-to-amino acid relationship of the genetic code. A DNA chromosome has a very long repeated nucleotide sequence (TTAGGG, repeated), called a telomere, at each end, whose main purpose is to prevent accidental linking with another chromosome. Two other sequences are required for replication during cell division: a replication origin and a centromere.

Genes

A gene is not an object, but a region of DNA that controls a hereditary characteristic. Genes have effects upon bodies, eye color, hair crinkliness, strength of aggressive behavior, and thousands of other attributes, all of which are called phenotypic effects. A gene usually corresponds to a sequence used in the production of one specific protein or ribonucleic acid (RNA). Its biological information must be copied by a cell to all its progeny. This includes the entire package: coding DNA sequences, non-coding gene-regulatory sequences, and non-functional sequences. Genes range in length from about 150 base pairs (e.g., the gene for insulin) to well over two million (e.g., the gene for dystrophin). The estimate for the number of genes in humans has decreased as our knowledge has increased, from 100,000 to perhaps as few as 20,000, with 25,000 now a commonly-accepted number. Polygenes are groups of interactive genes whose effects are additive.

The Human Genome

In vertebrates such as humans, "genome" carries the typical connotation of total chromosomal DNA. Although mitochondria have genes, they are not considered part of the human genome's three billion nucleotide pairs. A normal human cell has two copies of the genome, one from each parent, for a total of six billion base pairs. This digitally coded database is larger, in potential information content, than all 30 volumes of the Encyclopedia Britannica, three or four times over. However, only a few percent of that capacity is utilized. No one knows for sure why the rest, non-coding sequences often called "junk DNA," is there, but there seems to be evidence that parts of it may not be junk. About 8% of junk DNA consists of self-replicating virus-like DNA particles that infected our ancient ancestors.

An organism's complexity is not directly proportional to its genome size; some single-cell organisms have much more DNA than humans. Dogs and chickens have 78 chromosomes, 39 pairs. Crayfish have 200. It is interesting that chimpanzees share 98.9 percent of the human genome. They have an extra chromosome pair, but one human pair (chromosome 2) appears to be a fusion of two previously separate pairs because it has two centromeres instead of one.

Reading the Genome and Gene Expression

In the reading of a gene's codes, each "address" of paired autosomes offers alternative "letters." Sometimes these "alleles" are identical. If not, one reading might prevail over another, e.g., one ("dominant") leading to brown eyes, the other ("recessive") vainly specifying blue eyes. Sometimes, however, an alternative reading leads to some sort of compromise, resulting in a modified gene or something completely different (green eyes?)

Genes can not only be expressed (activated), but can be switched on and off. As scientists discover more about the epigenome ("above the genome"), a layer of biochemical reactions involving methyl molecules that turn genes on and off, they're finding that it plays a big part in health and heredity. Methyls are carbon-hydrogen molecules that affect gene activity. Modified or loosened by epigenetic factors, histones boost or inhibit gene expression. DNA tightly bundled around histones tends to shut down, its genes unexpressed. If histones are loosened, genes are expressed. Different molecules can attach to the dangling "tails" of histones, altering the activity of the DNA wrapped around them. Some attach directly to the DNA.

The epigenome tells genes what to do when and where. The epigenome can cause a gene's effect to be different according to whether it originated in the father's genome or that of the mother. Although twins have identical genomes, epigenetic differences can cause dramatic effects, such as one twin becoming autistic and the other quite normal. Exposure of DNA to methyls is believed to play an important role in

biological development because it restricts genetic information that will be passed along when cells divide and multiply.

The epigenome can be affected by environment, such as maternal behavior during early fetal or child development. It can even be affected during the formation of eggs and sperms. A poor environment can lead to stress, depression, drug abuse, diabetes, obesity, even heart disease in the adult, all possibly due to epigenetic factors. It follows that people should behave responsibly when creating and rearing children, ensuring that the epigenome remains “healthy.”

As cells divide over the years, epigenetic errors can creep into the new cells, with cancer a possible result. This is also one cause of aging.

Transposons

Transposons (“jumping genes”) are DNA segments that can hop around to different positions, sometimes interfering with active genes. They are classed as mutagens, and can damage the genome of the cell in different ways. They were discovered by Barbara McClintock in the 1940s and 1950s, earning her a belated Nobel prize in 1983. The most common form of transposon in humans is the Alu sequence, about 300 bases long. Over the past 65 million years, the Alu sequence has multiplied via an RNA-mediated transposition process until now there are hundreds of thousands of copies making up about 5 percent of the human genome. Diseases that are often caused by transposons include hemophilia A and B, severe combined immunodeficiency, porphyria, predisposition to cancer, and Duchenne muscular dystrophy. Their persistence in the human genome suggests that they may have good effects also, but why are there so many?

Mutations

Chromosomes have a limited lifetime, but their patterns tend to endure unchanged in replacement cells. Occasionally exposure to toxins, a cosmic ray, or malfunctions of cellular processes, among other things, may affect the DNA. Such changes, called mutations, over long time periods may let organisms adapt to new surroundings—or make them die out. However, they may not get started. Richard Dawkins writes (*The Blind Watchmaker*, 2006) that 5,000 DNA nitrogen bases degenerate per day and are immediately replaced by maintenance enzymes that recognize and fix the damage. The DNA is also protected by DNA-binding proteins like histones, which compact and organize DNA. These compact structures guide the interactions between DNA and other proteins, helping control which parts of DNA are transcribed.

Further information from *The Blind Watchmaker*: One source of mutations is a mistake in the DNA copying process during cell division. Copying is unbelievably reliable, but rarely a mistake may creep in. Cows and peas differ from each other in only two DNA “letters” of the 306 that define their histone H4 gene (humans also have H4). Their common ancestor, perhaps 1.5 billion years ago, must have had that same gene. How often has it been copied? Probably as many as 20 billion times. That’s pretty good copying. However, it could be that there were many more mistakes, and the mutant organisms either did not survive or did not reproduce. Character-copying fidelity can be measured, and it comes to one mistake in a billion copies. The difference between this, the mutation rate, and the lower rate of the mistake’s survival over time, is a measure of the effectiveness of natural selection in weeding out harmful mutations. Put another way, it takes five million generations to miscopy one percent of the characters. However, the DNA-copying mechanism has error-correcting capability, and many errors are

caught. Pseudogenes look like functional genes but contain many mutations that prevent their normal expression. Most come from the duplication of a good gene followed by the accumulation of damaging mutations in one copy.

Here is one way correction works: Every DNA molecule is composed of two strands. When a cell detects a defective "rung," that duplex is "repaired" by chopping out the entire region from both strands. No effort is made to determine which strand is correct. The gap is then filled by copying the same region on the other chromosome of the pair. All this editing happens when the two versions of the chromosome are paired closely together in the early stages of gamete (egg and sperm) formation. Some genes change at a high rate, with mutations that endure. Fibrinopeptides (produced during the clotting of blood) are an example, changing at a rate that matches the mutation rate. This means that the mistakes don't matter much, and natural selection therefore plays no part. Others, like the H4 gene, change rarely because mistakes tend to be corrected, either in the cell or by the process of natural selection.

The Sex Chromosomes

Human females inherit two copies of every gene on their two X chromosomes, whereas males inherit only one copy on their single X chromosome, except for "pseudoautosomal" genes (29 found so far) and a small number of "housekeeping" genes found on the Y that have counterparts on the X. The pseudoautosomal regions get their name because any genes located within them are inherited just like autosomal genes. Males have two copies of these genes: one in the pseudoautosomal region of their Y, the other in the corresponding portion of their X chromosome. That means a male can inherit an allele originally present on the X chromosome of his father and a female can inherit an allele originally present on the Y chromosome of her father. With only one X chromosome, are males at a disadvantage in the amount of gene product their cells produce? The answer is no, because one of the female's X chromosomes (from father or mother, no telling which) is inactivated for genes unrelated to sex characteristics. Inactive X chromosomes are called Barr bodies. What about those few genes that are found on the Y as well as the X? As it turns out, these genes somehow escape inactivation in females.

The X Chromosome

The X chromosome carries hundreds of genes, with few having anything to do directly with sex. However, the inheritance of these genes follows special rules. These arise because:

- Males have only one X.
- Most genes on the X have no counterpart on the Y.
- Any gene on the X, even if recessive in females, will be expressed in males.

Genes inherited in this fashion are called "sex-linked" or "X-linked." That is why women are frequent carriers of recessive X-linked traits (e.g., hemophilia) that are not expressed in their own phenotypes but have a 50-50 chance of being expressed in each son.

The Y Chromosome

The much smaller Y chromosome has far fewer genes (less than 100) than the X chromosome. Most are involved with essential cell house-keeping activities and sperm production. One of the former group encodes a component of ribosomes, meaning that every ribosome in a man's body is slightly different from those in a woman's. When any of the genes involved in sperm production are missing or defective

the result is usually very low sperm counts and subsequent infertility. One in six American couples is infertile. It is now thought that about one-third of those are unable to have children because the male lacks the necessary sperm-producing genes on his Y chromosome. *SRY* (for sex-determining region Y) is a gene located just outside the pseudoautosomal region. It is the master switch that triggers the events that convert the embryo into a male. Without this gene you get a female, so femaleness is the "default" program. If it is missing or defective, male anatomical traits will not develop, but other traits (e.g., androgen and testosterone levels) may. Due to hormone differences, as many as 15 percent of other genes are more active in one sex than the other. These considerations give Olympic organizers a big headache: "Should this athlete be considered a man or a woman?"

The Y chromosome, passed on only through males, does not participate in any significant exchange with the male's X chromosome. It remains unchanged down through the generations of men, except for rare mutations called markers. This fact has allowed geneticists to determine that every man has a single male ancestor (down the patriarchal line) dubbed Adam, who lived in east Africa about 60,000 years ago. The descendent lines of other men who lived at the time have died out. That number is based on an assumed mutation rate, and could be off by quite a bit. No, not by enough to get it down to a biblical number, as some web sites claim.

If most of the Y chromosome cannot pair with the X chromosome, how does it avoid the accumulation of mutations? The answer is that most of the active genes on the Y chromosome lie within eight vast palindromes, regions of the DNA that repeat sequences, but backwards. A palindrome has a very neat property: it can bend back on itself, forming a hairpin in which the two strands are aligned with nearly identical DNA sequences. This is the same sort of situation--alignment of nearly identical stretches of chromosomes--which permits the copy-edit of the X chromosome. Thus in the Y chromosome, mutations can be "corrected" by conversion to the undamaged sequence preserved on the other arm of the palindrome.

RNA and Protein Synthesis

Ribonucleic acid (RNA) is a nucleic acid consisting of a long chain of nucleotide units. RNA is very similar to DNA, with a four-letter alphabet, but differs in a few important structural details: RNA is usually single-stranded, while DNA is usually double-stranded. RNA nucleotides contain ribose while DNA contains deoxyribose (a type of ribose that lacks one oxygen atom), and RNA has the base uracil, rather than the thymine of DNA, to pair with adenine. RNA is central to the synthesis of proteins. It is fairly certain that DNA is descended from RNA, which has all the essential means of storing and expressing genetic information. However, the single-stranded RNA is unstable and easily damaged by enzymes. By doubling the RNA molecule and using deoxyribose sugar instead of ribose, DNA became able to pass on genetic information to the next generation with great reliability.

Enzymes

An enzyme is a catalytic protein, meaning one that assists in a chemical reaction. Enzymes are formed by stringing together between 100 and 1,000 amino acids in a specific unique order (as dictated by DNA), separated by peptide bonds. The chain of amino acids then gets folded into a unique shape. That shape allows the enzyme to act as a very efficient catalyst for speeding up a specific chemical reaction. Such reactions allow the cell to build things or take things apart as needed. This is how a cell grows and reproduces. There is a specific enzyme for each chemical reaction needed to make the cell work properly. For example, the sugar maltose is made from two glucose molecules bonded together. The maltase enzyme is shaped in such a way that it can break the bond and free the two glucose pieces. That

is all it can do, but it can do that very rapidly and efficiently. Other types of enzymes can put atoms and molecules together. Some have structural or mechanical roles, like microtubules in the cytoskeleton or myosin in muscle. There are a million enzymes in a typical cell, 2,000 kinds, giving the cell its particular shape and behavior. At the most basic level, a cell is really a little bag full of chemical reactions that are made possible by enzymes!

Messenger RNA

Protein synthesis generally consists of two major steps: transcription and translation. A gene contains both "coding" sequences that determine what the gene does, and "non-coding" sequences that determine when the gene is active (expressed). When a gene is active, its coding and non-coding sequences are transcribed by an enzyme called RNA polymerase. It reads the DNA's genetic code and produces a complementary RNA strand that will become messenger RNA (mRNA). The genetic code as transcribed is for RNA's code, not that of DNA, with T (thymine) replaced by U (uracil) as the transcription goes along. Introns, derived from the term "intragenic regions," are DNA regions within a gene that are not translated into proteins. Introns are present in precursor mRNA (pre-mRNA) and some other RNAs, and are removed by a process called splicing. After intron removal, the mRNA consists only of cleaned-up "exons" containing the information for the primary sequence of amino acids in a protein to be synthesized. The splicing process may have some indirect effect on the gene's expression. The mRNA is then free to migrate out of the nucleus.

Enzymatic RNA

Scientists have learned that RNA, and not just proteins, can act like an enzyme. Yale researchers obtained the first X-ray crystal structure of this "enzymatic" RNA. The image caught an RNA molecule as it spliced together two exons, the parts of a gene that code for proteins. Also visible in the image were a full-length noncoding intron and metal ions bound in the molecule's active site. This RNA acts like an enzyme so it can overcome an inherent hindrance to protein synthesis—the intron that separates the exons. With the help of the metal ions, the RNA connects the exons and removes the intron sequence. "This is the first RNA splicing complex to be visualized in molecular detail," said Scott A. Strobel, Ph.D., professor of molecular biophysics and biochemistry, and principle investigator of the study published in the journal *Nature*.

Transfer RNA

The mRNA moves the information contained in DNA to the cytosol. There the codes are again translated into amino acids by ribosomes, themselves consisting partly of a second type of RNA, transfer RNA (tRNA), with the mRNA acting as an adaptor. The tRNA contains about 75 nucleotides, three of which are called anticodons, and one amino acid. The tRNA reads the code and carries the amino acid to be incorporated into the developing protein. There are at least 20 different tRNA's - one for each amino acid. Part of the tRNA doubles back upon itself to form several double helical sections. On one end, a specific base triplet, called the anticodon, is used to actually "read" the codons on the mRNA. The reading is done by matching the base pairs through hydrogen bonding following the base-pairing principle. Each codon is read by various tRNAs until a match of the anticodon with the codon occurs, whereupon the amino acid specification is passed on to a ribosome.

Ribosomal RNA

Ribosomal RNA (rRNA) is the central component of ribosomes, the synthetic factories in the cell. It includes four different rRNA strands. Three of them are produced in the nucleolus (by chopping up one long strand), and one is produced outside and joins the others in the nucleolus. Ribosomal proteins from the cytosol enter the nucleolus and combine with the four strands to create the two subunits that will make up the completed ribosome. The subunits leave the nucleus through the nuclear pores and unite in the cytosol to form a ribosome. An average healthy cell can produce up to 10,000 ribosomes per minute,

and must have on hand about 30,000 proteins at any one time. The rRNA molecules are extremely abundant. They make up at least 80 percent of the RNA molecules found in a typical cell. The ribosome carries the enzymes necessary for protein synthesis. Once the backbone amino acids supplied by tRNAs are polymerized into a protein, the ribosome releases the protein and it is transported to the Golgi apparatus. The ribosome also attaches itself to mRNA and provides the stabilizing structure to hold all substances in position as the protein is synthesized. Several ribosomes may be attached to a single mRNA at any time.

microRNA (extract from the Smithsonian magazine, July 2009)

Most RNA is short-lived, serving as a mere messenger or intermediary in the construction of proteins. A tiny gene, only 70 bases long, does not make protein, as other genes do. Instead, it makes another kind of genetic material, which is now called microRNA. It is the gene's end product, and no mere messenger, as it suppresses the uncontrolled growth of cells, which we call cancer. "In probably every human tumor there are alterations in microRNA," says discoverer Carlo Croce, head of the Human Cancer Genetics Program at Ohio State University. These tiny molecules exert so much influence over the rest of the body that they are suspected of being involved in immune system, heart disease, schizophrenia, Alzheimer's disease, and Tourette's syndrome. Scientists estimate that humans have around 1,000 microRNA genes, which seem to control at least a quarter of our 25,000 or so genes.

Other RNAs

Small nuclear RNA (snRNA) is the name used to refer to a number of small RNA molecules found in the nucleus. These RNA molecules are important in a number of processes including RNA splicing (removal of the introns from nascent mRNA) and maintenance of the telomeres. They are always found associated with specific proteins and the complexes called small nuclear ribonucleoproteins (SNRNP), sometimes called snurps. RNA interference (RNAi) is a mechanism that inhibits gene expression at the stage of translation or hinders the transcription of specific genes. RNAi's targets include RNA from viruses and transposons, and it also plays a role in regulating development and genome maintenance. There are RNAs with other roles – in particular regulating which genes are expressed.

Heat Shock Proteins

A protein must not only have the right shape, but must also get to the right place at the right time. Heat Shock Proteins (HSPs) guard proteins from going astray in shape or destination. Those not folded properly are worked into the proper shapes. HSPs may also chaperone them to larger protein structures. HSPs are of great help to the immune system. They bring antigens from diseased cells to the attention of killer T-cells, who then know to seek out diseased cells and destroy them.

Cell Division

Mitosis

Cells divide in two different ways, mitosis and meiosis. In mitosis, the cells merely duplicate themselves, either to propagate more cells or to replace cells that are worn out. The cell first grows to a size that can support division and DNA replication, while maintaining its normal activities and doing some housecleaning. The first step in DNA replication is the separation of the two DNA strands that make up each chromosome. An enzyme called DNA helicase untwists the helix to form a Y shape called a replication fork. The replication fork moves down the DNA strand, splitting it down the middle into two single strands with "half rungs" of one nucleotide each. Next, an enzyme called DNA polymerase helps

new nucleotides line up next to the two separated strands, according to the rules of base pairing: adenine with thymine, and guanine with cytosine. These complete the “rungs” of two new chromosomes that are identical to the original. The process is repeated for each chromosome.

The duplicate chromosomes are joined near the middle by their centromeres, resulting in an X-shaped structure. The nuclear membrane disappears. The two centrioles move to opposite ends of the cell while a fan-like array called the mitotic spindle forms between them. When the spindle is completely formed, the spindle fibers align all the chromosomes at the center of the nucleus. Then they help to pull the duplicate chromosomes apart and push each group to opposite ends of the cell. The two groups are then surrounded by a protective envelope, thereby establishing two nuclei in the one cell. The chromosomes relax and resume their usual appearance of stringy tangle. The spindle fibers disintegrate and a nucleolus forms inside each nucleus. When the two nuclei reach opposite ends of the cell, the cell pinches in the middle, and final cleavage ("cytokinesis") happens. The result is two cells identical with the original one (but genes may operate differently). Besides the chromosomes, organelles have also been duplicated. Mitochondria multiply on their own to give each cell its needed number.

Meiosis

Meiosis is the type of cell division by which germ cells (eggs and sperms) are produced. It differs from mitosis in that chromosomes are duplicated without dividing them and there are two cell divisions, resulting in four cells that each have 23 unpaired chromosomes. First, the chromosomes are condensed and duplicated as in mitosis. Chromosome "homologous" pairs (one chromosome from each parent) form synapses, a step unique to meiosis. The paired chromosomes are called bivalents, and the connecting "chiasmata" enables the swapping of a portion of DNA between the two (but very little between the X and Y chromosomes). The process is called "recombination." The recombined chromosomes still have the same genes, but associated alleles may differ. That is the source of genetic diversity, which plays a huge role in the survival and adaptability of a species. Then cell division results in two cells, each with a full set of the 23 homologous pairs. With no further DNA change, the chromosomes are aligned in each cell, homologous pairs are separated, and each of the four resultant chromosomes ends up in one of the four cells resulting from a second division. In the male, each cell becomes a sperm, half with an X chromosome and half with a Y. In the female, the four resultant cells each have an X chromosome. Only one cell will become an egg, while the other three become "polar bodies," deficient in cytoplasm and organelles, slated for eventual destruction.

Fertilization and Development

The average human ejaculate contains around 180 million sperm. Each sperm cell is heterogametic, meaning it contains one of two sex chromosomes (X or Y). The female egg is homogametic, with all eggs having an X chromosome. While all a female's eggs are already in her body before birth, the male sperms are produced after puberty sets in. The male “determines” the sex of the child by the particular sex chromosome contained in the fertilizing sperm. If an X, the child will be female, with two X chromosomes. If a Y, it will be a male with one X and one Y.

When a sperm reaches and fertilizes the egg, their chromosomes combine to form a zygote with the full set of 46, but with a new combination of DNA distinct from either parent. The mitochondria from the sperm no longer function, so only the female mitochondria are passed on. They remain unchanged down through generations of women, except for rare mutations. This is analogous to the Y chromosome, transmitted only through males, except that both male and female zygotes get the female's

mitochondria. The entire human race (men and women) has a single female ancestor (down the matriarchal line) dubbed Eve, who lived in Africa perhaps 200,000 years ago (a more recent study says 150,000). While there were no doubt many other females at the time, evidence from our mitochondria shows that all their lines died out and only Eve's survived.

After a while the zygote divides mitotically, and divisions continue. The early cells are "stem cells," capable of becoming any type of cell. Then the cells start differentiating during division, as different chemicals congregate at each end of the dividing cell. These activate or modify genes' expression, gradually designing cells for their ultimate roles. We now know that differentiated cells can be "reprogrammed" to go back down the development chain until they are pluripotent, meaning they are like embryonic cells in having the capacity to evolve into many cell types.

Bacteria

While strictly speaking perhaps not part of the human body, the single-celled bacteria harbored in it greatly outnumber the body's cells, perhaps 10 times over. Some are beneficial, in fact essential to our existence, some are harmful, and some have no effect. They range from 300 to 1,000 species in the large intestine to two species of Demodex mites ("eyelash mites") living in the follicles of most eyelashes, especially those of older people. Don't worry, they're generally harmless. The human mouth is home to around 300 species of bacteria, with a few fungi and protozoa thrown in for good luck. There are more bacteria in the mouth than there are people on earth (a good argument for not "double-dipping" chips on the appetizer table). How do bacteria get into the body, since they are surely not present in the fetus? Answer: The newborn quickly acquires them from air breathed in, especially human breath, from milk ingested, and from other sources.

Conclusion

The human cell is obviously very complicated and deserves to be known for what it is: a prime example of how natural selection can give the appearance of highly ingenious deliberate design. In view of the clumsiness of some of its features, such as the multiple Alu sequences, pseudogenes, transposons, genetic disorders, and the need for help from a guest bacterium to produce adequate ATP, we cannot say the design is perfect--but it's awfully good. One of its seeming defects, occasional imperfect replication, sometimes harmful, makes evolution possible. Error-free copying would mean no changes in progeny and therefore no evolution.