Genetics: Present & Future

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When you plant a mango seed you always get a mango tree growing from the seed, never a coconut tree and vice-versa you never have a mango tree growing from a coconut. The reason for this is the genetic code that is embedded inside the seed that carries the blueprint for what type of a tree it should grow into. The same applies to all living organisms. The term "genetics" is an ancient greek term used to describe the study of the science of genes, heredity and variation in living organisms. The investigation of single genes is the primary focus of genetics, identified by some as "molecular biology". This is in comparison to genomics which involves studying the whole genome or complete set of genes found in an organism. Modern genetics was started by Gregor Mendel, a monk and scientist who traced the inheritance patterns of certain characteristics in pea plants and explained them through simple rules and ratios. Even though Mendel started this work in the mid 19th century, it was only in the early 20th century that the importance of his work was understood and the term "genetics" was used and popularized by William Bateson.

Later on in the 20th century, DNA or deoxyribonucleic acid was identified in 1944 by Avery, McLeod and McCarty as being responsible for transferring "genetic material". Then in 1953 the famous duo Watson and Crick determined the structure of DNA, the now familiar double helix shown in figure 1. As depicted the string of DNA is composed of sugars (blue pentagons), phosphates (cream-colored circles) and four types of nucleotides: Adenine (A), cytosine (C), guanine (G) and thymine (T). The A & T form two hydrogen bonds and G and C form a triple bond to form what is known as base pairing to assemble the double helix. All genetic material (other than in some viruses) exists as a combination of these four nucleotides with base pairing in a double helix and form the alphabet of all genomes, which is an organism's complete length of DNA. For example the human genome consisting of over 3 billion nucleotides, has various combinations of these A, C, G and T's. Only 22,000 to 25,000 genes are found encoded within the human genome. However, these genes only cover 2% of the 3 billion base pair genome and the remainder consists of non-coding regions which contain among other things, regions that regulate gene expression. To make things more interesting it was discovered that 99.9% of the genome is similar in all humans and our genome is 99% similar to the chimpanzee! Further details of the human genome project can be found at the following website: http://www.ornl.gov/sci/techresources/Human_Genome/home.shtml.

As outlined in figure 2 the genes carry the information that forms proteins that perform the various functions in the cells. The figure depicts the hemoglobin gene as

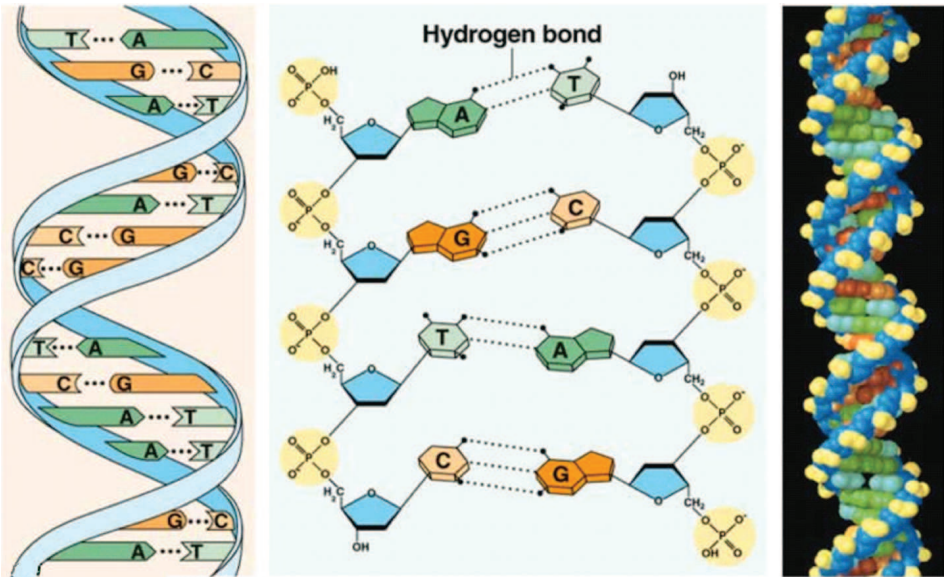

Figure 1

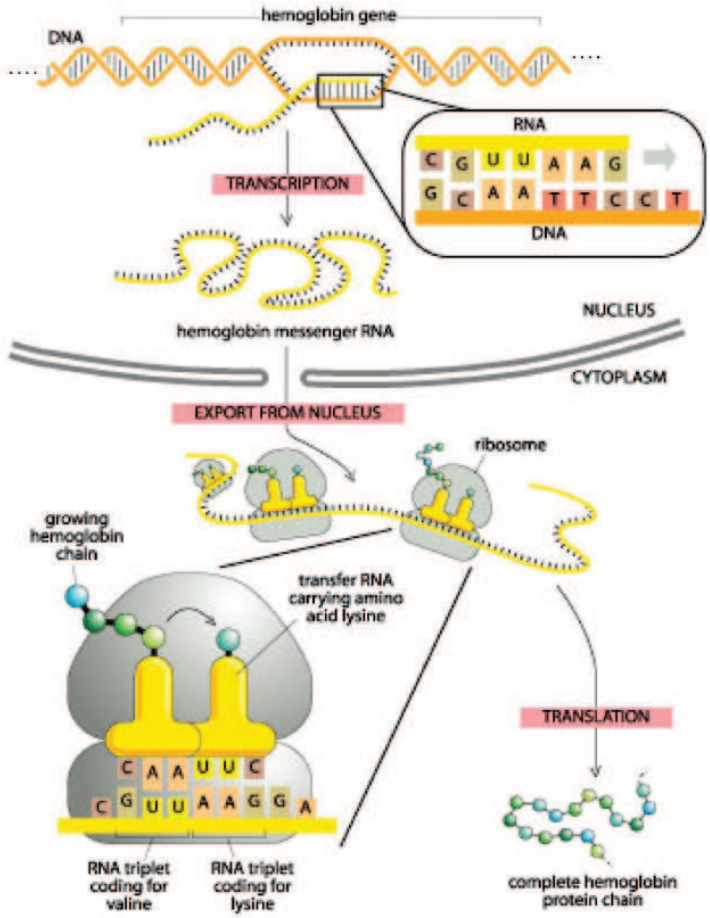

Figure 2

an example. In essence the proteins are the real work horses of each cell, giving each cell its form and function. As geneticists started to understand how to decipher the genes and the genomes of organisms, they increasingly started to study the functions of individual genes and the proteins that are eventually made from the instructions given in these genes.

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Procedures and discoveries that changed the field of Genetics

A number of discoveries have changed the field of genetics allowing it to expand in leaps and bounds to be at the advanced state it is in today.

One of the major developments was the ability to read the DNA molecule using chain termination DNA sequencing. This method was developed by Frederick Sanger in 1977. This revolutionalized the field and allowed scientists to read the nucleotide sequence of DNA molecules and identify genes. More details about this method can be found at this web site: http://jgi.doe.gov/education/how/

Currently, there are instruments that allow this type of sequencing in Sri Lanka at universities and private sector laboratories.

Another major development is the development of a technique called "polymerase chain reaction" or PCR. This method allows one to make millions or even billions of copies of a particular DNA sequence starting from just a few copies. While this method is a combination of several well established reactions no one had really tried it until Kary Mullis developed it in 1983 and won the Nobel prize for it in 1993. His Nobel lecture is interesting reading for scientists as well as non-scientists and can be found at this site: (http://nobelprize.org/nobel_prizes/chemistry/laureates/1993/mullis-lecture.html). This procedure which allows us to bypass the need to use bacteria for amplifying DNA is quicker and more convenient than using bacteria. PCR has become one of the most widely used indispensible techniques in medical and biological research laboratories for a wide range of applications. This includes the detection of various infectious agents, such as bacteria and viruses, the diagnosis of hereditary diseases and even genetic finger printing for paternity testing and forensics. As mentioned before it is a very powerful technique which allows us to amplify tiny amounts of

DNA to a large enough amount for other uses. Due to the lack of space I will not be going into detail in this article, but the following website explains the method in detail: www.dnalc.org/resources/animations/pcr.html

that have been completely sequenced and these sequences are available online at the following site: www.ncbi.nlm.nih.gov/sites/genome

We currently have the knowledge to identify a useful gene, clone it into bacteria and then express it to make the protein. Many useful proteins are made in this manner. One prominent example is insulin for diabetics. It used to be that insulin was purified from pigs for use in humans and this was very costly since one pig only gave a small amount of insulin. However, by cloning the gene and expressing it in bacteria or other types of cells we are able to make large amounts of insulin at a very cheap cost.

A number of laboratories in Sri Lanka do PCR-based diagnostics for various pathogens that cause Dengue, tuberculosis and HIV among many others. Even though the technique maybe relatively expensive it is fast and accurate.

Present

These above mentioned techniques among others have allowed us to understand the different genes and genomes to a level that has not been possible before. The field of genetics has rapidly moved forward and currently whole organisms are being sequenced and their genomes are freely available online for use by scientists and others. Table 1 depicts a list of genomes

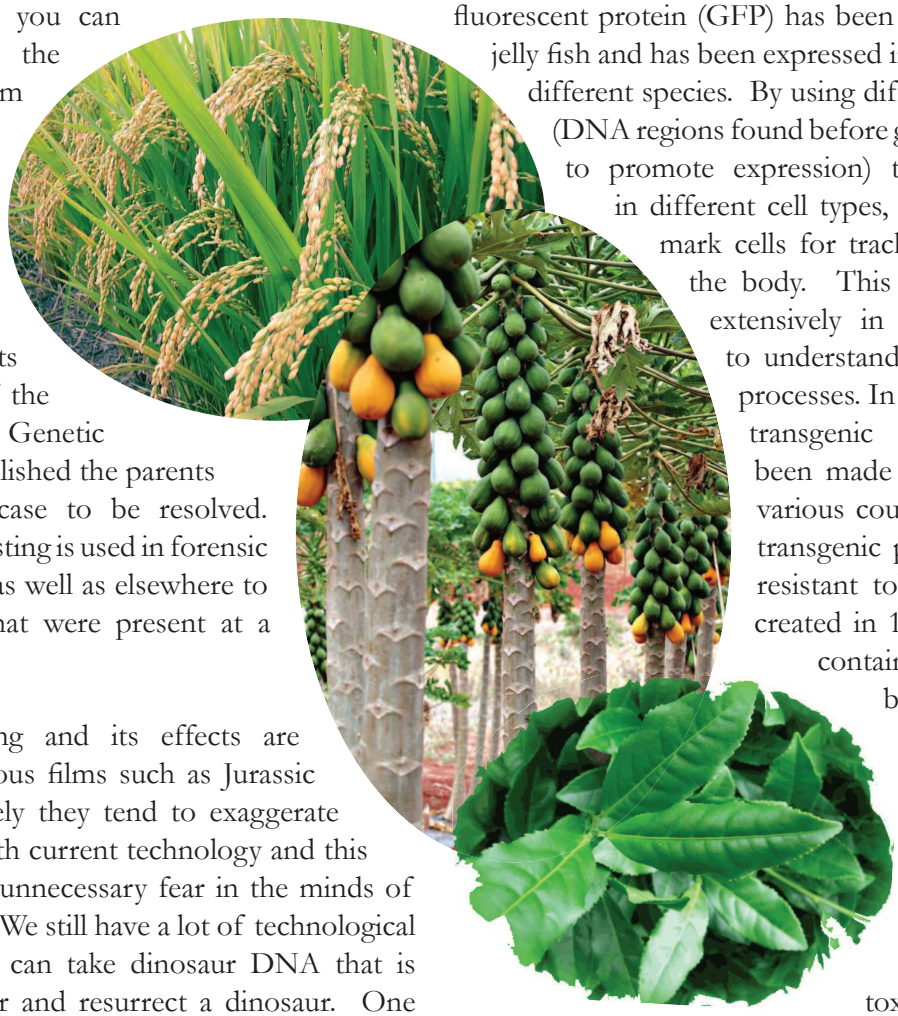
Table 1 Genomes that have been sequenced and the year of completion

- The first complete sequence of an organism – *Haemophilus influenzae* (1.8 Mb) - 1995
- *S.cerevisiae* bakers yeast (12.1 Mb) – 1996
- *C.elegans* round worm (97 Mb) -1998
- *D. melanogaster* Fruit fly (180 Mb) -2000
- *Arabidopsis thaliana* Weed (125 Mb) Dec 2000
- *H. sapiens* (3000 Mb) – Draft sequence 2001
- *Plasmodium* genome - 2002
- Rice genome - 2005
- Corn (Maize) - 2008

Knowing the unique DNA sequence of various organisms allows us to specifically identify them using techniques such as PCR. Molecular based diagnostics allows us to identify various pathogens. A number of laboratories in Sri Lanka do PCR-based diagnostics for various pathogens that cause Dengue, tuberculosis and HIV among m any others. Even though the technique maybe relatively expensive it is fast and accurate. Further detailed genetic studies of such pathogen strains allow more information about the pathogen to be gathered and valuable epidemiological data can be obtained. Knowing the sequence of human genome has also allowed doctors to identify changes in our genomes that make us vulnerable to various diseases. A specific mutation in the hemoglobin gene can cause sickle cell anemia and this can be identified using a genetic test. Cystic fibrosis, Down

syndrome and Muscular dystrophy are some of the debilitating disorders that can be identified by genetic tests even before the disease is apparent. Increasingly more mutations in genes are being identified that lead to increased susceptibility to various other diseases including cancers.

Another aspect of genomics that directly touches our lives is the ability to establish paternity in humans. By genetic testing you can confirm whether the child is really from those parents. The most well known paternity case in Sri Lanka was that of baby 81 who was claimed by a number of parents in the aftermath of the tsunami in 2004. Genetic testing clearly established the parents and allowed the case to be resolved. Similarly, genetic testing is used in forensic cases in Sri Lanka as well as elsewhere to identify persons that were present at a crime scene.



Genetic engineering and its effects are highlighted in various films such as Jurassic Park. Unfortunately they tend to exaggerate what is possible with current technology and this tends to create an unnecessary fear in the minds of the general public. We still have a lot of technological hurdles before we can take dinosaur DNA that is preserved in amber and resurrect a dinosaur. One needs to understand that having only the DNA is not sufficient and that we need the proper environment for the proteins to get transcribed in the proper sequence to make the proper organs at the correct time. This is much more complicated and humans have not been able to take DNA from an animal and have it grow into an organism without the proper "cells" from the same species to implant the DNA. Dolly the transgenic sheep that we have all heard of was done in a similar manner; the DNA was put back into egg cells from another sheep. Therefore we are still a long way away from making dinosaurs!

Even though we cannot create dinosaurs we are starting to insert useful genes into different organisms that can serve a useful purpose for humans. Such organisms are called "transgenics" and both transgenic animals and plants have been constructed. The gene of the green fluorescent protein (GFP) has been cloned from the jelly fish and has been expressed in various cells of different species. By using different promoters (DNA regions found before genes in genomes to promote expression) to express GFP in different cell types, they are used to mark cells for tracking them inside the body. This method is used extensively in transgenic mice to understand basic biological processes. In addition, various transgenic plants have been made and are used in various countries. The first transgenic plant, a pesticide resistant tobacco plant was created in 1983. This plant contained genes from a bacterium, (*Bacillus thurengiensis*) that kill insects, thus creating a pesticide resistant plant, preventing the need to spray toxic chemicals to kill the insects. Similarly one of the most successful genetically engineered (GE) crops currently in use is the Roundup (herbicide) resistant gene inserted in crops. Monsanto (the US company that developed it) have turned this product into a very profitable business since they also manufacture the herbicide Roundup (active ingredient is Glyphosate). This transgenic plant allowed farmers to stop the growth of other weeds by spraying the whole area

with Roundup, thus stopping weeds from growing, but not affecting their crop. Countries such as the United States have widely adopted GE crops. This is to a point where in 2010, 93% of Soya beans and ~75% of cotton plants grown in the US were GE crops. However, most of Europe has prevented the use of GE crops and until 2006 the European Union had a formal ban on GE crops. Now it is allowed in very limited areas, but heavily regulated. China was one of the first countries to allow the use of GE crops, while India has more recently approved the use of some GE crops, such as transgenic cotton.

Future

The field of genetics has matured to a level that many different areas rely on the information (or the DNA coding information) found in the various genomes. We are rapidly approaching a point where within the next few years almost all organisms that are of importance to humans would have been completely sequenced providing all the genetic information for further studies. Once this information is available the next step will be how we harness the knowledge to our benefit. Already one sees this happening in various areas.

While the use of GE crops has been widely successful in countries such as the US, it has not been adapted as widely in countries such as Sri Lanka and India with small farming plots and a bigger diversity of pests. But considering the growing demands for increased food production, pollution problems and production efficiencies, GE crops may need to be seriously considered as an option in the future.

Transgenic animals are another new area that is expanding due to new knowledge of genetics. Scientists have recently made a goat (named "Sweetheart") that has the human gene, antithrom bin, inserted in its genome. This allows antithrombin to be produced in its milk and can be easily purified for human use. This is the first drug produced in the milk of a genetically engineered animal that has been approved by the US Food and Drug Administration. The amazing thing about this is that we have done away with all the previous manufacturing facilities that were needed and once the goat is produced all you need to do is feed the goat and milk it. You need some expertise to purify the antithrombin from the milk and each goat can annually produce the equivalent of what we get from 90,000 blood donations. If it is necessary to expand production you breed the transgenic goats. This is the future of high end manufacturing of protein-based biopharmaceuticals.

What does Sri Lanka need to do to build up resources and take advantage of the knowledge offered in the field of genetics

Educate people about the true benefits of genetics and have them understand genetic engineering and its true potential. This will go a long way in making the benefits of genetics research widely available to the population. One such example is paternity testing in which the Police, Judicial officers and others in the field have been educated about the benefits and the relevant information has been disseminated. As a result the man or woman on the street accepts the results and trusts the result that is given from this paternity testing.

Provide grants and funding for setting up sequencing facilities and databases to genetically characterized plants and other living organisms found in Sri Lanka.

This should be setup as a complement to existing institutes such as the Plant Genetics Resource Center in Peradeniya and other Research Institutes in Sri Lanka.

The next step is training bioinformaticians and setting up databases for accessing the information as the need arises. Such a program is already being done by the Human Genetics Unit at the Medical Faculty Colombo for various human genetic variations found in the Sri Lankan population. Such databases can be expanded to include our indigenous plants and other unique organisms such as bacteria, and this will help to prevent piracy and protection of our indigenous resources.

As shown in table 1, many of the important plant species and animals have already been sequenced and the data is freely available. All the major Sri Lankan crops such as tea, rubber, coconut and rice have been sequenced. This knowledge can be harnessed to look at other varieties of the same species found in Sri Lanka and elsewhere. One such example is rice, in which Sri Lankan scientists can look for changes in genes in our local varieties which may have enhanced useful characteristics such as drought tolerance. Once the presence and sequence of such genes are known they can be bred into the more popular varieties of rice. This has been traditionally done in all the crops using phenotypic characterization (not using genetics) and takes a long time to develop a new variety. By using genetics and gene marking techniques such as "marker assisted selection", one can reduce the time period to generate the new strains. Focused research with adequate funding can thus drastically increase the number of new varieties and allow us to obtain them faster to be given to farmers.

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Another area that needs to be developed is the regulatory authorities for handling GE foods and plants that will inevitable come to our shores. Countries such as Sri Lanka have to setup the proper regulatory authorities with personnel knowledgeable on the science as well as social and economic aspects before the adaptation of genetically engineered crops. Even though the science is relatively clear, the economics and social aspects of adaptation of these GE crops has to be evaluated and thought out. Even though certain efficiencies can be gained by having GE crops it may upset the export markets (example; tea) we have carefully developed over the many years.

The field of genetics has developed rapidly over the last few decades and a proper understanding of these advances combined with the proper adaptation of new technologies can bring vast benefits to the people of Sri Lanka. It is the job of scientists and teachers to make sure the larger population understands this and accepts the vast benefits that this field can bring to Sri Lanka.

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