LESSONS from the Revolution of Molecular Biology

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"Freedom of access to scientific information will be critically important for Asian science and technology towards 21st century"

1. *Characteristics of changes in 20th century science : Information explosion*

Science in the 20th century is characterized by an increasing amount of scientific information. As a molecular biologist and physician, I have watched the dramatic accumulation of information about human disorders and human gene. In 1953, when I was born, Watson and Crick proposed the molecular structure of deoxyribonucleic acid (DNA). The double helix structure model provides us with profound insight into how information of life are stored and used. I first purified DNA from microorganism at age 15 as a member of the biology club at high school. The teacher indicated to me how to separate DNA and showed us that it was able to change the genetic characteristic of this microorganism. I entered the University of Tokyo medical school in 1971, at that time we did not have a molecular biology course. I thought that 100 years later, we may handle human DNA sequence. But actually the wave of molecular biology struck us so quickly, and immediately after graduating from the Medical School we faced a storm of information about human genes. Still human DNA seemed to have infinite information. However, today, human DNA is thought to consist from about 70 thousand genes encoded by 3 billion base pairs and 80 to 90% of its sequence will be determined within 2 to 3 years.

One of the reasons for this vast increase in the scientific information is the mode of 20th century. Science of each era is characterised by its paradigms. Once the paradigm becomes clear, many scientists can follow the method and theory, and can get much information relatively easily.

In the case of molecular biology, when double helix DNA model was proposed, many scientists/technologists realised that they could get much information by simply sequencing the DNA. Human DNA consists from only 3 billion base pairs, and currently using automatic DNA sequencer, one technician can determine nearly 10,000 base pair sequence. If 1,000 machines/technicians work 200 days a year, most of it will be sequenced within 2 years.

2. *Global aspect of scientific/technological change and intellectual property*

Another reason of this explosion of scientific information is globalisation. The large scale sequencing attempt started in France, then the worldwide effort started. Once technology for the atomic bomb was developed in the United States, other European countries and the former Soviet Union could easily develop it. Once the technology is developed, even by someone who has the confidence of success, the technology is developed by others relatively easily and quickly.

Immediately after succeeding in the DNA recombination experiment, Cohen and Boyer at the Stanford University applied for the patent, because they thought that this technology would change the method of life science and may earn a lot of money. Their prospect was right. It was proved when a venture biotechnology company Genentec earned millions of dollars from a gene, TPA, which prevents blood clotting and its product is useful in the emergency of heart attack patients. Of course, scientists of many other countries followed this way.

The technologies for molecular biology were mainly developed in the United States of America. The American industry and government learned a great deal from the previous electronics industry and automobile industry competition. In the 60s, 70s and 80s, they faced serious challenges from the Asian developing industries. When they made television, Japanese and other Asians followed. It dramatically increased the pace of technological development.

When the American industries faced these challenges they could not afford this fierce competition. Therefore, they set up a novel mechanism to protect their scientific/technological information. That is a system symbolised by the word "intellectual property".

We can see an example in the hepatitis type-C virus gene. The gene was cloned by a San-Franscisco based venture biotechnology company in late 80's. The patent covers not only the nucleotide sequence but also nearly all the related sequence claiming that the usage of a partial nucleotide sequence similar to their claimed sequence. Hepatitis C virus is the major causative gene for post transfusion hepatitis, which causes more than 10,000 deaths per year in Japan. However, the usage of this virus sequence in clinical tests is widely restricted by the patent. This situation became much more complicated when other companies' patents are involved. The hepatitis nucleic acid can be detected most easily using a special method named Polymerase Chain Reaction (PCR). The PCR technology was developed by another biotechnology company. The PCR is really a revolutional method to amplify DNA.

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The information concerning the viral nucleotide sequence, and the detection method can generate a lot of money everywhere around the world.

3. The age of CONTENTS science

In the case of human genome project, the most important information is 70,000 human genes. Formerly, scientists paid a lot of attention to the method of getting this information. But once the method to obtain information of these 70,000 genes has been indicated, people pay attention to the information encoded by the DNA sequence. We can sequence 70K genes and we will also soon be able to determine the major genetic difference as a difference in nucleotide sequence. We call the accumulated information in a particular field as CONTENT. The information is often handled by computers and also named as DIGITAL CONTENTS. We can analyse not only metabolic or structural information of human beings but also information concerning our physical ability, disease predisposition, emotion, intelligence, memory, sleep, sexual behavior or other aspects of human beings.

Life insurance companies may want to know about the personal predisposition to cancer. Police headquarters may want the DNA fingerprint of criminals. Professional sports managers may want the information of their team members' genetic characteristics. Even your school master or company employer may want your genetic code.

Previously in the field of biology, the information of living organism looks infinite. The nucleotide sequence of many viruses including hepatitis virus, HIV and others, many micro-organisms including E Coli, Yeast, have been determined. We are very near to finishing the human DNA sequencing project. When these sequences are determined, who has the intellectual property of these sequences? Currently there is a big controversy over this issue. The United States companies have applied patents of nearly 500,000 different partial human nucleotide sequences, named ESTs, which is actually the CONTENTS of our DNA. The patent office of European Union would deny the patentability of these partial DNA sequences. The difference between the US and EU patent offices may reflect the conflict between their industries, but may also reflect their cultural backgrounds. There are many unsolved problems concerning about the patentability of CONTENTS of human information including genome sequence.

One important issue missed out in these arguments is that these CONTENTS can provide many new resolutions to currently unsolved serious problems. We may overcome AIDS epidemic, we may find a new way to treat cancer, or even prevent cancer. For this purpose, we need an improved access to CONTENTS. According to the problem, the way to use these CONTENTS differs from each other. For example the way to solve AIDS epidemic may differ for each country. In Holland, the social agency delivers clean needles for drug addicts to prevent AIDS epidemic through the needle. This may not be a good method to prevent AIDS in Asian countries. We need an organised and intellectual way to use CONTENTS. There are many different ways to use the CONTENTS because of the complexity of the society and culture in Asian countries.

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4. Speedy monopoly vs. diversified pluralism

The speed of getting information will be profoundly enhanced in 21st century. However, the problem which scientists will face is not a monotonous one. For example, in the case of life science, there are many ways to understand life. When we analyse the human being, we can study the various levels including molecular level, protein, protein assembly (supramolecular structure), subcellular organella, cell, cell assembly, organ, individual human beings, human beings at various ages, time, society, and as a species. Actually 70,000 genes interact with each other, still current scientific theory has not succeeded in establishing a common resolution to more than that three-way interaction. The analytical method will not be limited to a single way. Many years will be needed to pick up the most important factor from many related materials. The research style of each scientist is different from each other. The research style of Asian researchers differs from that of an American researcher.

I do not want to be disrespectful to the United States law and science. In the United States, intellectual property is the right written in the patent law of the United States. The United States law would like to protect the profit of the inventor. In the United States, the science is considered as a competitive human effort, which is represented by a famous phrase "Publish or Perish". This phrase "Publish or Perish" means if you want to continue to be a scientist, you should publish your research results by your name, otherwise you cannot continue your job. In Asian countries, science is considered as an effort to get knowledge for human beings. The attitude may match the phrase, "Live and Let Live". The scientific knowledge is often considered as an asset of society and human beings. Therefore, the intellectual property should be determined by considering the balance of the inventor and the user. For example, if a company can claim the sequence of hepatitis virus, the knowledge should be used for the treatment of the patients first. Both the inventor and the user will benefit from the scientific accomplishment.

Considering the current enormous increase in the speed of getting CONTENTS, Asian society including Asian scientists and technologists will need to consider their identity. If they simply pursue the increase in the speed of getting knowledge, the future will not look bright They should pay much more effort to getting CONTENTS information such as human genome information. They also definitely need free access to these CONTENTS. Only by using the CONTENTS including the human genome sequence, will Asian researchers be able to provide a new solution to their societal need. To gain such access to CONTENTS, some new global guidelines will be needed immediately. Governments, industries and scientific societies of Asian countries must take part in this project following the international guidelines. At the same time, we need to promote life sciences of our own based on our cultural bases. For this important contribution, the dedication of Asian youngsters will be needed.