Pharmacoinformatics Infrastructure for Genome Based Personalized Medicine

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1 Introduction
One of the important application targets of the next genomic science and technology is personalized medicine. Personalized medicine is the idealized medical practice to give right drugs to right patients at right times. Finding SNPs is considered as a premise for this practice but it is by no means the sufficient effort. Good practice must be supported by well trained medical professionals who can easily access relevant data and knowledge. Such an informational environment would be called the infrastructure for personalized medicine [1]. New informatics is also needed in order to utilize these data and knowledge effectively. As the only national institution for pharmaceutical research we are trying to develop such informational infrastructure.

2 Method and Results
2.1 Design Concept
Figure 1 shows the component systems for the infrastructure. The Digital JAN [2] is the drug database for “the accepted names” of all drugs ever registered in Japan. In addition to the accepted names the database also has CAS Registry Numbers and Structure. The ADME Knowledge Base is the database for absorption, distribution, metabolism, and excretion of drugs. These data and knowledge are important to know how drugs are transported to various tissues and are chemically modified.

The Drug Target Knowledge Base is the database for target molecules of the drugs. A drug or its metabolite binds to some of the biomolecules that triggers a series of reactions and end up with the effects aimed by the prescriber. Although these target molecules are not yet identified for all the drugs, it was estimated that nearly half of them are receptors, one fourth of them are enzymes, and few of them are transcriptional factors. The link mechanism to SNPs is an interface program that fetch SNPs data for those biomolecules that are registered in the systems from public databases such as NCBI or Swiss-Prot.

2.2 Implementation of the Systems
Up to 2000 information was compiled in the Digital JAN Database, which is implemented on a PC based ACCESS. It was also put on the Web site. The ADME system is implemented for pilot study using only cytochrome P-450 (CYP) data [3]. These data are important to predict the so-called poor metabolizes and excess metabolizes. They are also important for predicting (so that preventing) adverse effects due to drug (or food and drug) interactions.
Drug Target Knowledge Base has been implemented mostly for receptors. Enzyme targets are still under development. However detailed knowledge was accumulated for an important nuclear receptor, i.e., estrogen receptors. Target molecules are linked both the Receptor Database (RDB) [4] and Cell Signaling Network Database (CSNDB) [5]. The SNPs data fetcher was implemented on CYP data and is being tested for receptor proteins in the Rector Database.

3 Discussions

Advances of genome analyses and related science & technology are accelerating discovery of drug targets and other important biomolecules. This discovery allows us to add new contents to our data and knowledge bases. The so-called gene networks, signal pathways, or protein-protein interactions are now attracting many bioinformatics researchers as the next target of genomic computing. Already there exist number of computer systems for metabolic pathways, signal transductions, and transcription factors. However these are not enough to realize personalized medicine. This is because these data or knowledge base has no direct link to real drugs that are used in today's clinical settings in Japan. One of the big obstacles was the lack of up dated digital data for the real drugs. Pharmaceutical companies are required to attach relevant information to each drugs on the market, but these information are not so easy to use nor enough for scientific reasoning. Thus collecting information for ADME and target molecules for each drug is very painstaking and costly job for researchers. To form some consortium supported by both pharmaceutical companies and academics would be a solution.

From personalized medicine viewpoint the present systems are only good for selecting right drugs for right patients. Problem still remains how to give right amounts at the right times. In order for that more pharmacokinetic data and right monitoring systems are needed. It is certain that DNA chip based diagnosis and patient-monitoring system will be used widely in the near future. How to implement these systems and to combine present systems are the next target.

References