Department of Pharmacogenomics · Genomic Drug Discovery Sciences (GDDS)

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Research Projects:

What's GDDS

The genomic drug discovery science is the science field of discovery of the new drug, the medicine of the effect to be higher and the medicine with few side effects, using the genome information. Our research projects are performed on major 3 themes; 1. Function of G protein-coupled receptors (GPCR), which are in cell membrane and play important roles on bio-reactions. 2. Development of microarray techniques, which are took notice as the techniques of comprehensive gene analysis. 3. Bioinformatics sciences, which is necessary to analyze a lot of information including genomic information.

GPCR

The Human Genome Project is now completed, and that enables access to every human G-protein coupled receptor (GPCR), which represents the single most important drug targets for medical therapy. Many of novel GPCR discoveries were based solely upon their shared sequence identities and characteristic seven transmembrane-spanning structure encoded therein. This sequence conservation allowed for powerful cloning techniques through DNA technology (in particular PCR technology) and in silico screening of GPCRs using genome or cDNA sequence data. Information from genome sequencing estimated the existence of 700-800 GPCRs in the human genome: about 250 of GPCRs are identified as receptors for known ligands, and the rest are still orphan receptors (oGPCRs). Recognized for the potential of oGPCRs as targets of novel drug discovery, oGPCRs have attracted a tremendous level of attention in terms of continued identification of their endogenous ligands and elucidation of their physiological functions.

Microarray

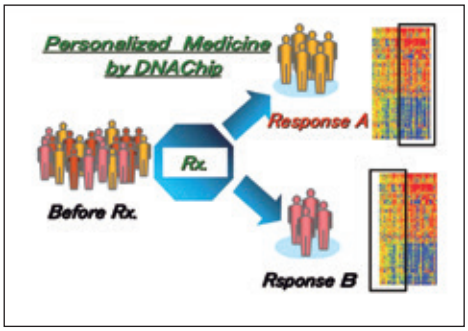
A microarray is one of the most important basic technology for drug discovery from the aspect of genomics. The focus of genome research will be shifted to functional analysis of genes including the determination of precise transcript unit as transcriptome.

The target validation is one of the critical point of drug discovery. The gene expression pattern (i.e. profile) of disease specific status could be obtained by DNA chip technology that makes it accelerate to find candidate molecules of drug target. Microarrays enable the comprehensive analysis of gene expression of various disease status including model animals and cellular activity. The process of target validation would be aided by the databases which conjugate the data of gene expression and that of pharmacology, physiology, biochemistry, molecular biology and so on. We are interested in the construction of databases of gene expression data, gene expression analysis of disease model animals and human disease status, and finally discovering the candidate molecule of the effective novel drug target and revealing the mechanisms of human disorders.

Pharmacogenomics

Pharmacogenomics is the study of how an individual's genetic inheritance affects the body's response to drugs. The term comes from the words pharmacology and genomics and is thus the intersection of pharmaceuticals and genetics. Pharmacogenomics holds the promise that drugs might one day be tailor-made for individuals and adapted to each person's own genetic makeup. Environment, diet, age, lifestyle, and state of health all can influence a person's response to medicines, but understanding an individual's genetic makeup is thought to be the key to creating personalized drugs with greater efficacy and safety. Pharmacogenomics combines traditional pharmaceutical sciences such as biochemistry with annotated knowledge of genes, proteins, and transcriptome scanning in particular.

Expression monitoring by DNA microarray is the most biologically informative application of this technology at present. Microarray technology has important applications in pharmacogenomics: drug discovery and development, drug safety and molecular diagnostics. DNA chips will facilitate the integration of diagnosis and therapeutics, as well as the introduction of personalized medicines.



Recent publications

- Takeuchi M, Hirasawa A, Hara T, Kimura I, Hirano T, Suzuki T, Miyata N, Awaji T, Ishiguro M, Tsujimoto G. FFA1-selective agonistic activity based on docking simulation using FFA1 and GPR120 homology models. Br J Pharmacol. **168**(7): 1570-1583, 2013.
- Ichimura A et al. Dysfunction of lipid sensor GPR120 leads to obesity in both mouse and human. *Nature*. **483**(7389): 350-354, 2012.
- Hirasawa A et al. Free fatty acids regulate gut incretin glucagons-like peptide–1 secretion through GPR120. *Nat. Med.* **11**: 90-94, 2005.