Correlation Analysis of Chemical and Biological Spaces toward in silico Drug Discovery

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With the completion of the human genome project, bioinformatics is expected as a promising tool in target gene discovery. Genomic information, however, provides no direct information for the drug discovery. The promise that chemical genomics, which integrates chemical knowledge with genomic (biological) knowledge, will improve the drug discovery process is very high. Chemical genomics aims to identify all possible chemical ligands and drugs of all target families. However, it is very hard to investigate relationships between chemicals and living organisms in a comprehensive manner. We are now trying to develop new informatics and data mining strategies with which biological and chemical data can be simultaneously processed by integrating of bioinformatics and chemoinformatics into a common platform.
In this study, we have developed a novel computational screening method, a chemical genomics-based virtual screening (CGBVS) which is fundamentally different from conventional methods such as ligand-based and structure-based virtual screening. We applied the CGBVS method to the ligand prediction of G-protein coupled receptors (GPCR). Five-fold cross-validation experiments showed that the prediction accuracy by the CGBVS method was significantly better than that of ligand-based method (91% v.s. 82%). Furthermore, in vitro binding assay of human beta-2 adrenoreceptor (b2AR) revealed high enrichment of active compounds in the highest scoring subsets (17/21 hit rate among the 50 top-ranked compounds). Some of these active compounds were structurally novel b2AR ligands that were undetected by the ligand-based method. These results suggest that the knowledge of chemical genomics is useful for virtual screening and hereby may lead to realize the genomic drug discovery.