STUDY ON HOMOLOGY MODELING OF 3-DIMENSIONAL PROTEIN STRUCTURE

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For anti-hypertension drug, the authors started “Structure Based Drug Design (SBDD) based upon homology modeling study on 3-dimensional protein structure” in 1985 before the computer graphics study is generally performed. The protein modeling of human renin which is the target angiotensinogenase for hypertension was carried out by using HGS Molecular models. Its target enzyme is containing aspartic acids in the catalytic site, and it has the 25% sequence identity for penicilopepsin determined experimentally. The inhibitor KRI-1230 was designed based upon the shape of the modeled active site. It was ascertained from the intravenous injection to marmoset that this drug is effective for the hypertention disease. At that time, we believed firmly that the homological protein modeling would become a greatly necessary tool in the SBDD study in recent future. Then we began making the soft programs such as sequence alignment and production of 3-dimensional protein structure. Thus, the system what is called BIOCES was made as the fundamental graphic system on which various application programs were executed. Moreover, we made the chimera modeling system in order to perform the homology modeling using some reference proteins determined from the X-ray and NMR experiments. From the use of those systems we have published 19 papers during 14 years since 1988. And it became possible that the plural proteins forming complex or multimer were made from the complex or multimer in the PDB database. Consequently, the FAMS (Full Automatic Modeling System) was developed. Using its FAMS, all the proteins coded on the genomes of various species had been modeled, and those modeling data were published to open from the RIKEN website as the name of FAMSBASE. Moreover, the FAMS program was developed to model the complex proteins as if the complex appears to be single protein in the proposal of a new algorism. We have continuously had the excellent results during recent 8 years until 2008 in the CASP contests of protein modeling. Also we have had good results in the CAPRI contests in relation to the docking prediction of the protein-protein interaction. Recently, we have developed a new SBDD program based upon bioinformatics using the 3-dimensional coordinates of proteins and binding ligand molecules in the PDB database.