

Structural Biology and Structural Genomics for Rational Drug Design

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The availability of the human genomic DNA sequence and the genomes of a wide range of other species has awakened big expectations in healthcare, agriculture, nutrition and many other fields. In addition to the rapidly expanding protein sequence universe derived by annotation of the genomic DNA sequences, the anticipated advances will have to be based on detailed knowledge of the proteome and other gene products of the organisms of interest. Coverage of the protein universe derived from the DNA sequences with three-dimensional structures is thus pursued with novel strategies of “structural genomics”. In this context my research team makes use of solution nuclear magnetic resonance (NMR) spectroscopy for protein structure determination and for collecting supplementary function-related data. The NMR method is unique when compared to structure determination by X-ray crystallography, in that atomic resolution structures and supplementary data can be obtained under solution conditions close to the physiological milieu in body fluids. By generating information on protein structure, stability, dynamics and intermolecular interactions in solution, NMR has an exciting role also in the longer-term challenge to advance from structural coverage of the protein sequence universe to new insights into protein functions and chemical biology.