Prediction of Protein Structure, Function and Druggability on a Proteomic Scale

Jeffrey Skolnick

University at Buffalo

A novel method for the prediction of protein function and druggability based on the sequence-to-structure-to-function paradigm has been developed. We first present recent results from the application of our structure prediction algorithm, TASSER, in CASP6 and then describe the structure prediction of all putative GPCRs in the human genome. Based on confidence criteria, 90% should have correct structures, and clustering shows that structurally similar GPCRs have similar function even when their sequences are diverse. We then describe our multimeric threading algorithm, MULTIPROSPECTOR, and its application to the prediction of protein-protein interactions in the S. cerevisiae genome. Next, we describe newly developed methods for the accurate inference of protein biochemical function and present results of the comprehensive analysis of all sequenced genomes and the automated assignment of proteins to metabolic pathways. Finally, we combine all these approaches into a pathway based method for the prediction of druggable protein targets and apply the resulting methodology to the human genome.