

Supplementary material

Method	Pros	Cons
Sequence based	Most known or reliable method ; Based on sequence homology	Many BLAST hits are either electronically annotated or hypothetical. Some phosphorylation sites or short motifs produce false positives
Structure-based	Global fold methods or active site characterization ; Structural homology	Global fold similarity does NOT correlate with functional similarity
Association based	Involves domains or phylogenetic profile	Lack of conserved proximity does not indicate lack of functional association
Proteomics and metabolomics based	PPI ; Gaps or holes in known pathways can be intuitively assigned : Function awaits a protein to be characterized to match that "gap"	False positives

Table 1: The pros and cons in the form of strengths and limitations of various methods used for functional annotation