TIMomics: Genome-wide Search for Evolutionary Relationships among TIM (triose-phosphate isomerase) Fold Proteins *via* Structural Genomics Approaches

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With more and more protein structures determined *via* world-wide efforts of structural genomics (SG), it becomes a common theme that many sequence unrelated proteins adopt the same folds. What are the origin and evolutionary pathways of these structure folds? How can we use this sort of information to predict protein structures with unrelated sequences? To answer these questions, we are trying to solve all possible TIM barrel proteins from a given genome. By using different methods and starting from SCOP TIM barrel PDB sets, we have searched exhaustively all potential TIM fold proteins from several complete genomes.

With the help of a high-efficiency and low-cost structural genomics platform set up at Peking University, China, we have chosen 288 (3x96) potential TIM fold genes from *B. subtilis* since 2005 Jan. as a pilot project for TIMomics. So far, we have got 259 genes PCR amplified and ready for subsquent cloning; a few dozen genes have already been cloned and expressed in *E. coli*, about 20 proteins have been purified and about 10 crystallized. We anticipate that we will be able to solve several dozens of protein structrures from the selected genes in the near future, in order to test our hypothesis and to study their structure, function and evolutionary relationships, and to answer the questions we proposed above.

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