

The Joint Center for Structural Genomics: A Multi-tiered Approach to Structural Genomics

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The JCSG (www.jcsg.org) has made substantial progress in the ultimate goal of HT structure determination by truly automated means. We have implemented a 3-tiered pipeline strategy where targets are characterized, categorized by behavior, and then processed in parallel by appropriate methods. Tier 1 is focused primarily on gathering experimental data on the proposed targets and is heavily reliant on complete automation and the processing of a large number of targets through initial crystallization trials. Targets are then either advanced towards structure determination by MAD or MR (Tier 2), or enter an appropriate salvage pathway (Tier 3). Salvage pathways have been developed which attempt to customize processing of smaller subsets of targets through parallel processing methods. Such pathways include NMR and DXMS screening, mutagenesis, protein refolding, protein co-expression, baculovirus protein expression and orthologs. These strategies have been successfully applied to a prokaryote (*T. maritima*) and eukaryote (mouse) proteomes.

Collaborations with the scientific community are an important part of the development, production and dissemination aspects of the JCSG. These collaborations are created, supported, and dynamically managed to match the programmatic needs while maximizing the leverage of available resources. (NIGMS/PSI (P50-GM 62411).

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