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The Joint Center for Structural Genomics: A Multi-tiered Approach to Structural Genomics. Marc Elslinger, A. Deacon, A. Godzik, S.A. Lesley, K.O. Hodgson, J. Wooley, K. Wuthrich, I.A. Wilson, The Joint Center for Structural Genomics, The Scripps Research Institute, 10550 North Torrey Pines Rd., La Jolla, CA 92037 USA.

The Joint Center for Structural Genomics (www.jcsg.org) pipeline is constructed around a flexible, 3-tiered approach to structural genomics, which is used to efficiently characterize, optimize and solve each target. This hierarchical strategy makes full use of parallel processing methods; however, it does not rely on a single processing protocol. Instead, it seeks to minimize the effort and resources to obtain a structure for every target of interest, regardless of whether they prove to be difficult or straight forward. Tier 1 is focused primarily on gathering experimental data on the proposed targets and is 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 or enter appropriate Tier 3 salvage pathways, which focus on identifying and creating parallel routes to retrieve more challenging targets. These pathways include alternative routes of expression, construct optimization, and alternative crystallization strategies. This behavior-driven approach is an efficient way to address large numbers of diverse targets and has been successfully tested for both prokaryote and eukaryote proteomes during PSI-1. Our current production center (JCSG-2) will continue to develop and optimize HT approaches to advance the frontiers of structural genomics through the determination of a large number of high-value targets that populate protein fold and family space.