Use of reductive methylation of proteins to increase crystallization efficiency at the Midwest Center for Structural Genomics

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The highest attrition rate in high-throughput structural genomics (SG) projects utilizing x-ray crystallography occurs at the step of obtaining diffraction quality crystals. The Midwest Center for Structural Genomics (MCSG) has developed and continues to optimize the high-throughput crystallization pipeline. The pipeline was set up with nano-liter crystallization robots such as Honeybee and Mosquito, and a Matrix Maker equipped with Crystal Monitor software for screening initial crystallization conditions and crystal optimization. As a part of effort to increase the success rate of obtaining diffraction quality crystals, chemical modification of proteins has been tested in the MCSG crystallization pipeline. Particularly, reductive methylation of lysine residues to alter the crystallization properties has been evaluated with more than 100 proteins, most of which have not been crystallized previously. Following the method described by Ivan Rayment (in Volume 276 of *Methods of Enzymology*) the proteins were methylated and screened using standard MCSG crystallization pipeline. Several structures have been obtained using this approach and detailed analysis and progress will be presented.

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