

W0553

Identification of Small Molecule Ligands for Structural Genomics Targets and their Application in Crystallization Trials. Evdokimova E.*, Skarina T.*, Kudritska M., Xu X., Egorova O., Pennycook-Brown M., Ezersky A., Edwards A.M., Yakunin A., Savchenko A., Ontario Centre for Structural Proteomics, Univ. of Toronto, University Health Network, 112 College St., Toronto, ON, M5G 1L6, Canada, evdokimo@uhnres.utoronto.ca, tskarina@uhnres.utoronto.ca, *Presenting authors

A large number of protein functions depend on the interactions with small molecules. The molecular mechanisms of these interactions are usually revealed through structural studies of protein-small molecule complexes. Structural Genomics targets poorly characterized protein families for large-scale three-dimensional structure determination. Identification of small molecule ligands for these proteins not only provides an insight into their function but also facilitates structural studies of these proteins.

At Ontario Centre for Structural Proteomics (Canadian and NIH-funded Centre affiliated with the Midwest Center for Structural Genomics in the US) we are using two main methods for identification of small molecule ligands of structural genomics targets: 1) generic enzymatic assays; 2) miniaturized high-throughput protein stability assays. Using these approaches, we have identified several potential ligands and enzymatic substrates for previously uncharacterized proteins. Interactions of these proteins with small molecules were confirmed by determination of their complex structures.