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Structural Genomics on Membrane Proteins. Kenneth Lundstrom, BioXtal, Epalinges, Switzerland.

Membrane proteins are targets for >70% of current drugs. Paradoxically, <1 % of the >25,000 structures in public databases are represented by membrane proteins. The expressability, low stability and inherent flexibility have made structural studies a major challenge. Large networks with broad expertise have been established to facilitate technology development of expression, purification and crystallization. The privately funded MePNet (Membrane Protein Network) consortium has focused on the expression of 100 therapeutically interesting G protein-coupled receptors (GPCRs). *E. coli*-based expression led to immunodetection of 50% of the GPCRs. Selected targets were produced in bacterial inclusion bodies in large-scale fermentation for purification and refolding attempts. Yeast-based expression in *Pichia pastoris* resulted in immunodetection of 94%, many showing high binding activity. Likewise, 95% of the GPCRs were expressed in Semliki Forest virus-infected demonstrating strong specific binding. Solubilization and purification of selected GPCRs from yeast and mammalian cell membranes has led to the first crystallization attempts. The EU-funded network, E-MeP, aims for structural characterization of 100 prokaryotic and 200 eukaryotic membrane proteins, including GPCRs, ion channels and transporters. Within E-MeP bacterial, yeast, insect and mammalian cell-based expression will be applied.