

You are cordially invited to a talk in the Edmond J. Safra Center for Bioinformatics Distinguished Speaker Series.

The speaker is Prof. William F. DeGrado, Department of Pharmaceutical Chemistry and Cardiovascular Research Institute, University of California

**Title:** "Analysis and design of proton transporters "

**Time:** Tuesday, 8 July 2014, at 11:15 (refreshments from 11:00)

**Place:** Britania 06, Life Sciences Faculty

**Abstract:** The mechanism of proton transport through membrane proteins is of general interest to multiple areas of biology. Using a variety of spectroscopic, crystallographic, and computational methods, we have investigated the mechanism by which protons are conducted through the M2 proton channel from influenza A virus, and used this information to design new anti-influenza drugs that target highly drug-resistant forms of the virus. A second topic of the talk will focus on the use of de novo protein design to test the mechanism by which a class of transporters uses proton gradients to drive the conduction of molecules into or out of cells. Transporters have been hypothesized to arise by physical association or gene duplication of primordial units, leading to an assembly with "frustrated symmetry" that rocks between two states with the substrate-binding site alternately accessing each side of the membrane. Rocker, a minimalist Zn<sup>2+</sup>/proton antiporter was designed to test these principles, although it bears no sequence similarity to any known natural protein. Structural, dynamic and functional studies indicate that Rocker is a primordial transporter, which recapitulates many of the properties of this class of proteins. These studies also demonstrate the feasibility of using de novo design to design membrane proteins with complex dynamic and functional properties.

**Host:** Prof. Nir Ben-Tal, [NirB@tauex.tau.ac.il](mailto:NirB@tauex.tau.ac.il), Life Sciences Faculty, Tel Aviv University