Transmembrane protein-mediated loading of synthetic compartments

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Compartmentalization, a prerequisite for the spatiotemporal control of biochemical pathways in cells, is an emerging concept in designing new materials for medical and technological applications. Synthetic nano- and micro-compartments (NCs, MCs) with their chemical versatility and superior stability provide the basis for developing catalytic compartments, artificial organelles or cell mimics furnished with specific biomolecules. However, a higher compartment loading efficiency and better permeability of the synthetic membrane remain hurdles that need to be overcome to increase the efficacy of *in situ* reactions. This interdisciplinary project aims to develop next-generation functional synthetic compartments whose composition is modulated by specific transmembrane proteins that deliver or selectively let molecules pass to the interior and test their activity *in vitro*. By inserting specific membrane proteins into the membrane of synthetic compartments, we plan to deliver protein cargo to the compartment interior or to allow a specific molecular flow across the membrane.

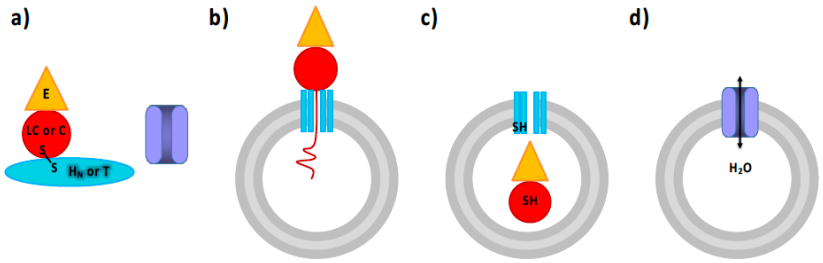

Fig. 1: Synthetic NCs and MCs equipped with membrane proteins for differentially loading the compartment interior. a) Membrane proteins variants comprising the catalytic domain (red), the translocation domain (light blue) and an enzyme of interest (orange), and a second membrane protein (purple). b) In the artificial membranes (grey), translocation domains change conformation to form a pore. c) Fusion proteins will enter inside the compartment where in the reducing environment, they separate from the translocation domain. d) Membrane protein inserted in synthetic membranes for the exchange of water and small neutral solutes.

Our study focuses on generating novel functional compartments by a combination of cutting-edge design of nanoscience-based compartments and state-of-the art methods in membrane protein expression and includes an array of methods for the detailed investigation of theses compartments *in vitro*. Importantly, this study takes advantage of a broad range of expertise and established techniques in the collaborating labs.