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A novel concept in membrane protein crystallization: Conjugated engineered-micelles

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We present a general strategy for producing crystals of integral membrane proteins which is conceptually different from crystallization procedures commonly employed. Our working hypothesis has been based on the idea that high quality crystals of membrane proteins can be produced via conjugating mechanisms which are capable of bringing detergent-solubilized membrane proteins into proximity and which, at the same time are: (1) Highly specific, mild and non-covalent; (2) capable of exerting control over both the optimal distance and binding affinity between detergent-protein complexes; (3) suitable for use with diverse membrane proteins, regardless of biological origin or size of the hydrophilic domains; and (4) simple to implement. These criteria are satisfied by a novel type of detergent micelles that we call engineered-micelles. Embedded in the engineered-micelles are specially synthesized hydrophobic molecules which may be conjugated to one another via specific interactions. Two examples of such molecules are hydrophobic [metal:chelator] complexes and complementary hydrophobic nucleoside base-pairs. These interactions lead to micellar aggregates with a variety of different architectures as determined by cryo-TEM imaging and which have been shown to provide necessary and sufficient conditions for the successful growth of membrane protein crystals.

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