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Engineered-micelles: A new concept for crystallization of membrane proteins

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I shall present a conceptually different approach to the long-standing problem of crystallization of integral membrane proteins. This approach is based on the idea that nucleation and growth of high-quality membrane protein (MP) crystals, permitting structure determination at atomic resolution, can be promoted by means of a detergent-micelle conjugation mechanism to bring the protein-detergent complexes (PDCs) into proximity. The interactions which produce conjugation must: (a) be highly specific, mild and non-covalent; (b) be sufficiently general to apply to membrane proteins regardless of their biological origin; and (c) be straightforward to implement in practice. These criteria are satisfied by a novel type of micelle that we have termed: Engineered-micelles. Engineered-micelles contain, in addition to the common surfactant, unique amphiphiles which interact to form conjugated micellar aggregates. We have constructed engineered-micelles based on three types of conjugation mechanisms: (i) hydrophobic [metal: chelator] complexes; (ii) the complementarity of hydrophobic nucleoside base-pairs; or (iii) hydrophobic +/- charged peptides. We have included these conjugating species in a variety of non-ionic detergent micelles, widely used in the crystallization of membrane proteins (e.g. OG, DM, DDM, C8E4). We found that, under the gentle conditions of our crystallization trials, the growth of membrane protein crystals was indeed observed only in the presence of conjugated engineered-micelles. I shall also discuss the extension of the conjugation concept towards a more flexible mechanism that would not only bring PDCs into proximity via specific means but, a priori, would permit a level of control over the inter-micellar distances. With the possibility of shortening\elongation of the conjugating molecules, the PDCs would then be positioned at distances that could take into account the size of the detergent micelles as well as the size of the hydrophilic domains of the integral MP.

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