Designed Coiled-coil Protein Origami Nanostructures

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Proteins are the most complex functional nanostructures, defined by the linear sequence of amino acids that can self-assemble into complex folds. Natural proteins are defined by a large number of weak cooperative long range interactions. In analogy to DNA nanostructures, based on strand complementarity, we devised coiled-coil protein origami (CCPO) which is based on the well-understood specificity of coiled-coil dimers (CC). CC dimer forming modules were concatenated into a single long polypeptide chain, where the CC modules form the edges of the self-assembling polyhedral scaffold. The principle was first demonstrated by the construction of a nanoscale tetrahedral cage from a single polypeptide chain composed of 12 coiled-coil forming segments1. In this case 6 edges of the polyhedron were defined by orthogonal CC dimers, measuring 5 nm. Design of the new CC building modules2 and computational design platform CoCoPOD enabled the design of protein origami cages that are able to self-assemble in vivo. The CCPO cages were extended to more than 700 residue proteins with tetrahedral, four-sided pyramid, triangular prism and trigonal bipyramid that fold efficiently, with kinetics and stability comparable to globular proteins3. Diverse chemical properties of amino acids enable introduction of functional sites and regulation of CC assembly. CC modules have been used to design artificial signalling pathways and fast information processing circuits in mammalian cells4. Additionally, in vivo folding of protein origami opens the prospects for new applications of this new type of designed nanostructures.

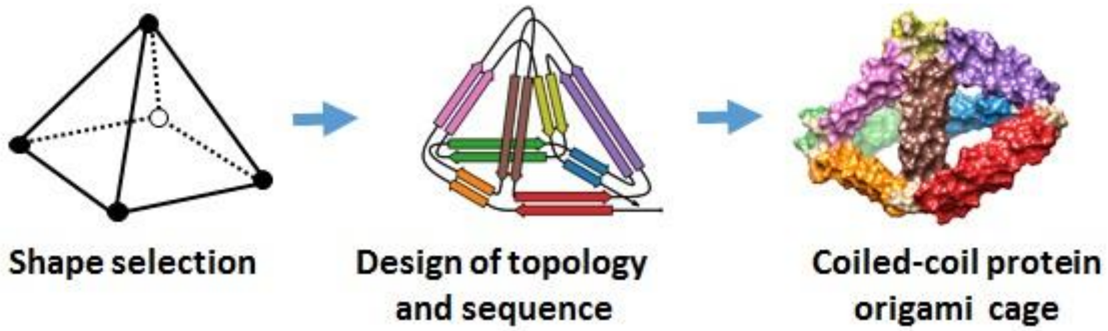

Figure 1: Principle of the design of coiled-coil protein origami nanoscale polyehedra composed of concatenated polypeptide modules.

References

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