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Protein capsids as molecular containers: Cargo loading and controlled release

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Statement of the Problem: Protein capsids form closed shell structures via self-assembly that can host various cargo molecules in their hollow interiors. These molecular containers can be useful for applications such as drug delivery, nanoreactors, and materials synthesis. These applications often require the encapsulation of cargo molecules followed by their eventual release from the capsid. However, general methods for loading and unloading cargo molecules are lacking. My research aims to endow protein capsids with the ability to encapsulate different cargo molecules and to develop non-denaturing cargo release mechanisms.

Methodology & Theoretical Orientation: The capsids formed by bacterial lumazine synthases (LS's) are attractive structures for engineering molecular encapsulation systems. Using DNA mutagenesis and covalent protein modification methods, LS capsids and potential guests were convergently engineered to generate interactions that are localized to the capsid interior and that can potentially be modulated by changing the solution conditions. Structural and functional characterizations of the resulting complexes are carried out using biochemical and biophysical techniques.

Findings: Using a charge complementarity strategy, engineered LS capsids were loaded with RNA cargoes during bacterial production. Similarly, a natural LS capsid was loaded with a protein bearing a peptide tag derived from its native guest. The protein cargo was released from the capsid by a mild change in the buffer conditions. Lastly, small-molecule cargo was loaded into an intact engineered LS capsid using a two-step thiol-disulfide exchange process. The resulting disulfide bond linking the cargo to the capsid can be broken by reducing agents, allowing diffusion of the cargo out of the capsid.

Conclusion & Significance: These strategies for reversible guest encapsulation extend the functional versatility of the LS capsid as a scaffold for bionanotechnology. The ability to control both cargo loading and release should be particularly useful for the development of new drug delivery systems.

Biography

Kenneth J Woycechowsky has expertise in the assembly, folding, function, and engineering of proteins. His work on protein capsid assembly and the engineering of protein capsids to construct novel molecular encapsulation systems helps lay the ground work for next-generation nanoreactors and drug delivery systems. He has experience in research and teaching at universities in China, the USA, and Switzerland. He obtained a BS in Chemistry from Penn State University and a PhD in Biochemistry from the University of Wisconsin-Madison. His research training emphasized a multi-disciplinary approach to tackling cutting-edge problems in protein structure and function. He is currently a Professor in the School of Pharmaceutical Science and Technology at Tianjin University.

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