^{3rd} International Conference on ANTIBODIES, BIO THERAPEUTICS & B2B & GENETIC AND PROTEIN ENGINEERING November 08-09, 2017 | Las Vegas, USA

De novo design and characterization of circular tandem repeat proteins

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Denovo protein design offers access to regions of protein fold space that have not been sampled during natural evolution, regions that may contain solutions to novel structural and functional challenges. *De novo* design can also produce proteins that are highly robust and stable-favorable attributes for subsequent functionalization by rational means. We recently reported the development and experimental validation of a computational method for design of closed tandem repeat protein architectures (a closed repeat architecture is one in which the N- and C-termini are juxtaposed). We have used this method to create a set of alpha-helical solenoid repeat proteins whose bundle handedness is opposite that found in analogous natural proteins. These designed proteins have toroidal architectures with up to 24 repeats, variable thickness and central pore dimensions ranging from 0 to 60 Angstroms in diameter. We are now expanding the topological diversity of the repeat units to access new geometries and functionalizing the designed scaffolds to create reagents for biomedical and industrial applications. A motivating hypothesis behind this work is that designed will prove to be valuable protein scaffolds for protein array and display by virtue of their solubility, stability tunable symmetry, modularity, and self-reinforcing architectures.

Biography

Barry L Stoddard has research interests in the structure, mechanism and engineering of proteins and enzymatic catalysts for basic research and biomedical applications. His lab conducts wide-ranging research on gene-specific endonucleases, the creation of suicide genes for biotech and medical applications, structural enzymology and protein engineering. He has coauthored over 160 research articles and reviews in these fields since 1990. In 2004, he was one of several recipients of the Newcomb Cleveland Prize from the American Association for the Advancement of Science (AAAS) for published work in the field of Protein Engineering.

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