Designer threads: New insight into protein fiber assembly

April 20 2010

Understanding how mixtures of proteins assemble and how to manipulate them in the laboratory has many exciting biomedical applications, such as providing scaffolds for the engineering of tissues that can replace diseased or damaged human tissues. Now, research published by Cell Press in the April 20th issue of *Biophysical Journal,* reveals new information about the kinetics of protein assembly and demonstrates how to manipulate conditions in order to provide different distributions of protein fiber lengths.

"Developing a good understanding of the relationship between the sequence of a protein fiber and its structure, stability and how it folds up and assembles together with other proteins is key and underpins our ability to design new protein-based materials for bioengineering," explains senior study author, Professor Derek N. Woolfson from the School of Chemistry at the University of Bristol in the United Kingdom. "It is also critical to determine the timescale of protein assembly so that the process can be fully controlled and accurately manipulated."

In previous work, Prof. Woolfson and colleagues designed two short peptides that, when mixed together, assembled to form fibers. These peptides were engineered to have "sticky ends" that interacted to form long fibers which exhibited a natural protein structural motif called the "alpha-helical coiled-coil"; a structure where fibrous proteins coil up like the strands of a rope. In the current study, the researchers used multiple sophisticated and complementary biophysical tools along with peptide engineering to gain further insight into the molecular process and timing

of going from the small nanoscale peptides to large micron-length fibers.

Using these techniques, the researchers were able to build a specific descriptive mathematical model for the self-assembly of the alpha-helical protein fibers. Prof. Woolfson's group was also able to demonstrate that they could intervene in the assembly process to manipulate the resulting fibrous structures with some precision. "This study and the resulting mechanism we propose present a potential route to temporal control of the assembly of fibers with future applications in biotechnology and nanoscale science and medicine," proposes Prof. Woolfson.

More information: Woolfson et al.: "The assembly pathway of a designed !-helical protein fiber." The Biophysical Journal, April, 2010. www.biophysics.org/

Provided by Cell Press