Engineer ramps up protein production, develops versatile viral spheres

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Scientists are taking the amazing protein-making parts out of cells and putting them into systems to mass-produce designer proteins for a wide variety of medical uses. At the annual meeting of the American Chemical Society Sept. 13 in San Francisco, Stanford engineering Professor James Swartz will discuss advances in such "cell-free" protein synthesis, including production of versatile, nanoscale viral spheres that can act as delivery trucks for a new class of potentially more effective vaccines.

"We want to make proteins that are important as pharmaceuticals and for other uses," says Swartz, a professor of chemical engineering and bioengineering at Stanford. "If we could produce them with great efficiency and at very low cost, that would be an important step."

He emphasizes: "A living cell has many unique demands for energy, such as for the synthesis of many types of molecules. We would like to focus all of those metabolic resources just on making our product."

Whole cells can be difficult for researchers to use for making custom proteins because they don't always tolerate the chemical changes a researcher needs to impose to make a specific product. Cell-free techniques, in contrast, can be more robust because they use just the protein-making machinery of cells. To harvest just the parts he needs, Swartz literally rips cells open by applying intense shear forces.

For one of his more recent contributions to developing cell-free

techniques, Swartz will receive the Gaden Award at the ACS meeting. The award is named for Elmer L. Gaden, the founding editor of the journal Biotechnology & Bioengineering, and recognizes the most outstanding paper of the year in that journal. Swartz, who holds the Leland T. Edwards Professorship in the School of Engineering at Stanford, will receive the award for a paper showing for the first time how glucose, the abundant sugar produced by photosynthesis and used in many organisms, can be used to power cell-free protein synthesis.

"We are delighted to honor Professor Swartz with the Gaden Award this year," says journal Editor Douglas S. Clark, a chemical engineering professor at the University of California-Berkeley. "His paper has been recognized by all of the editors for its originality and likely impact."

Versatile viral spheres

At the ACS session where Swartz receives the award he also will present one of the most recent innovations in his lab, the cell-free production of engineered viral capsids. The capsids are based on the outer shell of a naturally occurring virus that infects E. coli bacteria. They are formed when 180 copies of the same protein assemble into a nanoscale soccer ball.

"We think these little spheres, 27 nanometers in diameter, will form the basis for a new class of pharmaceuticals and a new class of materials," Swartz says. "For example, to date we've been seriously limited in our ability to both produce and to modify capsids to turn them into effective vaccines."

But now researchers in Swartz's lab, principally doctoral students Brad Bundy, supported by a Stanford Graduate Fellowship, and Aaron Goerke,supported by Merck & Co., Inc., have not only produced capsids cell-free for the first time, but also have attached uniquely reactive

amino acids to the capsid surfaces.

The amino acids allow the capsids to either stick to and carry specific proteins or stick to other capsids, allowing their assembly en masse. The tiny spheres could therefore transport targeted vaccines or medicines around the bloodstream or could be linked together in different configurations to make novel materials. Materials from assembled capsids could be light, strong and biodegradable, Swartz says.

Piggybacking vaccines on capsids may provide safer and more effective vaccinations than current methods, Swartz says. Most vaccines today work by introducing dead or weakened copies of viruses, mixed with other chemicals, into the bloodstream with the hope that they will provoke a strong, albeit general, response by the immune system. The process is akin to advertising a product to a random audience and hoping some consumers become interested.

With an engineered capsid, in contrast, a vaccine maker could attach a very specific protein designed to stimulate only the appropriate immune-system cells. A vaccine with these well-targeted capsids would be more likely than a traditional vaccine to elicit a strong and specific response. The capsid method is akin to advertising a product directly to the people who are most likely to want it.

Source: Stanford University