# Membrane protein kit may lead to better targeted drugs

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Many pharmaceuticals may soon become better targeted and more effective with the help of new technology developed at the U.S. Department of Energy's Argonne National Laboratory.

This technology, the Rhodobacter Membrane Protein Expression System, received one of this year's R&D 100 Awards. These prestigious awards, known as "the Oscars of Innovation," recognize the most important scientific and technological breakthroughs of the year. The winning invention, developed by Argonne biologists Philip Laible and Deborah Hanson, enables its users to easily generate large amounts of membrane proteins.

Membrane proteins are proteins embedded into the surfaces of cells that carry out vital processes necessary to the cells' survival. They act as gatekeepers, controlling which drugs can access the cell. These proteins can make or break a drug, and are so important in disease that more than half of all new drugs in development target membrane proteins.

For researchers to design better targeted drugs, they need to know the structure and functional characteristics of these membrane proteins. Determining these characteristics is difficult, because researchers need large amounts of membrane protein to characterize their functions and map their structures, and sources are scarce.

Few prior technologies were able to produce membrane proteins in large amounts, in part because membrane proteins are finicky and difficult to

work with. They cannot function in water, so the proteins must be protected by a layer of membrane almost immediately after they are generated inside the cell. Otherwise, they will degrade from exposure to an incompatible environment.

Laible and Hanson sought to change this. With their new kit, membrane proteins can be produced in unprecedented quantities. "This kit is the first of its kind to be designed specifically for the production of membrane proteins," Hanson said.

The kit has the capability to produce large quantities of protein because it uses Rhodobacter, a type of bacteria that naturally produces many internal membranes, providing the cell with greater capacity to sequester more foreign membrane proteins. Because Rhodobacter is also easy to culture, Laible and Hanson hope that someday the cells will be used as "factories" for membrane proteins.

The Rhodobacter system avoids the challenges that have typically dogged membrane protein manufacture through the innovation that Hanson and Laible developed. In the kit, membrane proteins are synthesized at the same time as the membranes that house them. "It's the intricate coordination of these events that allows the whole system to work," Laible said. This breakthrough shortens the proteins' exposure to inhospitable environments, preventing them from degrading.

The two processes occur together because they are triggered by the same signal: oxygen. A drop in oxygen levels both tells the Rhodobacter cell to synthesize the desired membrane protein and prompts it to generate more membrane. As a result, this kit affords researchers greater control. This trigger can be set automatically, left overnight without the need for a researcher's presence, or initiated manually by the researcher.

Laible and Hanson say that pharmaceutical companies stand to gain the

most from this new technology, due to the prominence of membrane proteins in drug design. The Rhodobacter system is currently available through Argonne, and the researchers are seeking industry partners.

Provided by Argonne National Laboratory