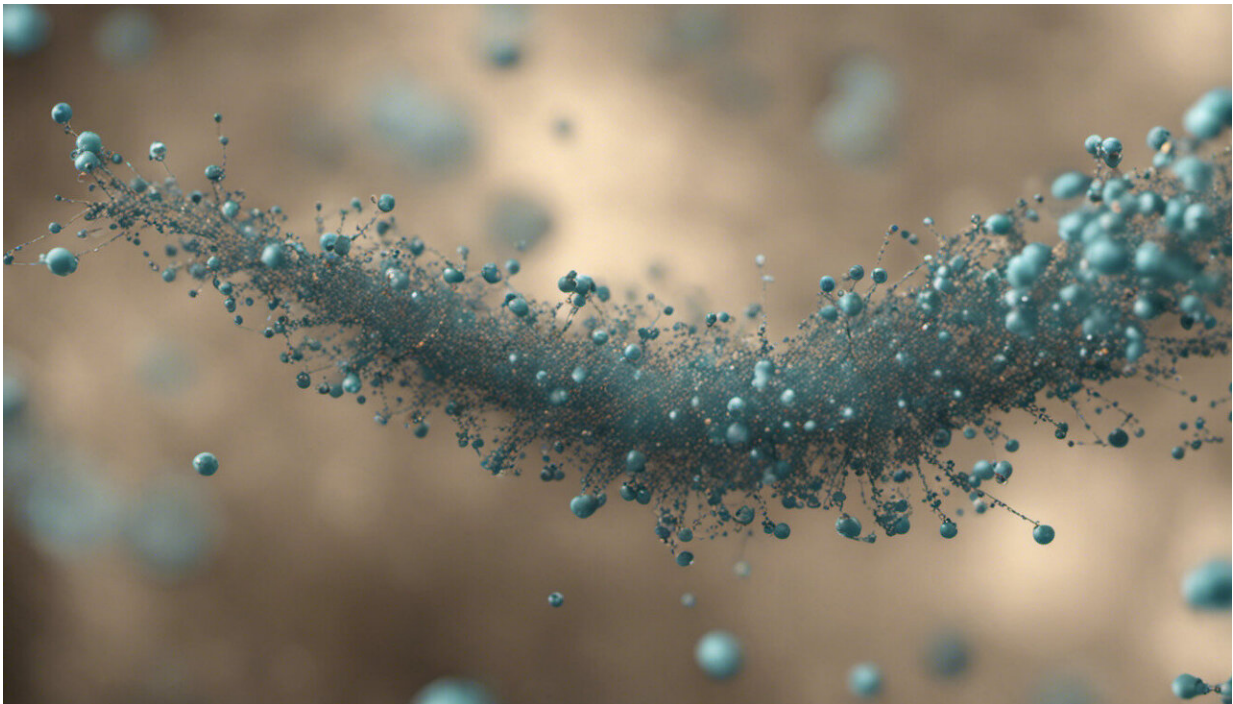


# Supercharged proteins enter biology's forbidden zone

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Credit: AI-generated image ([disclaimer](#))

Scientists are reporting discovery of a way to help proteins such as the new generation of protein-based drugs -- sometimes heralded as tomorrow's potential "miracle cures" -- get past the biochemical "Entrance Forbidden" barrier that keeps them from entering cells and doing their work.

The new technique, described in the monthly journal, *ACS Chemical Biology*, represents a new use for an engineered form of green fluorescent protein, the topic of the 2008 Nobel Prize in Chemistry that is one of the most important research tools in biosciences.

In the report, David Liu and his colleagues describe the difficulty of delivering proteins from the outside of mammalian [cells](#) into their interiors.

For that reason, nearly all of the blockbuster drugs that are proteins must do their work on the exterior of cells, activating [receptors](#) that send signals to the interior. This constraint greatly limits the scope of protein-based drugs. Liu's solution: Attaching proteins to molecules of "supercharged" [green fluorescent protein](#), which they mutated to give it a very high positive charge. When the hybrid proteins bump into the surface of a cell, they get pulled inside by negatively charged [molecules](#) called proteoglycans.

Liu and his team tested the hybrid proteins on five types of cells, and found that they were extremely good at carrying their protein cargo inside. In fact, the supercharged [protein](#) was up to 100 times better at getting proteins into cells compared to other approaches. The delivered proteins were able to go to their target locations in the cell, such as the nucleus or cytoplasm, and perform their jobs. "To our knowledge, this is the first report of functional delivery of an enzyme into retinal cells in vivo," the researchers state.

**More information:** "Potent Delivery of Functional Proteins into Mammalian Cells in Vitro and in Vivo Using a Supercharged Protein", *ACS Chemical Biology*.

Provided by American Chemical Society

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