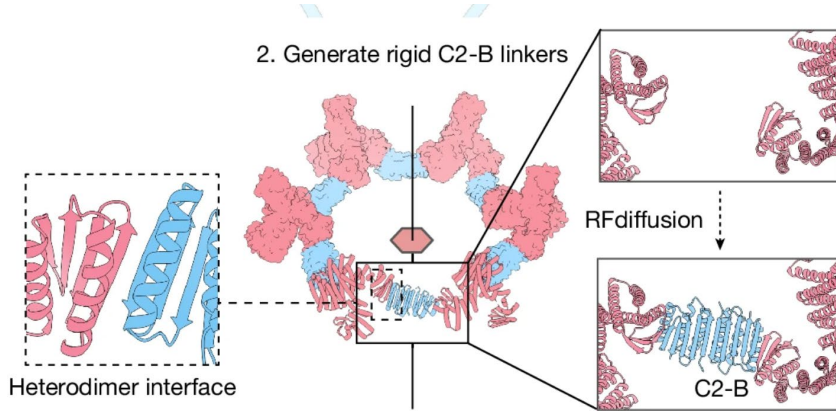


Customizable Protein Cages for Drug Delivery to Cells



Design strategy for generating spherical protein cages. Protein cages form when pentagons and hexagons (red) combine to create the curvature needed for a closed, spherical structure. Rfdiffusion, which is a generative protein design method, was used to create dimeric linkers (blue) that rigidify the curvature and connect the protein building blocks to direct proper self-assembly. X-ray crystallography validated the linker structure and cryo-EM revealed the cage architecture.

S. Wang, Y. Xie, D. Chmielewski, C. Weidle, T. Shu, G. Ahn, R. D. Kibler, C. Hernandez, W. Chen, D. C. Duran, A. Carr, A. K. Bera, S. Lee, J. Decarreau, A. Kang, E. Brackenbrough, E. Joyce, K. Wu, A. J. Borst, A. Favor, B. Huang, F. DiMaio, L. J. Holt, and D. Baker, "De novo design of quasisymmetric two-component protein cages," *Nature* **655**, 251–257 (2026).

Scientific Achievement

Researchers computationally designed two-component protein cages that assemble into virus-like spherical cages with programmable size and function.

Significance and Impact

These customizable cages provide a new platform for biologic drug delivery and for studying how large biomolecular assemblies move and organize inside cells.

Research Details

- Protein components were designed to assemble into curved hexagonal lattices with pentagonal defects that close into spherical cages ranging from 40 to >200 nm in diameter.
- X-ray crystallography at the FMX beamline provided a high-resolution structural validation of a key linker protein component, the C2-B- α 20 linker.
- Functionalized cages delivered ribonucleoprotein cargo into cells and served as probes of size-dependent cytoplasmic diffusion and protein localization.