Building molecular 'cages' to fight disease

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(Phys.org) -- Researchers at the University of Washington in Seattle and the University of California, Los Angeles (UCLA) have developed a computational approach to designing specialized proteins that assemble themselves to form nanoparticle cages that can be used to deliver drugs to tumors and other sites of disease. Published in the journal Science, this research could be utilized to create nanoparticle cages from any number of different proteins, with potential applications across the fields of medicine and molecular biology.

UCLA investigator David Yeates led this study. He and his colleagues used computer models to identify two proteins that could be combined to form perfectly-shaped three-dimensional puzzle pieces. Twelve of these specialized pieces fit together to create a molecular cage a mere fraction of the size of a virus.

The specifically designed proteins intermesh to form a hollow lattice that could act as a vessel for drug delivery. In principle, it would be possible to attach a recognition sequence for cancer cells on the outside of the cage together with a chemotherapeutic agent. As currently designed, the assembled protein cages are porous enough that a drug placed inside would likely leak out during the delivery process. The investigators are now conducting computer modeling studies to design a new molecular cage with an interior that will be better sealed.

In a second paper that was also published in Science, Dr. Yeates and University of Washington colleague David Baker describe how they created similarly designed molecular cages using multiple copies of the

same protein as building blocks. The scientists control the shape of the cage by computing the sequence of amino acids necessary to link the proteins together at the correct angles. This alternative method represents a more versatile approach in theory because it requires only one type of protein to form a structure, Dr. Yeates said.

This work is described in two papers titled, "Structure of a 16-nm cage designed by using protein oligomers," and "Computational design of self-assembling protein nanomaterials with atomic level accuracy." Abstracts of these papers are available at the journal's website.

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