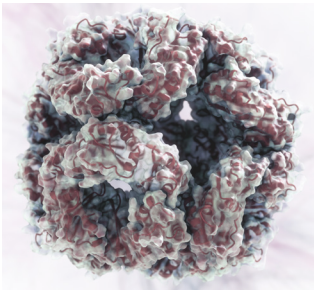
THE UW INSTITUTE FOR PROTEIN DESIGN



Self-assembled nanoparticle designed in the Baker group.
Illustration rendered by Vikram Mulligan, Ph.D.

Today's projects, tomorrow's solutions
UW Medicine researchers are exploring designed proteins as the basis for:

- Life-saving vaccines for flu, HIV, malaria and other deadly infectious agents (using antigen designs that mimic key pathogen proteins)
- Targeted drug delivery and gene therapy (using smart nanoparticle protein packages)
- Destruction of cancer cells (using proteins designed to regulate other proteins responsible for cancer cell growth)
- Diagnosis of vitamin deficiency, toxins, flu and other important substances (using small stable "affinity" agent proteins with built-in protein sensors that emit light or change color on binding to the target substance)
- New approaches to treat type 1 diabetes, arthritis, multiple sclerosis and other autoimmune disorders (using protein designs that interact and modulate or block immune cell targets)
- Treating celiac disease (with a new oral enzyme therapy to break down gluten)
- Prevention of Alzheimer's disease (using designed proteins to bind the toxic malformed amyloid or tau brain proteins)

Protein design: going green
In addition to tackling challenges in human health, proteins may hold promise in healing the environment. Our researchers envision proteins designed to break down pollutants in water, soil and air — and proteins that will lead to biofuels.

Proteins: the Workhorses of Life

Proteins fulfill the instructions of DNA. They are responsible for digesting food, building tissue, transporting oxygen through the bloodstream, dividing cells, firing neurons, powering muscles. Proteins do nearly every job, at every moment, within the body.

Disease results when the proteins that orchestrate human life malfunction. **At the same time, proteins hold great promise for the future of medicine — and other fields as well.**

Over the last century, countless drugs have been developed to target and correct malfunctioning proteins in the body. Yet in recent years the pace of discovery has slowed dramatically, resulting in few effective new drugs despite billions of dollars of investment by public and private sources. Science clearly needs a new strategy — and proteins are the key.

The power of proteins

At UW Medicine, scientists are pioneering the field of **protein design,** engineering brand-new proteins to serve as therapeutic and diagnostic tools. This field has the potential to significantly reduce the time and cost it takes to improve medical care.

The power of proteins lies in their exquisite precision. Most of today's drugs are derived from **small molecules** that seek out and bind to target proteins in the body, where they work to correct errors and change the course of a disease. In many cases, however, these drug molecules are too small to be precise or potent when it comes to the body's proteins, which are **large molecules.** Once in the body, small-molecule drugs can bind too weakly to their target protein or miss it entirely, limiting drug benefits. Or they can bind to the wrong protein, causing negative side effects.

Imagine drug molecules that are themselves proteins — large, robust, precisely focused proteins able to identify their target in the body and bind tightly to it. Such drugs would be more effective and result in fewer side effects than small-molecule medicines.

A number of protein-based therapeutics exist today, primarily in the form of **antibodies** used to treat autoimmune conditions and inflammation. The benefit of antibodies — which are very large protein molecules — is their specificity. The downside is that they are exceedingly expensive to develop, and antibodies and other existing protein-based drugs address only a small number of diseases and conditions.

David Baker, Ph.D., leads the global effort to design new proteins. In addition to pioneering protein design, he and his team have developed a computational program, Rosetta, that is the world standard for researchers in academia and industry working to understand protein structure. Computational power is at the heart of protein design, and the Rosetta software — with its ability to rapidly sort through large data sets — will allow speedier discoveries at lower costs.

Baker has received numerous awards for his work. He holds faculty appointments in the University of Washington's departments of biochemistry, genome sciences, physics, computer science, chemical engineering and bioengineering. He graduated with a bachelor's degree from Harvard in 1984 and a Ph.D. from the University of California, Berkeley, in 1989. Among many achievements and distinctions, Baker has served on the editorial boards of the *Proceedings of the National Academy of Sciences* and *Protein Science,* is a Howard Hughes Medical Institute investigator, and has received the prestigious Sackler Prize in Biophysics.

Unlike antibodies, designed proteins are synthetic proteins, making them cheaper and faster to generate. Moreover, harnessing the ability to engineer new proteins will open up far-reaching possibilities.

Researchers at UW Medicine see the potential not only for vastly improved drugs for a whole range of diseases and conditions, but for earlier, more accurate diagnoses — even for the prevention of disease. Our researchers see the power of proteins to revolutionize medicine, and they are at the forefront of this revolution.

Harnessing the potential of proteins

UW Medicine scientist David Baker, Ph.D., recognized worldwide for his breakthroughs in understanding proteins and in manipulating them for new purposes, is the leading architect of protein design. Already Baker and his colleagues have designed a number of proteins with new functions, including HIV vaccine candidates and influenza virus inhibitors.

The **University of Washington Institute for Protein Design** will take this work to new levels. Under Baker's leadership, the institute will marshal deep institutional strengths — in biochemistry, genome sciences, biological structure, pharmacology, immunology, computational biology and a host of other disciplines — to advance the potential of protein design.

The UW Institute for Protein Design will unify a multidisciplinary cadre of people — not only the University's faculty, scientific staff, postdoctoral fellows and graduate students, but also partners from collaborating institutions and from the computer and biotechnology industries. Together, they will bring extraordinary expertise to bear on a singular focus.

With this depth and breadth of talent — and with a state-of-the-art facility in the new Molecular Engineering and Sciences Building on the UW campus — the institute will be a magnet for new talent, a wellspring for new ideas and a source of new hope and promise.

The power of private support

The UW Institute for Protein Design is an ambitious endeavor. Our success will rely on our ability to recruit key faculty to contribute new areas of expertise to the effort, to fund postdoctoral fellows equipped to bridge disciplines in this new science, and to develop the sustainable infrastructure that will enable the research to take flight.

Private support will be critical in building this world-class institute. Investments from visionary philanthropists will have an impact in donors' lifetimes, while serving as a legacy for future generations of researchers, physicians and patients.

For more information

For more information on the UW Institute for Protein Design, please contact Katherine Cardinal, senior director for philanthropy, at 206.616.0412 or cardinal@uw.edu. Thank you for your interest in our work.