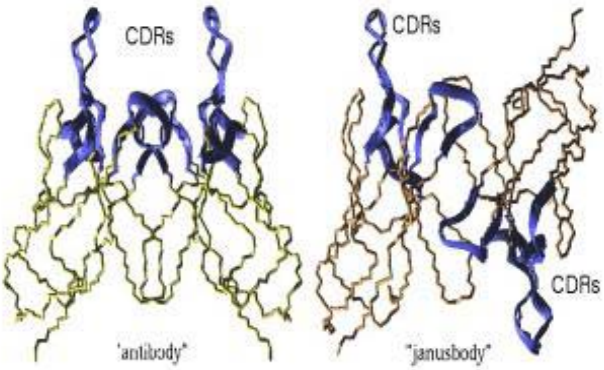
Argonne NATIONAL LABORATORY

Technology Development and Commercialization

JANUSBODY. Synthetic Molecules that Pack a Punch

A Compact, Bivalent Designed Protein Consisting of a Dimeric Assembly of a Single Antibody Domain



Argonne researchers have synthesized surrogate molecules, called "Janusbodies," that pack a significantly greater punch per unit mass than do conventional antibodies. The Janusbody — so named because its two "business-end" binding sites face in opposite directions — is produced by flipping one of its folded amino-acid "domain" segments. The resulting synthetic bodies retain their capacity to bind to specific "target" compounds (called antigens), but with their interaction area greatly enlarged; at the same time, their thermal stability — which determines "shelf life". — is increased by a factor of thousands (potentially, millions). Janusbodies are the key to fast, inexpensive, and highly accurate tests for diagnosing diseases and detecting low-concentration contaminants.

Immunoassay (IA) technology depends on the ability of antibodies — constituents of biological immune systems — to bind selectively to particular "target" molecules. Antibody fabrication has shifted toward production in bacteria, rather than in animals, and the use of fragments—such as the Fv, the smallest functional antibody construct to date — rather than whole antibodies. However, the two domains of the Janusbody dimer (so called because the molecule is made up of two subunits), despite their opposite orientation, are actually identical. Thus, in contrast to conventional antibodies and even Fvs, which require modification of two different genes, only a single gene must be modified to alter or change the Janusbody's target molecule.

The multibillion-dollar immunodiagnostic industry uses antibodies for testing the safety of blood units (screening for the presence of hepatitis or HIV, for example), spotting cancer indicators, and determining levels of hormones, as well as in immunotherapy treatments. Every time someone uses a home pregnancy kit, for instance, an IA test is involved. Because every application requires a different protocol, each test for a particular kind of target —infectious disease, cancer antigen, or toxic compound — must be performed separately. Thanks to their engineerable high-affinity for targets and low affinity for molecular mimics, as well as the potential ease and cheapness of multiple, redundant tests, Janusbodies promise rapid, highly accurate identification of contaminants, detection of illicit materials, and diagnosis of disease.

By modifying the binding properties of individual Janusbody strains and matching them to targets of interest via phage display techniques, a "library" of tailored Janusbodies, each specific to a particular compound, can be developed. Production of large quantities of the desired Janusbody can then take place using bacterial expression systems. The approach is highly practical; no critical new technology or scientific "breakthrough" is needed to take the Janusbody technology from feasibility testing and prototyping to commercial readiness.

Janusbodies lend themselves to a multitude of real-world applications. Examples include (1) Large-scale, affordable screening of meats, grains, and other foods for bacterial contamination (such as E. Coli and salmonella), fungi, and pesticides; (2) injection in humans as a general-purpose antitoxin against disease or antidote to poisons; and (3) water testing for all known pathogens at once. Use of Janusbodies as a reliable means of detecting the presence of particular compounds will also lead to biosensor applications that provide improved environmental monitoring and criminal forensics.

Over the past two years, Argonne scientists have learned to reproduce Janusbodies in quantity and stabilize them; with feasibility demonstrated, the project is now in the prototype design/optimization phase.

For More Information

For more information, contact Argonne's Office of Technology Transfer (800-627-2596, partners@anl.gov)