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Spotlights on Recent *JACS* Publications

FLU PROTEIN REACHES THE NUCLEUS BY BURNING A SALT BRIDGE

Martin Blackledge, Darren Hart, and colleagues reveal a temperature-dependent control on the binding of a component of the influenza A RNA polymerase complex (DOI: 10.1021/jacs.5b07765). The discovery sheds light on how a crucial viral protein enters the nucleus after a host cell is infected with the virus.

Influenza A is one of the two main viruses that cause seasonal flu in humans; it also infects other mammals and birds. Researchers want to know exactly how the virus propagates in host cells. In one important step of this process, a component of the virus's RNA polymerase complex called basic protein 2 (PB2) interacts with the adaptor protein importin α1 to gain entry into the nucleus. But the detailed mechanism has so far been unclear.

Using solution-state NMR, small-angle scattering, and single-molecule FRET, the team shows that this interaction is regulated by a temperature-dependent dynamic equilibrium between open and closed states of a heterodimer at the C terminus of PB2. At cooler temperatures, a salt bridge between the two domains stabilizes them in a closed state, the form they adopt in the complex. At warmer temperatures like those in the body, the heterodimer adopts a more flexible conformation that allows it to interact with importin to enter the nucleus.

Deirdre Lockwood, Ph.D.

ENZYME DESIGN MADE EASIER WITH MINIMALIST MODIFICATION

By modifying a single residue in the protein calmodulin, Ivan Korendovych and colleagues have engineered an esterase whose activity competes with that of rationally designed enzymes made with more complex approaches (DOI: 10.1021/jacs.5b07812).

To design artificial enzymes with new and useful functions, researchers have typically used complex computational approaches for directed evolution and made catalytic antibodies. However, both of these methods require substantial resources and can yield disappointing activity levels and poor protein stability.

Now Korendovych and co-workers demonstrate a minimalist approach to directed enzyme evolution that involves altering a single amino acid in a non-enzymatic protein, calmodulin. The team computationally models introducing a histidine residue, which has been shown to catalyze ester hydrolysis, into the hydrophobic cavity of calmodulin at 10 individual sites. When prepared and tested experimentally, one such mutant, dubbed AlleyCatE, has activity that bests that of previous *de novo*-designed esterases and is comparable with that of some catalytic antibodies.

The authors have successfully used this single-mutation approach to create other enzymes from calmodulin as well. The method could represent a simpler and cheaper way to design functional proteins, by identifying leads for further optimization, and could also help clarify natural protein evolution.

Deirdre Lockwood, Ph.D.

NEW LIGHT-HARVESTING MOLECULAR SYSTEM WITH TUNABLE PROPERTIES

To create artificial photosynthetic systems for solar energy conversion, scientists must apply knowledge about photosynthetic processes to the design of self-assembling components that mimic them. The ideal candidate for an artificial photosynthetic system would have the ability to perform ultrafast intermolecular charge transfer, accept and stabilize electrons, and harvest light over a large range of the solar spectrum.

Researchers led by Oren Scherman, Werner Nau, Michael Wasielewski, and J. Fraser Stoddart have now taken a step forward with the design of a system that takes advantage of the energy and electron transfer dynamics of a series of perylene diimide/cyclophane interlocked systems (DOI: 10.1021/jacs.5b10329).

The team describes how altering the chemical environment of this class of molecules impacts the properties of the system and their potential to serve as optoelectronic materials. Namely, with the selection of just the right heterocycles for use as extending units, the researchers discover they can tune the material's photophysical properties, as well as its capacity to accumulate electrons and transfer energy. The information garnered from this study may help pave the way toward the development of switchable, photoactive, mechanically interlocked systems and light-harvesting arrays for applications in photovoltaic devices.

Christine Herman, Ph.D.

PACKING AFFECTS HYDROGEN PRODUCTION FROM RENEWABLE ENERGY MATERIAL

One type of renewable energy material involves light-absorbing molecules, which pass energy to catalysts that generate fuel such as hydrogen. The light-absorbing portion of the material is typically a stack of aromatic molecules, the supramolecular arrangement of which impacts the energy conversion efficiency of the material.

Samuel Stupp and his colleagues want to learn more about how aromatic packing impacts H_2 production in these materials (DOI: 10.1021/jacs.5b10027). The researchers have synthesized seven perylene monoimide molecules, each with a different length of carboxlate linker dangling from the imide. They study the nanostructures of the hydrogels formed from each molecule using X-ray diffraction and crystallography and then examine the gels' electronic properties using absorbance spectroscopy. Finally, they connect each material to a nickel catalyst that produces H_2. Molecules with linkers of intermediate lengths produce the most H_2, because the packing of the aromatic rings provides higher orbital overlap, which the researchers think leads to better charge splitting upon light absorption.

Aside from showing their relevance to solar fuel production, this comparison between physical structure and electronic properties could be relevant to fields like crystallography and supramolecular self-assembly.

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