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DRUMMING UP INTERACTIONS BETWEEN PROTEINS THAT ARE NATURAL STRANGERS

David Margulies and colleagues have designed a synthetic chemical transducer able to reversibly control the catalytic activity of a common cellular enzyme, with implications for cancer therapy (DOI: 10.1021/jacs.5b01123).

Many signaling proteins are allosteric proteins that change their structure in response to environmental stimuli. Researchers want to develop synthetic analogues to such proteins so that they can carry out signal transduction pathways not found in nature. With such analogues, proteins overexpressed in cancer cells might be able to activate enzymes that cleave prodrugs which kill those same cancer cells.

Here, the authors present a "transducer" compound that is a hybrid of a DNA aptamer that binds platelet-derived growth factor (PDGF) and small molecules that inhibit the glutathione-*s*-transferase (GST) enzyme. Adding or removing free PDGF in the cell culture medium causes the transducer to change shape, enabling PDGF to reversibly activate and inactivate GST, which is not its natural binding partner.

This transducer, by activating GST, effects the GST-mediated cleavage of an anticancer prodrug and the release of nitric oxide, which is toxic to cancer cells. Some cancer cells secrete high levels of PDGF, suggesting that synthetic transducers could be used to relay the release of a cytotoxic molecule.

Deirdre Lockwood, Ph.D.

GRAPHENE AND METALS SHARE NEW CHEMISTRY

Graphene—a sheet of carbon atoms arranged like chicken wire—has been studied extensively in isolation, revealing interesting electronic, physical, and optical properties. Now, as researchers study how graphene interacts with other materials, the impact of its chemistry may eclipse all that we have learned about its physics.

Richard Berndt, Marie-Laure Bocquet, and their teams investigate how graphene behaves on the surface of iridium, a transition metal, at very low temperatures (DOI: 10.1021/jacs.5b05558). Graphene is a single layer of atoms with highly mobile hovering electrons, so it can be heavily influenced by the character of its supporting substrate. On a transition metal surface, graphene becomes chemically activated by the underlying metal and able to bond with other species. Here, the researchers use scanning tunneling microscopy to identify a bond formed through an unusual reaction between iridium-supported graphene and phthalocyanines, molecules of interest for photovoltaics applications. The researchers' modeling and calculations indicate that this new reaction should also work for a wide range of related molecules.

Though graphene's commercial uses are limited at present, applications in development include filtration, energy storage, composite strengthening, and more. The novel chemistry revealed here hints at unexpected opportunities for chemical functionalization and tailoring of graphene-containing materials.

Jenny Morber, Ph.D.

NEW ASSAY REVEALS DETAILS OF VESICLE FUSION

Many biological processes rely on tiny cargo-carrying sacs called vesicles. Neurotransmitter release, exocytosis, vesicle trafficking, and other biological processes depend on the fusion of these phospholipid vesicles to each other or to a larger cell. The fusion is facilitated by proteins called SNAREs that work like tethers. Although researchers have spent years investigating how SNAREs and other regulatory proteins govern vesicle fusion, many details are unknown.

Now Kimoon Kim, Nam Ki Lee, and colleagues have developed an *in vitro* assay that allows them to study the dynamics of vesicle fusion (DOI: 10.1021/jacs.5b05385). One vesicle contains half of the reagents needed for a highly sensitive fluorescence experiment; another vesicle contains the other half of the reagents. When the two vesicles fuse, the SNARE-mediated fusion process can be tracked by measuring the fluorescence emitted as the reagents mix.

With the assay, the researchers show that the vesicle fusion process, guided here by neuronal SNAREs, undergoes "flickering": the pore that forms between the two fusing vesicles opens and closes at least twice. The first fusion pore opening is the most time-consuming step. The investigators say their assay can be extended to the analysis of other short-lived and dynamically rapid biological processes.

Rajendrani Mukhopadhyay, Ph.D.

NEW POLYMERIZATION METHOD COMBINES THREE STEPS INTO ONE

Chemists can now accomplish in a single shot what previously required three separate steps. Researchers led by Tae-Lim Choi describe a new method for olefin metathesis—a synthetic transformation yielding new carbon−carbon double bonds—that is the first to combine ring-opening, ring-closing, and cross metathesis in a one-pot reaction to yield well-defined polymers (DOI: 10.1021/jacs.5b06033).

The team designs multiple unique monomers containing cyclopentene moieties and uses them to create polymers via tandem ring-opening/ring-closing metathesis polymerization. The reactions are carried out without side reactions, such as cross-linking or depolymerization, to produce a distinct polymer microstructure. The researchers also demonstrate metathesis polymerization of multiple olefins, crossing the dicyclopentene monomers with diacrylate monomers to create an A,B-alternating copolymer.

Previous attempts to combine two or more transformation steps in polymer synthesis typically resulted in ill-defined polymers with random microstructure, and almost all past methods for olefin metathesis polymerization yielded polymers with simple repeat units resulting from a single type of transformation. Because polymers are used in countless ways worldwide, the ability to synthesize well-defined materials in a straightforward manner may have a significant positive impact.

Christine Herman, Ph.D.

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