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Spotlights on Recent *JACS* Publications

IMMUNO-EDITING WITH "EPITOPE SURROGATES"

There is tremendous interest in "drugging" the adaptive immune system, for example to dampen auto-immune disease or to stimulate an anti-cancer response. However, current immune-targeted drugs are limited in that they cannot distinguish one immune response from another, resulting in general immunosuppression or stimulation. Ideally, researchers would like to target only the "good" or "bad" immune responses with a new generation of drugs.

In a new Perspective, Thomas Kodadek and colleagues review the development of chemical tools for differentiating various antigen-specific antibodies, B cells, and T cells with the goal of modulating specific adaptive immune responses (DOI: 10.1021/jacs.6b02954). They describe libraries of synthetic peptide variants (peptoids and peptoid-inspired conformationally constrained oligomers), from which "epitope surrogates" representing antibody targets in chronic lymphocytic leukemia are isolated. These molecules could ultimately be used to target cytotoxins specifically to leukemic B cells—a strategy called "immune editing".

Also discussed are strategies for editing T-cell responses, building diagnostic panels for autoimmune and other diseases, and identifying key autoantigens. The scientists conclude by discussing DNA-encoded libraries, which would allow millions of compounds to be screened against antibodies and other immune targets. "The stage is now set to attempt to discover antibody biomarkers that would have enormous diagnostic utility, such as for early stage cancers or neurodegenerative diseases," they write.

Jeffrey M. Perkel

RESEARCHERS STRIKE GOLD WITH NEW SCREENING APPROACH

For some crystalline materials, photoluminescence properties can be altered by applying mechanical forces such as grinding, crushing, or ball-milling. This phenomenon is known as luminescent mechanochromism, and one of its potential applications is in sensing and recording devices. Over the past decade, researchers have found it difficult to control the properties and behavior of mechanochromic compounds. For now, the discovery of new mechanochromic compounds happens either serendipitously or as the result of modifications made to known mechanochromic compounds. But researchers led by Hajime Ito and Tomohiro Seki have taken a step toward changing that limitation with the design of a new screening method for mechanochromic complexes with desirable properties (DOI: 10.1021/jacs.6b02409).

The team set out to discover mechanochromic gold isocyanide complexes that undergo a desired, yet rare, crystal-to-crystal phase transition. The screening approach, which the team uses to assess 48 complexes that they have prepared, consists of three basic steps that involve identifying emissive complexes, evaluating changes in the emission color of the complexes upon mechanical stimulation, and identifying the complexes that undergo crystal-to-crystal phase transition. The authors say the approach can serve as a model for screening mechanochromic complexes to discover those with desired phase transitions.

Christine Herman, Ph.D.

HARDER THAN A ROCK: SUPERHARD TUNGSTEN TETRABORIDE ALLOYS

Richard Kaner and co-workers have developed a new class of superhard metallic materials that also have excellent thermal stability properties (DOI: 10.1021/jacs.6b02676). Superhard materials are useful in applications including drilling, precision cutting, and wear protection. While diamond is the hardest natural mineral, due to its high-density structure of covalent carbon−carbon bonds, synthetic superhard materials offer a practical and inexpensive alternative.

The authors present a new strategy for synthesis of superhard materials that exploits extrinsic effects such as manipulation of the material's grain morphology. More conventional intrinsic methods used previously had instead relied on developing materials with new compositions and crystal structures.

The new superhard materials are synthesized from alloys of tungsten tetraboride with varying amounts of group 4 transition metals, including titanium, zirconium, and hafnium. Differences in grain morphology are observed by scanning electron microscopy. These alloys set new hardness records under high stress, as measured by the commonly used Vickers indentation test. This approach opens possibilities for further development of superhard materials by alloying other metals with tungsten tetraboride.

Dalia Yablon, Ph.D.

BREAK TO MAKE: A NEW ROUTE TO SILYLENES

Carbenes possess intriguing reactivity due to the neutral divalent central atom and have become an important component of main group chemistry. Silylenes, the silicon analogues of carbenes, are usually transient species that require special stabilization in order to be isolated.

Thomas Müller and co-workers have now developed an entirely new strategy to selectively prepare stabilized hydridosilylenes from the fragmentation of silanorbornadienes induced by N-heterocyclic carbenes (NHCs) (DOI: 10.1021/jacs.6b02824). Experimental data and theoretical analysis suggest that these NHC-stabilized silylenes, possibly generated in a one-step concerted reaction, are equivalent to neutral silyl anions.

This unprecedented yet generally applicable discovery has added a convenient alternative route to stabilized silylenes. More importantly, the concept of NHC-induced fragmentation has enriched the fundamental understanding of main group element reactivity. It may also be suitable to synthesize other carbene and silylene congeners, such as germylenes and phosphinidenes.

Xin Su, Ph.D.

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ROSETTE NANOTUBES: JUST ADD WATER

In the future, materials that can stitch up cells, generate renewable energy, or shrink electronics are likely to include nanotubes. To develop nanotubes with customizable dimensions and properties, researchers need to understand the molecular forces that drive the self-assembly and structure of these nanomaterials. In a new study, Hicham Fenniri and coworkers have examined the role that hydrogen bonding plays in the self-assembly of a rosette nanotube (DOI: 10.1021/jacs.6b02420).

The rosette nanotube is composed of a self-complementary G^C molecule, which is a hybrid of guanine and cytosine and has the capacity to hydrogen bond with itself. The nanotube assembles in stepwise fashion: first, the molecule forms rosettes, a ring of six G^C molecules, through hydrogen bonding, and then these rings stack atop one another to form a hollow nanotube.

Because the nanotubes are not easily crystallized, the researchers turn to solid-state nuclear magnetic resonance spectroscopy to decipher, on a molecular level, how the hydrogen bonds hold the nanotube together. It turns out that water is essential to nanotube formation. Water drives self-assembly by facilitating hydrophobic interactions between the rings of each layer in the nanotube. Plus, water in the nanotube channel directly bonds with the G^C molecules to stabilize the tube.

Erika Gebel Berg, Ph.D.

NEW WAY TO CATCH A KAT

Post-translational modifications can have a strong influence on a protein's cellular function or activity. For example, acetylation of the amino acid lysine impacts a number of enzymatic and epigenetic signaling pathways. A family of enzymes called lysine acetyltransferases, known in scientific shorthand as KATs, effect this post-translational modification. But scientists have struggled to comprehensively study KATs and their regulation in cells. Now Jordan Meier and colleagues have developed a system to globally capture and study KATs (DOI: 10.1021/jacs.6b03036).

The researchers incubate cell lysates with a resin-bound general KAT inhibitor, thereby capturing all of the KATs in the mixture on the resin. When other possible KAT inhibitors are added to the solution, they prevent the KATs from sticking to the resin. Using their system, the team finds that KATs are susceptible to inhibition by an important compound called coenzyme A (CoA). In particular, one KAT, called NAT10, which has been implicated in some cancers and the aging disease progeria, appears to be most sensitive to feedback inhibition by CoA. These findings suggest that NAT10 may play a novel role in linking metabolism with cell signaling.

Meier and colleagues conclude, "This platform provides a powerful tool to define the potency and selectivity of reversible stimuli, such as small molecules and metabolites, that regulate KAT-dependent signaling."

Rajendrani Mukhopadhyay, Ph.D.

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