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# Spotlights on Recent *JACS* Publications

## TARGETING THE TRANSTHYRETIN TETRAMER

Though most notoriously associated with neurological disorders such as Alzheimer's and Parkinson's diseases, amyloidogenesis—a process in which a protein aggregates and becomes toxic—is also thought to cause numerous other diseases including type 2 diabetes and cataracts. Now, Jeffery Kelly and co-workers report a strategy for preventing aggregation of transthyretin, a protein in the blood that transports the hormone thyroxine and whose amyloidogenesis is associated with several conditions affecting the central nervous system, the peripheral nervous system, and the heart (DOI: 10.1021/ja311729d).

In order to function properly, proteins must adopt specific three-dimensional structures. Unfortunately, mutations or other structural abnormalities can disrupt protein structure and lead to amyloidogenesis. Normally, transthyretin exists as a tetramer, but transient dissociation of the tetramers and subsequent misfolding can lead to the formation of aggregates. Careful analysis of the three-dimensional structure of transthyretin enables the investigators to design small molecules that permanently attach to the thyroxine binding site and stabilize the tetrameric structure, preventing aggregation. Fortuitously, several of the inhibitors also become fluorescent upon attaching to the protein, suggesting they may have potential as imaging agents. These inhibitors are valuable tools for investigating the biology of transthyretin amyloidogenesis and also have potential diagnostic and therapeutic applications. **Eva J. Gordon, Ph.D.**

## DICHALCOGENIDE SEMICONDUCTOR MATERIALS MADE EASY

Liying Jiao and co-workers have developed a way to control the growth of crystalline molybdenum sulfide semiconductor by using molybdenum oxide microcrystals as templates (DOI: 10.1021/ja4013485). Semiconductors are incredibly important devices and are used in solar cells, light-emitting diodes, transistors, and many other electronic components. Transition metal dichalcogenides, including $MoS_2$, are emerging as important materials in semiconducting because they have the desired characteristics of both an intrinsic large bandgap and flexibility.

The researchers expose the rhomboid $MoO_2$ microplates to sulfur gas at high temperatures and anneal them at high temperatures for varied durations to produce highly crystalline $MoS_2$ flakes with controlled number of layers. The single-crystal domain size in the obtained $MoS_2$ flakes is around 10 $\mu$m in diameter, much larger than has been grown by other chemical methods. In addition, these synthesized flakes perform as well as mechanically exfoliated flakes, which are more difficult to make in a controlled manner.

The new method of producing $MoS_2$ semiconducting materials improves on earlier attempts that have produced either low-quality materials or crystals that are too small or too variable in size and shape. This simple solution may make dichalcogenide semiconductors cheaper to synthesize, which could have an effect on the future price and availability of consumer electronics. **Leigh Krietsch Boerner, Ph.D.**

## LIQUID CRYSTALS TRANSLATE CHEMICAL SIGNALS INTO VISUAL CUES

Due to their extraordinary physical properties, liquid crystals (LCs) have captured the interest of researchers looking to develop new methods for the sensitive, multiplexed detection of biological targets. Now, a new approach to label-free biosensing, developed by Daniel K. Schwartz and co-workers, combines the specificity of aptamers—nucleic acid sequences engineered to recognize specific molecular targets—with the rapid, real-time detection achievable with aqueous/LC interfaces (DOI: 10.1021/ja400619k).

When the team introduces an aptamer solution to the aqueous/LC interface, the aptamer molecules adsorb and cause the LC to transition from a vertical to a tilted/planar orientation. Upon addition of the small-molecule target solution, the aptamer molecules bind to the small-molecule targets and undergo a conformational change that causes the LC to revert to its original orientation. The researchers use polarized light to detect the changes in LC orientation that correspond with the aptamer–ligand binding.

By studying two different aptamer–ligand pairs, the team discovers that relatively subtle changes in aptamer conformation can have dramatic effects on LC reorientation, which could make it possible to develop highly multiplexed aptamer-based sensors, or "aptasensors", that hold potential for applications including environmental monitoring and molecular diagnostics. **Christine Herman, Ph.D.**

## TUMOR-TARGETING NANOPARTICLES FIND THE SWEET SPOT

Jie Zheng and colleagues have created tumor-targeting nanoparticles that are small enough to be cleared through urine but still effectively target cancerous tumors (DOI: 10.1021/ja401612x).

With passive tumor targeting, researchers hope to treat cancer without sickening the patient and harming healthy tissues. Until now, tumor-targeting particles have suffered from a dilemma that hampers their clinical use. If the particles are too small, the body clears them from tumors too quickly, thereby lowering their targeting efficiency. If particles are too large, they can accumulate at toxic levels in the liver and spleen.

To circumvent this apparent paradox, the authors coat tiny gold nanoparticles with a peptide called glutathione. In tests with live mice, the nanoparticles move quickly out of healthy tissues, accumulate at tumor sites at high concentrations, provide clear images of tumors, and pass out of the body through the bladder. When compared against dye molecules commonly used for in vivo imaging, the coated nanoparticles accumulate at the tumor site at a concentration 10 times greater than the dye, and clear from normal tissues more than 3 times

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faster, which make them more suitable for rapid detection of tumors. By combining efficient renal clearance of small molecules with long tumor retention of conventional nanoparticles, these coated gold nanoparticles make promising candidates for cancer diagnosis and therapy in clinical practice. **Jenny Morber, Ph.D.**


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