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Spotlights on Recent *JACS* Publications

CONJUGATE SEARCHES OUT AND DESTROYS PROSTATE CANCER TUMORS

Haiyen Zhau, Bogdan Olenyuk, Jean Shih, and colleagues have designed a monoamine oxidase A inhibitor—near-infrared dye conjugate that holds promise for targeting and treating tumors in prostate cancer (DOI: 10.1021/ja512613j).

Prostate cancer is the second leading cause of cancer-related deaths for men in the U.S., but most current treatments such as chemotherapy, radiation therapy, and surgery, are only effective for patients with its early stages and significantly decrease their quality of life. The search for new therapies to effectively combat prostate tumors of all grades is an ongoing, multidisciplinary endeavor.

In order to selectively target prostate cancer cells, the team has designed a strategy to inhibit a protein involved in the progression of the disease. The protein, monoamine oxidase A (MAOA), is an enzyme that degrades certain biomolecules and releases hydrogen peroxide, eventually leading to DNA damage, accelerated tumor growth, and metastasis in prostate cancer.

But because MAOA is also expressed in the central nervous system and elsewhere in the body, the researchers needed to find a way to deliver a MAOA inhibitor directly to tumors. To accomplish this goal they have developed a conjugate, combining a MAOA inhibitor, clorgyline, with a near-infrared dye that specifically targets tumors. The conjugate reduces MAOA activity in mouse xenograft models of prostate cancer and is a promising novel agent for treating the disease.

Deirdre Lockwood, Ph.D.

SEMICONDUCTOR SURFACE PROTECTION LETS RESEARCHERS FLAKE IT OFF

Like graphite, molybdenum disulfide (MoS_2) and tungsten disulfide (WS_2) are composed of paper-like sheets of atoms held together by weak out-of-plane forces. Like graphene, sloughed-off single layers of these materials demonstrate optical, electronic, and chemical properties distinct from those of their bulk counterparts. Potential applications of MoS_2 and WS_2 sheets include flexible electronics, photovoltaics and sensors. However, processing is a problem. Chemical separation, or exfoliation, of these sheets in liquids changes their properties, and additional processing is needed to recover their semiconducting nature.

Stanley Chou, Jiaxing Huang, Vinayak Dravid, and colleagues modify the surface of exfoliated MoS_2 in a one-step process that enables its transfer from water to inert organic solvents (DOI: 10.1021/ja5107145). With the sheets suspended in high boiling point solvents, researchers can tune semiconducting properties through heating, with minimal fear of oxidation. Maintaining the sheets in liquid also eases assembly into application-friendly films and patterns, or secondary substrates. This technique, which allows faster, easier chemical exfoliation than currently possible, is potentially extendable to WS_2 and similar materials. Researchers who had previously struggled to produce high-quality MoS_2 can now flake it off with a bit more confidence. An important material class just got easier to produce.

Jenny Morber, Ph.D.

AN ENOLASE IN THE (GENOMIC) NEIGHBORHOOD

John A. Gerlt and co-workers report the discovery of a novel enzyme, a member of the enolase superfamily characterized by the ability to abstract a hydrogen atom from a carbon adjacent to a carboxylic acid group (DOI: 10.1021/ja5103986). Though the precise functions of many of the tens of thousands of members of the enolase superfamily cataloged to date are not known, these enzymes play key roles in the metabolism of carbohydrates and amino acids. The new enzyme A0NXQ8, identified in the bacteria *Labrenzia aggregata*, is the first in its class found to function as an amino acid dehydratase.

The gene encoding A0NXQ8 resides between those encoding two members of another enzyme superfamily, the proline racemase family. The authors deduce that proline or a proline derivative may be a substrate of A0NXQ8. By screening a library of proline analogues, they determine that A0NXQ8 catalyzes the dehydration of a hydroxyproline.

Characterization of A0NXQ8 offers new insight into the metabolic pathways used by *L. aggregata* and the range of functions exhibited by enolases. In addition, these findings highlight the utility of the genomic neighborhood of genes encoding uncharacterized proteins to decipher their function.

Eva J. Gordon, Ph.D.

POLYMER-BASED NANOPARTICLES CARRY LOADS OF ANTI-CANCER DRUG

The ideal nanoparticle-based therapeutic is able to provide sustained release of high drug concentrations directly to diseased tissue, resulting in fewer systemic side effects and reduced dosage requirements compared to conventional treatments. As an added bonus, drugs with poor solubility, such as the anti-cancer compound paclitaxel, can be encapsulated within nano-sized micelles composed of amphiphilic polymers at high concentrations, which allow large doses of the drug to be administered without the need for toxic carriers to dissolve them.

Now, Karen L. Wooley and co-workers report a new method for improving paclitaxel delivery, which involves the use of polyphosphoester-based nanocarriers (DOI: 10.1021/ja512616s). The researchers demonstrate paclitaxel can be loaded into the self-assembled biocompatible and biodegradable micelles at high concentrations—up to 4.8 mg/mL, orders of magnitude higher than the <2.0 μg/mL aqueous solubility of the drug alone—forming well-defined nanoparticles. The team performs shell cross-linking to prevent rapid micellar dissociation and finds the cross-linked particles are more structurally stable, delay the release of drug, and are retained in the lungs of mice for almost twice as long as their un-cross-linked counterparts. The results open up numerous questions for future investigations and serve as an important first step in the exploration of polyphosphoester-based nanotherapeutics for the treatment of metastatic lung cancer.

Christine Herman, Ph.D.

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