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Spotlights on Recent *JACS* Publications

TELOMERES: LIKE BEADS ON A STRING

Telomeres are repetitive sequences of DNA located at the ends of chromosomes. Unlike other DNA in chromosomes that codes for proteins, telomeres serve to protect the ends of the chromosomes from deteriorating and have been implicated in various normal and pathological processes, including aging and cancer. Interestingly, telomeres are enriched in two of the four nucleotides that make up DNA—guanine and cytosine—and the very end is composed of just a single strand of guanine which can fold up into highly stable structures called G-quadruplexes. Most biochemical studies of G-quadruplexes have employed strands that are significantly shorter than those in cells. Studies of long telomeric DNA under more physiologically relevant conditions would give valuable insight into how telomeres function naturally.

Daisuke Miyoshi, Naoki Sugimoto, and co-workers use various biochemical techniques including polyacrylamide gel electrophoresis, circular dichroism, and ultraviolet spectroscopy to examine the structure, energetics, and hydration of G-quadruplexes (DOI: 10.1021/ja305384c). Based on the results, they propose that long telomeres adopt a bead-on-a-string-like structure composed of G-quadruplex units with structured linkers between two units under physiologically relevant molecularly crowding conditions. These studies contribute to continuing efforts to understand these intriguing parts of the chromosome and target them for therapeutic applications. **Eva J. Gordon, Ph.D.**

MOLECULAR SIEVE "TRAPDOOR" SELECTIVELY LETS THE BIG GUYS IN

Aluminosilicate molecular sieves, called zeolites, are important industrial tools since they can separate gases on the basis of their size. What types of molecules they can adsorb depends on their pore size. Separation of gaseous mixtures occurs when the sieves adsorb smaller molecules into their interiors, leaving the larger ones behind. While effective, this process is limiting if scientists need to separate and store a larger molecule from a mixture of gases.

Paul Webley and co-workers have synthesized a class of chabazite zeolites that act more as a trapdoor than a sieve (DOI: 10.1021/ja309274y). Instead of separation by size, this system lets molecules through that can induce a cesium cation in the pore to move temporarily, and thus let the molecule in. The researchers examine the mechanism both experimentally and theoretically, and they find that the ability to open the molecular door is based on paying an energy toll. This penalty is easier for "strong" molecules to pay than "weak" ones, regardless of size, effectively creating sieves that can separate mixtures with a "size inversion". The chabazite materials, made up of zeolites arranged in layers of double six-ring prisms linked by tilted four-membered rings, are highly selective for carbon dioxide over methane and nitrogen. These new materials could have significant implications for future gas separation, storage, and catalysis technologies. **Leigh Krietsch Boerner, Ph.D.**

RESEARCHERS DEVISE REVERSIBLE PROTEIN MONOLAYERS

The ability to immobilize functional proteins on surfaces is very important to the development of microarrays, biosensors, and drug screening, as well as for basic research. A rich literature exists for immobilization chemistry, but less well developed is the technology to make such interactions reversible. Now Luc Brunsveld, Pascal Jonkheijm, and colleagues describe an electrochemically controlled system for reversibly coupling proteins to self-assembled monolayers (DOI: 10.1021/ja308450n).

The system involves tethering a protein (in this case, yellow fluorescent protein, or YFP) to a ferrocene via a linker that includes a reactive thiol bond. That conjugate is then added to a self-assembled monolayer of β-cyclodextrin, which binds the ferrocene to form a monolayer of fluorescent protein. Oxidation of ferrocene to ferrocenium reverses the reaction.

Using surface plasmon resonance, the authors find that YFP dimers (linked by a disulfide bond between linkers) bind β-cyclodextrin with higher affinity than YFP monomers, resulting in a monolayer in which 16% of β-cyclodextrin molecules are occupied. The resulting monolayer is functional (i.e., fluorescent) but impermanent: It could be repeatedly formed and disrupted electrochemically. "Such systems are currently of interest for fabricating adaptive biomimetic interfaces," the authors write. **Jeffrey M. Perkel**

MESSING WITH THE MISMATCHES

The fidelity of the DNA replication process is critically important for proper functioning of the cell. The mismatch repair pathway, in which mismatches that arise within genomic DNA are fixed, is one of several mechanisms the cell has devised to quality-check DNA replication in the nucleus. The improper functioning of this pathway has been implicated in many types of cancer, suggesting that compounds that can target cells with mismatched DNA could be valuable tools for diagnosing and even treating certain cancers.

Toward this goal, Jacqueline Barton and co-workers generate several compounds referred to as rhodium metalloinserters that can precisely target mismatched DNA (DOI: 10.1021/ja3090687). These compounds can preferentially target cancer cells that are defective in repairing mismatches over healthy cells with an intact mismatch repair pathway. They then use a technique called inductively coupled plasma mass spectrometry to detect where in the cell the compounds end up. While all the compounds were found in the nucleus where genomic DNA is located, the authors also found that some of the rhodium metalloinserters tended to accumulate in the mitochondria of the cell as well, and these compounds were less specific for the mismatch repair-deficient cancer cells than those that preferred the nuclear environment. These results suggest that controlling subcellular location is an important design element for compounds that target mismatched DNA, a finding that

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could guide the development of anticancer diagnostics and therapeutics. **Eva J. Gordon, Ph.D.**

UP WITH FUNCTIONALITY, UP WITH PORE SIZE IN METAL–ORGANIC FRAMEWORKS

Metal–organic frameworks (MOFs) are crystalline constructs with potential applications in gas storage and separation, as well as sensing, biomedical, and catalysis applications. Generally, they are built by combining building blocks such as metals and organic ligands. As such, the size and functionalities of the MOF pores are built right into the frameworks by judicious choice of the building blocks. However, adding functional groups to the ligands reduces the pore size of the MOFs because they take up more space, limiting the type of the molecules that they can adsorb. But in a new method devised by Hong-Cai Zhou and co-workers, adding functionality to MOFs actually increases pore size instead (DOI: 10.1021/ja3085884).

In lieu of assembling the completed ligands into MOFs, the researchers incorporated ligand fragments. Zhou and co-workers truncated their systems, swapping the laterally functionalized biphenyl dicarboxylate in the terphenyltetracarboxylate unit with the functional group itself. The functional group on the fragment is no longer part of the structure of the MOF, but instead dangles alongside. As a result, there is a larger pore space, but with the same binding moiety, in the dicopper paddlewheel-based structures. Additionally, changing this group can affect the uptake and release of carbon dioxide, which is potentially applicable to carbon dioxide capture and sequestration as well. **Leigh Krietsch Boerner, Ph.D.**

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