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Spotlights on Recent *JACS* Publications

SOLID-STATE NMR REVEALS HOW A KINKY PEPTIDE SLAYS MICROBES

The innate immune system has a particularly effective tool for stamping out attacks by a wide world of enemies including bacteria, fungi, and viruses: positively charged α-helical antimicrobial peptides (AMPs). The potency and broad-spectrum activity of AMPs has stoked the interest of scientists hoping to learn their secrets and develop new medications for the war against drug-resistant bacteria.

To kill pathogens, AMPs insert themselves into and disrupt the microbial membrane, but the details are fuzzy. Solving structures of proteins in membranes is notoriously difficult; thus, 3D structures of AMPs in their relevant membrane context are scarce. Now, in a breakthrough, Myriam Cotten and colleagues have generated structures of helical AMPs—the highest resolution to date—immersed in a lipid bilayer with solid-state nuclear magnetic resonance (NMR) spectroscopy (DOI: 10.1021/ja411119m).

The researchers have solved the structures of two homologous AMPs, piscidin1 (p1) and piscidin 3 (p3). Of the pair, p1 is the more potent antimicrobial. Differences in the two structures could provide insight into what makes an AMP an effective killer. While both peptides have a distinct kink, the angle of the kink differs between p1 and p3, perhaps accounting for their gap in potency. The work provides insights that will help in the design of AMPs with novel and potent antimicrobial activity.

Erika Gebel Berg, Ph.D.

METAL CENTROCHIRALITY DIRECTS ASYMMETRIC CATALYSIS

Metal-based asymmetric catalysis—a major component of modern asymmetric synthesis—profoundly relies on organic ligands with point or axial chirality, or both. On the other hand, the intrinsic chirality at metal centers in certain complexes could also presumably provide ideal environments to induce asymmetry. However, efforts to exploit such highly desirable features have met with great challenges, mainly due to racemization of metal complexes.

Having demonstrated an asymmetric catalysis directed by the ligand sphere of a stereogenic Ir(III) center, Eric Meggers and co-workers now successfully modify the Ir(III)-based system to enable immediate chirality transfer from the metal center (DOI: 10.1021/ja4132505). The unusual stereochemical robustness and the lability to ligand substitution of this catalyst are both crucial for the efficient and highly enantioselective Friedel–Crafts additions between indoles and α,β-unsaturated 2-acyl imidazoles.

The researchers make a promising and possibly paradigm-shifting breakthrough in asymmetric catalysis methodology. Ready access to metal centrochirality may not only obviate the need for complicated chiral ligands but also open new avenues for many other asymmetric catalytic reactions.

Xin Su, Ph.D.

SNAPSHOTS OF NANOPARTICLES IN ACTION REVEAL THEIR INTERACTIONS

Jwa-Min Nam and co-workers have studied the simultaneous interactions between many freely moving nanoparticles with very high resolution, thereby quantifying in situ the particles' growth kinetics (DOI: 10.1021/ja501225p). This study goes beyond current single-particle studies that are limited by a variety of factors such as harsh environmental conditions (not in situ), disruption of particle dynamics, and restrictions to the range of motion or number of components that can be tracked at one time.

Here the authors study the interactions between DNA-modified nanoparticles that are confined in a lipid bilayer where the particles move freely in two dimensions. The researchers image these systems with dark-field microscopy and then conduct simultaneous analyses of individual couplings over a large surface area, revealing different particle cluster growth kinetics.

By tracking the interactions from multiple reaction sites with single-particle resolution, snapshots of the dynamic nanoparticles in action in solution can now be distinguished from the ensemble average. These methods can be applied to study a variety of interactions between nanoparticles and molecules including DNA, RNA, proteins, membranes, and chemical ligands and to develop highly quantitative and sensitive chemical and biological detection platforms. Detailed information on processes such as colloidal nanocrystal growth, assembly mechanisms, and reaction kinetics may be obtained from these types of investigations.

Dalia Yablon, Ph.D.

DNA DAMAGE DELIVERS A KNOTTY CROSS-LINK

Kent Stephen Gates and colleagues find that DNA sites with a common type of modification can react with the nucleobase adenine to cause cross-linking that could harm cells (DOI: 10.1021/ja410969x).

Both spontaneous chemical reactions and exposure to mutagens or toxins can cause a common type of DNA damage that leads to the formation of abasic sites, which do not contain a coding nucleobase. These abasic sites are present as an equilibrating mixture of a cyclic hemiacetal and a ring-opened aldehyde. Gates and co-workers have previously shown that the aldehyde form of abasic sites can react with a guanine residue on a complementary DNA strand. Now they show that a similar reaction can take place with adenine residues. Both reactions create a cross-link between two complementary strands of DNA.

Cross-linking between complementary DNA strands can functionally damage DNA by blocking the strand separation required for replication and transcription. As mammalian DNA contains up to 200,000 abasic sites per cell, the authors suggest that this cross-linking has the potential to cause biological problems such as cancer and cell death.

Deirdre Lockwood, Ph.D.

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