JACS
JOURNAL OF THE AMERICAN CHEMICAL SOCIETY
Spotlights
pubs.acs.org/JACS

# Spotlights on Recent *JACS* Publications

## A NEW FUNCTION FOR FIBRILS

To explore enzyme function and develop new drugs, scientists often turn to small organic molecules that control enzyme activity. Molecules that inhibit or turn off enzymes are by far the most common. In contrast, compounds that turn on enzyme activity are more challenging to discover and therefore less prevalent.

Now, James Wells and co-workers have discovered a synthetic small-molecule activator of procaspase-3, a protease that, when activated, is involved in cell death, immune function, and brain development (DOI: 10.1021/ja208350u). When the researchers studied the mechanism by which the small molecule activated procaspase-3, they were surprised to find that instead of participating in a one-to-one interaction with the enzyme, the compound assembles into very small fibers called nanofibrils that in turn interact with and activate the enzyme. Interestingly, these fibrils may act in the same way as natural structures in the cell that activate enzyme function, such as amyloid-$\beta$ (A$\beta$) peptide. The authors showed that A$\beta$ peptide fibrils can also activate procaspase-3, which may be linked to amyloid-$\beta$ neurotoxicity in Alzheimer's disease.

Understanding the way this unusual small molecule works paves the way for the design of additional nanostructures capable of caspase activation. Moreover, this understanding can aid research into the mechanisms by which natural and synthetic fibrils influence enzyme function in both normal and disease-related processes. **Eva J. Gordon, Ph.D.**

## METHOD TAKES THE GUESS WORK OUT OF DENDRIMER VESICLE FORMATION

Researchers can now predict the size and properties of a vesicle on the basis of the primary structure of its molecular precursors, thanks to a method developed by Virgil Percec and co-workers (DOI: 10.1021/ja208762u).

The team studied dendrimers, which are branched amphiphilic molecules possessing both polar and apolar character. Dendrimers can self-assemble into nanosized vesicles known as dendrimersomes, and scientists are interested in developing dendrimersomes because these hollow vesicles can encapsulate drugs and biomolecules for applications in both basic research and medicine. For example, researchers can tailor dendrimersomes to mimic cell membranes and perform fundamental biological studies to better understand how cells grow and divide. Alternatively, dendrimersomes encapsulating DNA, proteins, or therapeutic molecules can be developed for applications in nanomedicine.

Dendrimersomes have a number of advantages over traditional lipid-based vesicles, such as increased stability, uniformity, and the ability to be tuned to have a specified size and shape by altering the composition of their dendrimer precursors. Prior to this study, researchers could not systematically predict the properties of vesicles, such as size, membrane thickness, and stability, from the structures of their precursors. This method will take some of the guess work out of dendrimer research and speed the development of dendrimersomes as useful cell membrane mimics. **Christine Herman**

## NMR METHOD ASCERTAINS NATURE OF MEMBRANE PROTEIN ASSOCIATIONS

A three-step method developed by Charles Sanders and co-workers should enable scientists to use solution-phase NMR to more rigorously study the interactions between membrane proteins, which underpin the extensive biological chemistry that occurs within cell membranes (DOI: 10.1021/ja208972h). When researchers use NMR to study protein-complex formation in cell-membrane mimics called micelles, they run the risk of misinterpreting shifts in the spectra. For instance, protein A and protein B might interact nonspecifically because the micelles confine them near each other.

Together, the new method's three steps draw a unified picture about what is going on between the proteins. The researchers first determine whether proteins A and B are interacting with each other, and then how strongly the two proteins interact. Finally, paramagnetic spin labeling of different parts of protein A yields information about the complex's architecture and confirms that the interaction between the two proteins is specific.

The team learned that CD147, a membrane protein involved in cellular development, forms a specific, albeit weak, complex with the transmembrane domain of amyloid precursor protein (APP). APP is processed into the amyloid-$\beta$ peptide that plays a central part in Alzheimer's disease. CD147 has been shown to reduce levels of amyloid-$\beta$ in the past, but it was not known whether the protein interacts directly with APP until now. **Lauren Wolf**, *C&EN*

*C&EN*: adapted from *Chemical & Engineering News* with permission.

**Published:** December 20, 2011




dx.doi.org/10.1021/ja211405x | *J. Am. Chem.Soc.* 2012, 134, 2–2