

## Spotlights on Recent *JACS* Publications

### ■ POKING HOLES IN MEMBRANES WITH PH-TRIGGERED PEPTIDES

Membranes are the guard walls that protect the insides of cells from unwanted guests that could cause harm. Large molecules, such as proteins, have a particularly difficult time breaching the membrane divide. Scientists would like to develop ways to poke holes in cell membranes, allowing, for example, macromolecular medications to enter the cytosol to either heal a cell or, in the case of cancer, eliminate it. The key to such an approach is to avoid universal cellular permeabilization and to target certain cells selectively.

William C. Wimley, Kalina Hristova, and colleagues focus on using pH to induce selectively a peptide to form macromolecule-sized pores in membranes (DOI: [10.1021/jacs.6b11447](https://doi.org/10.1021/jacs.6b11447)). The researchers screen a peptide library looking for candidates that form membrane pores at low pH, but not at physiological pH. Through multiple iterations, they hit on potent pore formers at pH 5–6 that are essentially inert at pH 7.

These pH-sensitive peptides could help deliver molecular cargo via endosomes, which have an acidic interior. Endosomes carry macromolecules captured via endocytosis through the cell. Typically, these molecules are disposed of, but pore formation would allow them to escape into the cytosol. Similarly, the microenvironment around cancer cells is acidic, offering an opportunity to poke holes in malignant cells to usher in chemotherapeutics.

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