STRUCTURAL BIOLOGY

Taming crystals' whimsy

Molecularly imprinted polymers act as 'smart' nucleants for protein crystallization.

More often than not, protein crystallization relies on a random search for conditions that allow crystal nucleation and growth. As in speed dating, the hope is that at least one of the interactions will lead to 'instant chemistry' and a rewarding relationship. Nucleating agents added to the crystallization conditions can sometimes act as chaperones and guide proper interactions for crystal inception. But given the idiosyncrasies of individual protein targets, can nucleants really provide a more rational screening approach?

"MIP MIP hooray!" exclaims Naomi Chayen from Imperial College London. In collaboration with Sub Reddy from University of Surrey, Chayen reported the use of molecularly imprinted polymers (MIPs) as 'smart' crystallization nucleants. Polymerized in the presence of protein, MIPs retain cavities which are complementary to the protein's structure and exhibit selective rebinding. As Chayen simply puts it, they are "made by proteins for proteins," and either a local increase in protein concentration or statistical coincidences in cavity orientation could explain their nucleating function.

The researchers tested seven MIPs on cognate proteins and three additional targets. Six of the polymers induced crystallization of nine proteins, often in conditions that otherwise would not yield crystals. Cognate polymers always worked best, but noncognate MIPs could sometimes enhance crystallization as well. Although some proteins crystallized in the absence of imprinted polymers, crystals grown in the presence of MIPs typically diffracted to higher resolution. Three of the targets did not readily crystallize in the absence of MIPs or in the presence of traditional nucleants. Remarkably, up to 10% of the MIP-containing conditions yielded promising hits for these challenging targets.

According to the researchers, cognate MIPs can be synthesized with very small amounts of protein and should be applicable to a variety of systems, including protein complexes and membrane protein targets. "What is so marvelous here is the simplicity," says Chayen. Regarding the applicability for high-throughput crystallization screening, she adds: "This is the first [type of] nucleant, which is not solid but really a gel, that you can dispense easily and use with automation and robotics."

Petya V Krasteva

RESEARCH PAPERS

Saridakis, E. *et al.* Protein crystallization facilitated by molecularly imprinted polymers. *Proc. Natl. Acad. Sci. USA* **108**, 11081–11086 (2011).