Synopses of Research Articles

Simple Peptides Stabilize Mighty Membrane Proteins for Study

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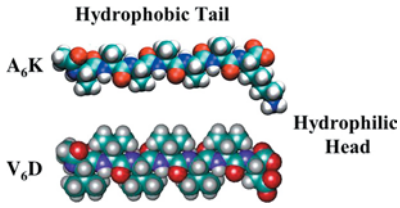
Cell membranes are largely made of proteins, and membrane proteins account for about a third of all genes. Despite their importance, they are devilishly hard to isolate and stabilize, and therefore are hard to study. The problem lies in their structure: membrane proteins have at least one hydrophobic domain, composed of a stretch of water-repelling amino acids, which holds the protein snugly in the lipid membrane. Purifying such a protein in an aqueous medium makes the hydrophobic parts aggregate, destroying the protein's delicate three-dimensional structure and often disrupting its function. The alternative is to extract the protein with a detergent, a two-headed "Janus" molecule with both hydrophobic and hydrophilic ends. The protein remains surrounded by the hydrophobic ends, while water clusters at the hydrophilic ends, easing the protein out of the membrane and into solution, where it can be studied.

To date, though, relatively few complex membrane proteins have been successfully purified with available detergents. In this issue, Shuguang Zhang and colleagues show that a simple amino acid–based detergent can successfully stabilize the dauntingly large protein complex photosystem I (PS-I), an integral part of the photosynthetic machinery.

The molecule they made, abbreviated A_6K, links six units of the hydrophobic amino acid alanine to one of the hydrophilic amino acid lysine. The authors used it to stabilize PS-I and then attached the detergent–protein complex to a glass slide, allowed it to dry, and examined the stability of PS-I by testing its fluorescence. Intact PS-I emits red light with a characteristic peak wavelength; as it degrades, this peak subsides and is replaced by another, bluer peak. Even the two best standard detergents did poorly at maintaining the red peak. In contrast, the spectrum after A_6K extraction was almost a perfect match for the normal one, indicating the complex was largely intact after drying. Furthermore, the complex appeared to remain stable for up to three weeks on the glass slide.

The potential applications of this work are severalfold. PS-I itself remains to be fully characterized, and this stabilization technique offers new means to explore its properties. In addition, an isolated and stabilized form of PS-I may hold some promise as an alternative energy source, since it generates an electric current in sunlight. Perhaps most importantly, the full potential of such simple amino acid–based detergents has only begun to be explored. It is likely that either this one, or others like it, can be used to isolate and stabilize hundreds of other membrane proteins, allowing them to be studied in detail for the first time.



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The designed short peptide (protein fragment) detergents look like matches and behave like lipids or oil molecules that repel water at one end but attract water at the other end

Kiley P, Zhao X, Vaughn M, Baldo MA, Bruce BD, et al. (2005) Self-assembling peptide detergents stabilize isolated photosystem I on a dry surface for an extended time. DOI: 10.1371/journal.pbio.0030230

miRNA Processing: Dicer-1 Meets Its Match

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In recent years, the control of gene expression by small RNA molecules has emerged as a major new mechanism for gene regulation. The small RNAs interfere with the expression of their target gene by reducing its transcription, triggering the destruction of the gene transcript, or inhibiting its translation into a protein. This discovery has not only altered views of gene regulation, but also provided molecular geneticists with powerful new tools with which to study and manipulate the function of any gene. The biology of these small RNAs is, therefore, under intense scrutiny.

Small RNAs are generated by specific pathways, the elements of which are being rapidly discovered. In this issue of *PLoS Biology*, two groups have identified a missing piece in one such pathway—in the fruitfly *Drosophila*. The pathway under investigation leads to the production of a type of small RNA called a microRNA (miRNA). These are 21–23 nucleotides in length, and are involved in regulating the expression of many genes. miRNAs start life as a much bigger transcript called a pri-miRNA, which is processed in two steps. First, it is converted into a shorter pre-miRNA, by the action of two proteins: Drosha, an RNAse III enzyme; and Pasha, which contains double-stranded RNA binding domains (dsRBDs). The pre-miRNA is then transported to the cytoplasm and is trimmed again into a double-stranded miRNA by a different RNAse III enzyme called Dicer-1.

In a separate pathway, RNAs called small interfering RNAs (siRNAs) depend on the Dicer-2 RNAse III and a dsRBD protein called R2D2 for their function. These pathways are also conserved in other organisms. Thus, a pattern emerges: the functions of small RNAs tend to require the combined actions of an RNAse III and a dsRBD protein. But why doesn't Dicer-1 have a partner? The answer, provided by the two studies from the labs of Phil Zamore and Haruhiko and Mikiko Siomi, is that we just hadn't found it yet.

The two groups took different approaches to finding Dicer-1's partner. Zamore's group looked for genes resembling other dsRBD-encoding genes, while the Siomi lab did a functional screen for new genes specifically implicated in miRNA processing. They both homed in on a new gene with great similarity to R2D2, and showed that loss of function of the gene results in the accumulation of pre-miRNAs—very similar to loss of Dicer-1 function, which suggests that the two genes act together in the same pathway. The new potential partner of Dicer-1 was given the name *loquacious (loqs)*, because failure to process the miRNAs in turn causes increased levels of expression of the target genes for the miRNAs.