PROTEOMICS

RNA-binding proteome redux

Scientists exploit the basic physicochemical properties of protein–RNA complexes to paint a dynamic portrait of the RNA-binding proteome.

Substantial efforts have been directed toward defining the full extent of the RNA-binding proteome (RBPome) over the past decade. Most of those efforts have relied on the cross-linking of protein to RNA followed by sequence-specific isolation of the resulting complexes. Although this method has proved successful at providing large repertoires of RNA-binding proteins (RBPs), drawbacks include the need for sizable amounts of material and complex workflows.

To address these limitations, a group from the Cambridge Center for Proteomics, led by Kathryn Lilley, Eneko Villanueva, Tom Smith, and Rayner Queiroz, took advantage of the well-known tendency of proteins and RNA to partition into organic and aqueous solvents, respectively. The scientists demonstrated that once

proteins were cross-linked to RNA by UV irradiation, the protein–RNA complexes—which combine the properties of each of their individual components—could be specifically and efficiently isolated from the aqueous–organic interface for downstream analysis by mass spectrometry and RNA sequencing. The approach is termed OOPS, short for “orthogonal organic phase separation.”

Analysis of the protein and RNA components isolated by OOPS demonstrated that both coding and noncoding RNAs with sizes greater than 60 bases are isolated without bias, and the RNA-binding sites could be inferred from the lack of sequence coverage caused by cross-linking at the point of interaction. The group also used OOPS to define a first bacterial protein–RNA interactome. Finally, they used OOPS to

document dynamic changes in RNA-binding patterns during cell cycle progression in human cells.

Because of its simplicity and relatively reduced material requirements, OOPS promises not only to facilitate the cataloging of protein–RNA interactions, but also to provide a system-wide view of the RBPome by enabling studies of its dynamics.

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Research papers

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