Protein recognition and disorder: A debate

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The extent to which three-dimensional structure is required for protein recognition and function is an area of vigorous debate with clear implications for protein engineering. Two differing viewpoints have been put forward in two articles published in *F1000 Biology Reports* today.

In structuring their arguments, the authors were encouraged to consider the opposing viewpoint, examine the points put forward and critique them in their own articles. This novel collaborative approach has given rise to a considered exchange of ideas and may consequently stimulate further research in the field.

In their article entitled "The case for intrinsically disordered proteins playing contributory roles in molecular recognition without a stable 3D structure", Keith Dunker (Indiana University School of Medicine) and Vladimir N. Uversky (Russian Academy of Sciences and University of South Florida) argue that the lock and key model of protein recognition cannot be upheld as a universal truth. They argue that some proteins without a rigid structure, intrinsically disordered proteins (IDPs), still have function.

In contrast, Joël Janin (Université Paris-Sud) and Michael J.E. Sternberg (Imperial College, London), in their article "Protein flexibility, not disorder, is intrinsic to molecular recognition", argue that a protein's function in the real world environment of the body's cells is dependent on the structure of that protein, and that protein recognition requires regions of complementary structure binding to each other. Janin and

Sternberg also note that many proteins seem to be disordered in the test tube but are in fact proteins waiting for partners (PWPs), which then adopt fully ordered structures in the presence of other components of the cell required to perform a function.

To counter the argument put forward by Janin and Sternberg, Dunker and Uversky conclude that the major difference between ordinary proteins and IDPs is that the former fold first and then bind to their partners while that latter remain disordered until they bind their partners. Furthermore, some IDPs can be much more dynamic than just "waiting for a partner", with the ability to switch from one partner to another and change structures while changing the partner.

Commenting on the two articles, Richard Henderson, MRC Laboratory of Molecular Biology, Cambridge said: "Both articles are by leaders who have given a great deal of thought to the function of proteins that appear to be intrinsically unfolded. Their different emphases will no doubt stimulate experiments as well as debate in the Structural Biology community. Time will tell us whether one or both models reflect how nature uses these structures."

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