

“The (zinc) *finger* is connected to the (EF) *hand*; the hand is connected to the *arm* (-adillo repeat)” -

Modularity in Protein Structure

At a fundamental level, nature appears to operate by taking a limited number of units and combining them in a myriad of ways to create a much larger portfolio of entities. The four DNA bases combine to code for 20 amino acids (or, we have heard recently, 22) and the 20 amino acids combine to make a vast array of different proteins. There is, however, an additional level of combination intermediate between these two. Rather than simply have many proteins that are each built from scratch, the 20 amino acids instead combine to make a more limited number of structural units that can be mixed and matched to create proteins with different functions. These units are known as domains, and PROSITE (<http://www.expasy.ch/prosite/>) currently lists around 1,500 different domains – a very small number compared to the total number of proteins known (currently over 600,000).

In this issue's *Showcase on Research*, we are examining protein domains in several different ways. In the first article, Grant Booker reflects on the existence of domains, and makes some elegant comparisons to show how a particular structural scaffold can be adapted to different functions and how different domains can be co-opted to carry out similar functions. In the second article, Jacqui Matthews discusses zinc-binding domains in their various guises. Following her article, Jörg Heierhorst tells us about FHA domains, which function as phosphothreonine binding modules. Finally, Jackie Wilce zooms in further and describes a current project that is focused on understanding the RNA-binding domain from a transcriptional coregulator, HuR.

I hope you enjoy reading these articles and that they provoke some thinking and discussion amongst protein domain fans.

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Protein Lego - Modularity in Protein Structure

Guest Editor: Joel Mackay

- What a Difference Domains Make
Grant Booker
- Zinc Fingers - Folds for Many Occasions
Jacqueline Matthews and Margaret Sunde
- FHA Domains as Phosphothreonine Binding Molecules
Andrew Hammet, Brietta Pike, Carolyn McNeas, Lindus Conlan, Nora Tenis and Jörg Heierhorst
- RNA-Binding Proteins which Affect mRNA Translation or Stability
Jackie Wilce, Peter Leedman and Matthew Wilce

Cover Illustration -

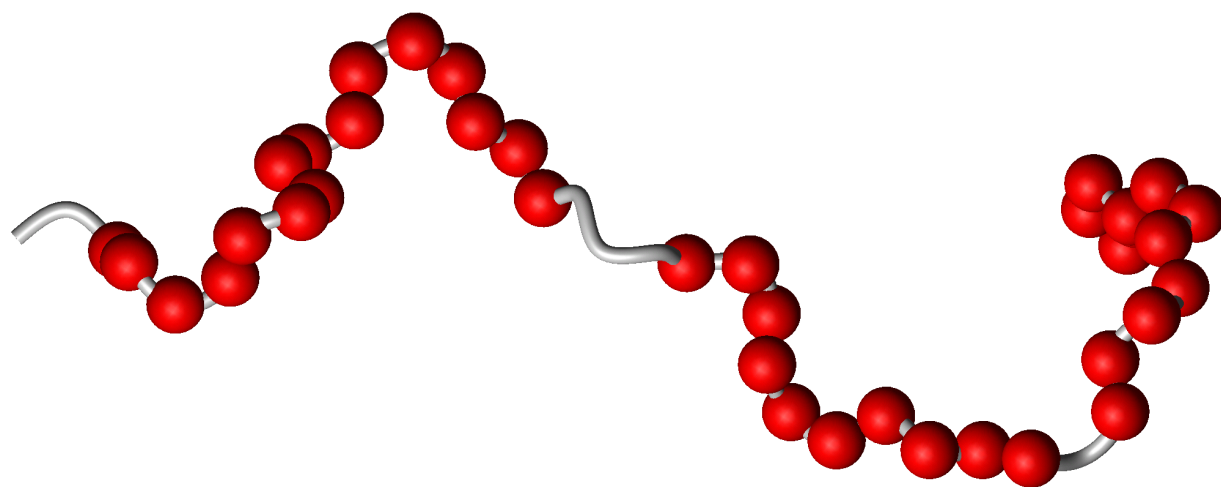
Mysterious and Intriguing Domains

Many proteins are built up from one or more domains. Sometimes the extent of this modularity is rather remarkable. Here is shown a schematic illustration of the *Xenopus laevis* transcription factor Xfin. Zinc finger domains are depicted as red spheres on the grey polypeptide chain. This protein contains 37 classical zinc finger domains that together comprise over 90% of the protein sequence. No functions have been yet ascribed to most of these domains and it is intriguing to ponder over what they all might do!



In the Next Issue . . .

In December, Showcase on Research will be on **Diabetes** – *Guest Editor: David James*



Front Cover Image