3.6: Protein Domains, Motifs, and Folds in Protein Structure

The structures of two different proteins shown below share a common PH (Pleckstrin Homology) domain (maroon).

These two and many other proteins have this domain, allowing them to bind a molecule of phosphatidyl-inositol triphosphate that is generated as part of a common cell-signaling pathway. The implication of this common domain is that a cell can have signaling pathways that allow it to respond to different signals that lead to the same response, albeit under different conditions and probably at different times. Proteins are typically described as consisting of several distinct sub-structures, discussed below.

A. Domains

A structural domain is an element of the protein’s overall structure that is stable and often folds independently of the rest of the protein chain. Like the PH domain above, many domains are not unique to the protein products of one gene, but
instead appear in a variety of proteins. Proteins sharing more than a few common domains are encoded by members of evolutionarily related genes comprising **gene families**. Genes for proteins that share only one or a few domains may belong to **gene superfamilies**. Superfamily members can have one function in common, but their sequences are otherwise unrelated. Domain names often derive from their prominent biological function in the protein they belong to (e.g., the calcium-binding domain of calmodulin), or from their discoverers (the PH domain!). The domain swapping that gives rise to gene families and superfamilies are natural genetic events. Because protein domains can also be "swapped" by genetic engineering to make **chimeric proteins** with novel functions.

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### B. Motifs

Protein **motifs** are small regions of protein three-dimensional structure or amino acid sequence shared among different proteins. They are recognizable regions of protein structure that may (or may not) be defined by a unique chemical or biological function.

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### C. Supersecondary Structure

**Supersecondary structure** refers to a combination of secondary structure elements, such as beta-alpha-beta units or the helix-turn-helix motif. They may be also referred to as structural motifs. “Google” [Supersecondary structure](https://en.wikipedia.org/wiki/Supersecondary_structure) for examples.

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### D. Protein Folds

A **protein fold** refers to a general aspect of protein architecture, like helix bundle, beta-barrel, Rossman fold or other "folds" provided in the [Structural Classification of Proteins](https://www.rcsb.org/structure/) database. Click [Protein Folds](https://www.rcsb.org/structure/) to read more about these structures.