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# Molecular Modeling to Study Protein Function

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A protein's structure and interactions are key to understanding its function. Skeletal muscle is filled with high molecular weight proteins that evade experimental determination of structure. Commonly, structures of single protein domains are used to overcome this hurdle. In addition, recent developments in molecular modeling enable solid testable predictions that further understanding of protein function.

When a structure is available from a homologous protein or domain, alignment tools enable the creation of a 3 dimensional model based on the homologous structure. By aligning the two dimensional amino acid sequence of the protein of interest to the amino acid sequence of the other protein for which a structure is available, computer models can model the 3 dimensional structure of the protein of interest [1]. Such modeling of the 94 kDa muscle protease Calpain 3 led to testable hypotheses into the effects of specific mutations that cause the disease Limb Girdle Muscular Dystrophy 2A [2].

When two structures or structural models are available, computer algorithms called docking algorithms can calculate the predicted surface interaction to determine likely interaction sites [3]. Such experiments offered support for a cleavage motif in Calpain 3 [4]. The docking algorithm predicted that a small protein containing a putative cleavage motif would have maximum surface interaction with its cleavage motif at the active site of the protease, consistent with it being a substrate. One note is that the calculations involved are complex and this method works best with smaller structures.

When no homologous models are available, one can use the amino acid sequence to predict secondary structures like alpha helices and beta-sheets. Specific programs like LOCATE [5] enable screening for protein domains in very large protein sequences. LOCATE enabled the identification of large hydrophobic domains in the lipophilic giant apolipoproteins B and I/II [5,6].

Finally, when no models are available to aid in prediction of structure or interactions, one can turn to the literature. There is a wealth of information available in written text, and real interaction partners will leave traces by association in the literature. This assumption led to the method of concept profiling [7], in which terms are associated into clouds by co-occurrence in Medline abstracts [8,9]. Proteins with high degree of overlap have a higher chance of being real interaction partners. This method led to the prediction and experimental confirmation of β-parvin as an interaction partner of Calpain 3 [8].

Protein structure is a great way to understand protein function. When structure is hard to experimentally determine, molecular modeling offers a powerful alternative.

## References

1. Arnold K, Bordoli L, Kopp J, Schwede T (2006) The SWISS-MODEL workspace: a web-based environment for protein structure homology modelling. Bioinformatics 22: 195-201.
2. Garnham CP, Hanna RA, Chou JS, Low KE, Gourlay K, et al. (2009) Limb-girdle muscular dystrophy type 2A can result from accelerated autoproteolytic inactivation of calpain 3. Biochemistry 48: 3457-3467.
3. Krippahl L, Moura JJ, Palma PN (2003) Modeling protein complexes with BiGGER. Proteins 52: 19-23.
4. de Morrée A, Lutje Hulsik D, Impagliazzo A, van Haagen HH, de Galan P, et al. (2010) Calpain 3 is a rapid-action, unidirectional proteolytic switch central to muscle remodeling. PLoS One 5: e11940.
5. Segrest JP, Jones MK, Mishra VK, Anantharamaiah GM, Garber DW (1994) apoB-100 has a pentapartite structure composed of three amphipathic alpha-helical domains alternating with two amphipathic beta-strand domains. Detection by the computer program LOCATE. Arterioscler. Thromb 14: 1674-1685.
6. Smolenaars MMW, de Morrée A, Kerver J, Van der Horst DJ, Rodenburg KW (2007) Insect lipoprotein biogenesis depends on an amphipathic beta cluster in apolipophorin II/I and is stimulated by microsomal triglyceride transfer protein. J Lipid Res 48: 1955-1965.
7. Jelier R, Schuemie MJ, Veldhoven A, Dorssers LC, Jenster G, et al. (2008) Anni 2.0: a multipurpose text-mining tool for the life sciences. Genome Biol 9: R96.
8. van Haagen HH, 't Hoen PA, Botelho Bovo A, de Morrée A, van Mulligen EM, et al. (2009) Novel protein-protein interactions inferred from literature context. PLoS One 4: e7894.
9. van Haagen HH, 't Hoen PA, de Morrée A, van Roon-Mom WM, Peters DJ, et al. (2011) In silico discovery and experimental validation of new protein-protein interactions. Proteomics 11: 843-853.

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