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At the root of characterizing disease states and of life-saving treatments is a thorough understanding of the fundamental processes that control cell behavior, including those that make cells move, signal, grow, and replicate. With this information, scientists can more easily predict how cells will respond in various situations: to threats and to opportunities.

In "Structure and Plasticity of Endophilin and Sorting Nexin 9," published in the October issue of Structure, Holger Sondermann and his co-workers provide insight into the molecular mechanism of a fascinating class of proteins that regulate endocytosis, a cellular program for membrane and cargo trafficking, receptor recycling, and nutrient uptake. In this study, the researchers compare and contrast proteins involved in modulating membrane shape through their structure and which might provide insight into their regulation. Investigations depict how these proteins interact with membranes and how this event might alter their activity.

"This basic science is the precursor to breakthrough discoveries that will advance the health and well-being of animals and people," said Sondermann, the Robert N. Noyce Assistant Professor in Life Science and Technology at the College of Veterinary Medicine and a 2008 Pew Scholar. "We need to understand the basic mechanisms of cell regulation and control in order to understand the molecular basis for disease. Elucidating the structure, function and regulation of proteins has the potential to provide knowledge about how we can then work on treatments and cures.

The study of multi-domain proteins and the regulatory principles involved in controlling their cellular function is still a very active but demanding field. We have much work to do."

The results of this research shed new light on mechanisms with both conserved and distinct molecular properties employed by proteins that have in common a particular domain (a building block of a larger protein) that allows them to interact and deform cellular membranes during cargo uptake. Interestingly, although the two proteins, Endophilin and Sorting nexin 9, have such a domain in common and have similar cellular function, the domains appear to have distinct biophysical properties. The work also highlights the complexity in protein architecture and regulation: Similar domains, when appearing in a different context in various proteins, may have evolved to adopt new regulatory mechanisms or functions. It is the context in which these domains develop that determines which functions are conserved and which provide them with a distinct cellular role.