Serpentine-shaped protein identified

The factors that govern normal cellular function or dictate disease states are manifold, and many of them are yet to be discovered. Often though, the answer lies in the function of proteins that contribute to a certain pathway or process. For instance, Dr. Holger Sondermann's work in understanding the role and molecular mechanism of certain proteins involved in neuronal signaling may bring us closer to understanding the pathology of diseases, such as Huntington's.

Dr. Sondermann and his colleague, Qi Wang, study the proteins involved in membrane trafficking that control the presentation of cell surface receptors, specifically those that facilitate neuronal transmission. Through a biological process called endocytosis, receptors are removed from the plasma membrane and internalized into a cell for degradation or recycling. For this to happen, a membrane bud has to form that is ultimately pinched off, yielding a vesicle that can be absorbed into the cell. The fission step is facilitated by enzymes and adaptor proteins that impose forces on the membrane.

In the post-genomic era, we deal with an extensive parts list describing the molecular content of cells, but it requires detailed studies such as ours to elucidate the function and interplay between the individual entities, proteins, membranes, and DNA," said Dr. Sondermann. "We are very excited when we determine the structure of a protein at atomic resolution. The interpretation of the structure allows us to propose how a protein may fulfill its job and how it may be regulated. We then use biochemical assays to test our hypotheses to provide a direct correlation between structure and function."

Sondermann and his team wanted to identify and understand the molecular mechanism responsible for fission, when the neck between the plasma membrane and the budding vesicle forms during endocytosis.

While it is well accepted that Dynamin, an enzyme, is responsible for the final fission process, our research implicated a protein called Pacsin (or Syndapin) capable of introducing constriction points at the membrane neck or membrane tube without the presence of Dynamin. Structural and biochemical studies were conducted in the Sondermann lab to reveal the mechanism and motifs responsible for the specific membrane-sculpting capability of Pacsin.

Often multiple, similar proteins are present in the cell, and it is important to assign specific functions to particular proteins so that eventually we can describe fundamental cellular processes at a molecular level. Most notably in the case of Pacsin, the structural studies revealed a serpentine shape of the protein, rather than the expected crescent shape, which suggests, Dr. Sondermann said, that it has unique features that distinguishes it from other F-BAR domain- containing proteins. These insights were recently published in the **Proceedings of the National Academies of Sciences**.