A new 'bent' on fusion

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(PhysOrg.com) -- Success in soccer sometimes comes with "bending it like Beckham." Success in cellular fusion -- as occurs at the moment of conception and when nerve cells exchange neurotransmitters -- requires that a membrane be bent before the merging process can begin, University of Wisconsin-Madison researchers have shown.

The scientists offer the first concrete evidence that a protein called synaptotagmin plays a critical role in initiating fusion by bending a section of a target membrane. The protruding dimple provides a small point of contact that can fuse with another membrane with less effort.

The finding, reported in the current issue (Aug. 21) of *Cell*, answers important questions relating to one of the most fundamental processes in biology.

"Fusion occurs when a sperm and an egg combine to make a person and when a virus such as HIV invades an immune cell," says senior author Edwin R. Chapman, a Howard Hughes Medical Institute professor in the physiology department at the UW-Madison School of Medicine and Public Health.

Fusion also takes place when cells deliver molecules onto their surfaces or exchange them with each other, as occurs during the transmission of messages between neurons at specialized structures called synapses. And fusion is the same process that lets the dozens of compartments working within cells transfer their contents to one another.

The process typically begins when a vesicle, or bubble-like container, buds off a donor compartment and travels to an "accepting" compartment.

"Fusion is an elementary issue that biologists have pondered for a long time," says Chapman, a synaptotagmin expert who has contributed significantly to understanding the protein's role in fusion during nerve cell communication. "It's something I've been thinking about since 1992."

A study by one group of scientists led to the theory that synaptotagmin bends the target membrane to begin fusion, but the theory had never been tested. That study used vesicles that already were highly curved, so it was not clear what bending effect synaptotagmin was actually having on them.

The Chapman team addressed the problem by creating vesicles with different degrees of curvature, including some that were only slightly curved. By exposing the differently curved vesicles to mutated synaptotagmin, which lacked membrane-bending capability, the researchers showed that the target membrane must be bent for fusion to occur.

To find a way to compensate for the mutated synaptotagmin's inability to bend membranes, Chapman's group turned to a protein that controls the bending of membranes when vesicles are returned to their original form during fission, which involves the splitting apart of membranes in a process called endocytosis. The researchers found that the endocytic protein overcame the fusion deficiency.

"Nobody had ever done this," notes Chapman, "although L.V. Chernomordik had suggested that fission and fusion proceed via similar intermediate structures. He was right."

Source: University of Wisconsin-Madison (news : web)