Team shows how dynamin mediates membrane constriction and scission

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Cells continually form membrane vesicles that are released into the cell. If this vital process is disturbed, nerve cells, for example, cannot communicate with each other. The protein molecule dynamin is essential for the regulated formation and release of many vesicles.

Scientists of the Max Delbrück Center for Molecular Medicine in the Helmholtz Association (MDC) and the Institute for Biophysical Chemistry of Hannover Medical School (MHH), together with researchers from the Freie Universität Berlin and the Leibniz-Institut für Molekulare Pharmakologie (FMP), have now elucidated the regulated process by which the molecular "motor" dynamin assembles into a screw-like structure. Moreover, they demonstrated how specific mutations impair the function of dynamin, for example in the congenital muscle disorder centronuclear myopathy or the neuropathy Charcot-Marie-Tooth disease. The researchers' study represents an important contribution to the development of new therapeutic approaches.

To transmit signals, nerve cells release neurotransmitters that are packed in vesicles. These vesicles are formed through membrane invaginations of the cell wall which are constricted and severed by dynamin. First, a chain of dynamin molecules wraps around the neck of the budding vesicle in a spiral. In a second energy-dependent step, the dynamin spiral is constricted, and the vesicle is released into the cell.

The researchers elucidated the 3-dimensional structure of the basic component of the spiral. It consists of four dynamin molecules, called a

dynamin tetramer. "For the first time we could determine how the dynamin tetramers assemble into a spiral," said Dr. Katja Fälber from the Crystallography Department of the MDC. "The structure also explains why this process only occurs on membranes: Only there do rearrangements in the dynamin tetramer take place that release the contacts for spiral formation," said Professor Oliver Daumke.

More information: Crystal structure of the dynamin tetramer, *Nature*, DOI: 10.1038/nature14880

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