A dynamin mutant defines a super-constricted pre-fission state

Dynamin family members are large GTPases found throughout the cell and are involved in numerous membrane fission and fusion events. The founding member, dynamin, plays a role in endocytosis by organizing into helical assemblies at the base of nascent clathrin-coated vesicles. Formation of these oligomers concomitantly stimulates the intrinsic GTPase activity of dynamin, which is necessary for efficient fission during endocytosis. Recent evidence suggests that the transition-state of dynamin’s GTP hydrolysis reaction may serve as a key determinant of productive fission.

To examine these structural changes and understand how they contribute to membrane fission, we solved the structure of a transition-state-defective dynamin mutant, K44A (K44ADyn), using cryo-EM and real space helical image processing techniques. This structure displays a 2-start helical symmetry and is tightly constricted with an inner luminal diameter of 3.7 nm, reaching the theoretical limit for spontaneous fission. Computational docking reveals that a GTP ground state conformation of dynamin is sufficient to achieve this final ‘super-constricted’ state and shows how the 2-start helical arrangement generates the most efficient packing of dynamin tetramers around the membrane neck. These data suggest a new model for the assembly and regulation of the minimal dynamin fission machine.