# Hotspots on the dynein stalk mediate communication in the motor domain

Stefan Niekamp, Nicolas Coudray, Nan Zhang, Ron Vale and Gira Bhabha

Skirball Institute, NYU school of medicine

For any molecular motor protein to produce motility, communication between the catalytic site of energy production and the site of the protein that engages with its track is essential. For many motor proteins, such as kinesin, these two sites are very tightly coupled to each other in space. For the microtubule based motor protein dynein, the catalytic AAA ATPase domain is spatially distant from the microtubule-binding domain (MTBD), and the two are separated by a ~135 Å coiled coil stalk. It is evident that the stalk must mediate communication between the AAA ring and the MTBD. However, the mechanism by which it does so has remained elusive. To better understand the role of the stalk in dynein motility, we carried out a bioinformatics study of 534 dynein sequences, and found that the length of the stalk is remarkably well conserved. Using outlier sequences, we designed a panel of mutations in the yeast cytoplasmic dynein background, and assessed the effect of these insertions and deletions on dynein motility. Our data point to three locations in the stalk that are important for mediating communication between track binding and catalytic site, and we show that the exact length of these regions is critical for maintaining this communication.