Kinesin-1, Kinesin-3, and fast transport of axonal organelles in *Drosophila* motor neurons

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We have developed methods for time-lapse fluorescence microscopy and tracking of single organelles in the motor axons of Drosophila to address questions about mechanisms axonal transport: 1) which motors move each organelle type and 2) how are those movements controlled? Mitochondria simultaneously bind kinesin-1 and dynein to drive saltatory motion along axons. However, each mitochondrion has an ~ 50-fold preference for a primary direction. How does a mitochondrion "know" and enforce its preferred direction of transport? To identify potential regulatory mechanisms for mitochondria and vesicle transport, we have done a number of genetic screens centred on distal neuropathy defects that are caused by microtubule motor mutations. Those screens have identifiedAPLIP1/Jip-1, a scaffolding protein for the JNK regulatory pathway as having important influences on transport. Most recently, we have identified a Jip-1 associated JNK pathway that regulates kinesin-cargo binding. We hope that defining such transport regulatory pathways will eventually lead to the development of therapeutic agents that will help suppress the neurodegeneration caused by motor neuron diseases like HSP.