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Title: Incorporating Motility in the Motor: Role of the Hook Protein Family in Regulating Dynein Motility

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Abstract: Cytoplasmic dynein is a retrograde microtubule-based motor transporting cellular cargo, including organelles, vesicular intermediates, RNA granules, and proteins, thus regulating their subcellular distribution and function. Mammalian dynein associates with dynactin, a multisubunit protein complex that is necessary for the processive motility of dynein along the microtubule tracks. Recent studies have shown that the interaction between dynein and dynactin is enhanced in the presence of a coiled-coil activating adaptor protein, which performs dual functions of recruiting dynein and dynactin to their cargoes and inducing the superprocessive motility of the motor complex. One such family of coiled-coil activating adaptor proteins is the Hook family of proteins that are conserved across evolution with three paralogs in the case of mammals, namely, HOOK1–HOOK3. This Perspective aims to provide an overview of the Hook protein structure and the cellular functions of Hook proteins, with an emphasis on the recent developments in understanding their role as activating dynein adaptors.

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