Supplemental Data

Mutations in BICD2 Cause Dominant Congenital Spinal Muscular Atrophy and Hereditary Spastic Paraplegia

Figure S1. A Proposed Disease Mechanism for DCSMA Caused by Mutations in BICD2

(A) The proposed pathomechanism of DCSMA due to mutations in BICD2. In early embryogenesis, Bicaudal related protein-1 (BICDR-1) sequesters Rab6 positive vesicles to the pericentrosome preventing their anterograde transport to growth cones.

(B) In late embryogenesis (Post day 10 in mice), BICDR-1 is down regulated, allowing anterograde transport of Rab6 positive vesicles part mediated by BICD2 from the Golgi to the growth cone required for neurite extension (Silencing of Rab6 and overexpression of BICDR-1 in late embryogenesis impairs neurite outgrowth). (C) In the case of mutant BICD2, the increased binding affinity to the dynein/ dynactin complex shifts the balance in favour of retrograde transport and impairs transport of Rab6 positive vesicles to peripheral growth cones - impairing neurite outgrowth.
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