

P037 ARF6 interaction with JIP4 controls a kinesin-I to dynein/dynactin switch mechanism regulating endocytic recycling during cytokinesis

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Late steps of cytokinesis and abscission require trafficking of endomembranes to the midbody. ARF6, a small G protein implicated in polarized membrane recycling, localizes to the midbody and controls the completion of cytokinesis. We identified JNK Interacting Protein 3 (JIP3) and JIP4 as new effectors of GTP-ARF6. These proteins scaffold the MAPK signalling pathway and control bidirectional movement of axonal vesicles by interacting with microtubules (MT) motor subunits, Kinesin Light Chain (KLC1) and dynactin. We demonstrated that KLC1, dynactin and GTP-ARF6 interact with the same domain of JIP3/4. Importantly, JIP3/4 do not bind both motors simultaneously, and ARF6 association with JIP3/4 promotes a KLC1 to dynactin switch. In HeLa cells, we implicated the ARF6/JIP4 pathway in the completion of cytokinesis and demonstrated that ARF6 and JIP4 control endosome trafficking to the midbody. KLC1 and dynactin were also clearly involved in the transport of membrane toward the midbody. Additionally, we found that both ARF6 and JIP4 are required for the recruitment of dynactin to the midbody. We thus propose that ARF6 controls membrane delivery to the midbody and abscission by interacting with JIP4 and regulating its association with motors.