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Title: Arf-like GTPase Arl8: Moving from the periphery to the center of lysosomal biology

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Abstract: Lysosomes are dynamic organelles that not only mediate degradation of cellular substrates but also play critical roles in processes such as cholesterol homeostasis, plasma membrane repair, antigen presentation, and cell migration. The small GTPase Arl8, a member of Arf-like (Arl) family of proteins, has recently emerged as a crucial regulator of lysosome positioning and membrane trafficking toward lysosomes. Through interaction with its effector SKIP, the human Arl8 paralog (Arl8b) mediates kinesin-1 dependent motility of lysosomes on microtubule tracks toward the cell periphery. Arl8b-mediated kinesin-driven motility is also implicated in regulating lytic granule polarization in NK cells, lysosome tubulation in macrophages, cell spreading, and migration. Moreover, Arl8b regulates membrane traffic toward lysosomes by recruiting subunits of the HOPS complex, a multi-subunit tethering complex that mediates endo-lysosome fusion. Here we provide a brief review on this recently characterized lysosomal GTPase and summarize the studies focusing on its known functions in regulating lysosomal motility and delivery of endocytic cargo to the lysosomes. We also explore the role of human Arl8b and its orthologs upon infection by intracellular pathogens.

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