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Abstract:

Lysosomes are membrane-bound cell organelle containing hydrolytic enzymes which help in the degradation of damaged organelles, aggregated proteins. They also regulate vital cellular functions, including autophagy. The endocytic pathway routes the cargos taken up from the environment towards lysosomes for degradation. These cargos bind to receptors in the plasma membrane and are incorporated into vesicles that are carried to early endosomes, where the receptors are separated and returned to the cell surface and then from early endosomes, it is then moved to late endosomes and further to lysosomes where the lysosomal hydrolytic enzymes digest the proteins. The endocytic pathway involves multiple fusion and fission events where small GTPases, tethering factors and SNAREs play important roles. In recent discoveries, the small GTPase Arl8b has emerged as a major regulatory GTPase, which localizes on lysosome. Recently the lab has established that the Rab7 effector PLEKHM1 simultaneously binds Rab7 and Arl8b, and this binding results in the late endosomes and lysosomes fusion. The interaction of Arl8b and PLEKHM1 is through N terminal RUN Domain. Through this study, we aimed to purify Arl8b and the RUN Domain of its downstream effector PLEKHM1 to study their interaction and eventually aimed to find the residues responsible for the interaction of PLEKHM1 and Arl8b.

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