Eukaryotic cells have an elaborate endocytic system that is specialized totake up materials from the environment and route it to the lysosomes fordegradation. The endocytic pathway is marked by multiple fusion andfission events whose regulation involves an interplay of small GTPases,tethering factors and SNAREs. HOmotypic fusion and Protein Sorting (HOPS)complex is an evolutionarily conserved multisubunit tethering factor thatmediates vesicle fusion with lysosomes. The mechanism of mammalian HOPSaction and its crosstalk with other lysosome proteins is only beginningto be understood. In the first part of this thesis, we demonstrate thatthe small GTPase Arl8b interacts with, and recruits HOPS complex tolysosome membranes. Depletion of HOPS subunit Vps41 results in defects in cargo trafficking to lysosomes that were rescued upon expression ofwild-type but not an Arl8b-binding-defective mutant, suggesting thatArl8b-dependent localization of HOPS complex to lysosomes is required for cargo degradation. Since the discovery of Arl8b, an ever-increasing numberof its interaction partners have come into light, inclusive of the RUNdomain-containing proteins. In the second section of the thesis, we haveidentified that Arl8b interacts with the RUN and FYVE (RUFY)domain- containing proteins, Rabip4' and Rabip4/RUFY1, via their RUNdomains. Arl8b depletion results in striking displacement of endogenousRabip4(s) from the endosomal membranes to the cytosol that can be rescuedupon expression of siRNA- resistant Arl8b. Future studies will be useful togain insights into how Arl8b regulates the membrane localization ofRabip4(s) and significance of Rabip4(s) interaction with Arl8b in membranetrafficking.