# Functional analysis of RacGAP ARHGAP22

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Rho small GTPases control cell morphology and motility through the rearrangement of actin cytoskeleton. ARHGAP22 is a member of Rac-specific GAP (FilGAP) family, and implicated in the regulation of tumor cell motility. However, little is known concerning the cellular localization and mechanism of regulation at the molecular level. Whereas FilGAP binds to FLNa and localizes to lamellae, we found that ARHGAP22 did not bind to FLNa. Forced expression of ARHGAP22 induced enlarged vesicular structures containing the endocytic markers EEA1, Rab5, and Rab11. Coiled-coil domain of ARHGAP22 is responsible for targeting of ARHGAP22 to the vesicular structures. Endogenous ARHGAP22 is also co-localized with EEA1- and Rab11-positive endosomes but not with trans-Golgi marker TGN46. When constitutively activated Rac Q61L mutant was expressed, ARHGAP22 is co-localized with Rac Q61L at membrane ruffles, suggesting that ARHGAP22 is translocated from endosomes to membrane ruffles to inactivate Rac. Forced expression of ARHGAP22 suppressed lamellae formation and cell spreading. Conversely, knockdown of endogenous ARHGAP22 stimulated cell spreading. Thus, the results may suggest that ARHGAP22 might control cell morphology by inactivating Rac but its localization is not mediated by its interaction with FLNa.