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The ESCRT pathway and ubiquitin-binding ability of Tsg101 are required for dynamic Src trafficking and v-Src-mediated invadopodia formation and invasion

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ESCRT proteins including Tsg101 are well-established for their role in formation of multivesicular bodies and sorting ubiquitinated endosomal cargoes to lysosomes via their ubiquitin-binding domains. However, genetic ablation studies in mouse models and human cell lines show ESCRT proteins and Tsg101 are required for proliferation, cell viability, and malignant phenotypes of cancerous cells. Utilizing a conditional Tsg101 knockout mouse embryonic fibroblast (MEF) cell line, we show that Tsg101 is indispensible for Src function. Dynamic trafficking of Src at endosomes and translocation of active Src to focal adhesions and invadopodia are impaired when expression of Tsg101 is lost. Blocking Vps4 function by expression of a dominant negative form of Vps4 has similar effect. Viral expression of wildtype Tsg101, but not the N45A mutant, which has lower binding affinity to ubiquitin, restores invadopodia formation and invasivenss of Tsg101-deleted v-Src MEFs. Together, our study reveals a surprising positive role of Tsg101 and probably ESCRT pathway in promoting Src signaling that requires its ability to interact with ubiquitin.

Biography

Chun Tu obtained her ph. D from Washington University at St. Louis in 2004. Her postdoctoral work under Dr. Hamid Band at Northwestern University and University of Nebraska Medical Center focused on how lysosomal trafficking affects Src signaling and invadopoida-associated matrix-degradation and invasion. She is currently an instructor working in Dr. Mien-Chie Hung's lab at University of Texas MD Anderson Cancer Center.