Head and neck squamous cell carcinoma (HNSCC) is highly aggressive tumor and despite various treatment options available, HNSCC patients are still faced with a high chance of recurrence and/or metastasis, with a 5-year survival rate of only about 50 percent. Thus understanding the metastatic process is of high importance and is highly significant for the development of novel treatments. Abnormal cell migration and invasion modulated by integrin-mediated interactions between the extracellular matrix (ECM) and the actin cytoskeleton are key components of metastasis. We recently identified that high expression of Rho-GEF binding protein α-catulin correlates with the ability of human squamous cell carcinoma cells to invade and metastasize. We showed that α-Catulin is preferentially expressed at the tumor invasion front and in the invasive streams of cells with minimal expression in the normal oral epithelia. Our in vitro data show that an upregulation of α-catulin expression correlates with the transition of tumor cells from an epithelial to mesenchymal morphology and knockdown of α-catulin in hHNSCC cell lines dramatically decreases the migratory and invasive potential of those cells in vitro and metastatic potential in xenotransplants in vivo. α-catulin deficient cells exhibit defects in actin dynamics, Rho signaling and directional migration. Performed by us transcriptional and biochemical analyses of tumors deficient in α-catulin demonstrate that its ablation prevent tumor cells from invading the surrounding stroma which is accompanied by changes in expression of genes involved in cell migration and invasion mediated by RhoGTPases, including integrins, CD44, its shedding enzyme ADAM10 and HGF/Met receptor. We hypothesize that α-catulin might be an important mediator in ECM-integrin-Rho pathway signaling by acting as a scaffold for Rho complex distribution that results in proper spatial activation of signaling downstream from ROCK during tumor progression. Therefore we developed conditional mouse model of α-catulin to investigate its role in SCC invasion. This mouse model will be combined with the model of invasive squamous cell carcinoma. Using this system we aim to contribute to better understanding of molecular mechanism of signal transduction by the catulin-Rho/ROCK downstream from integrins in metastasizing squamous cell carcinoma cells in order to identify novel strategies for HNSCC treatments and prevent cancer cell metastasis.