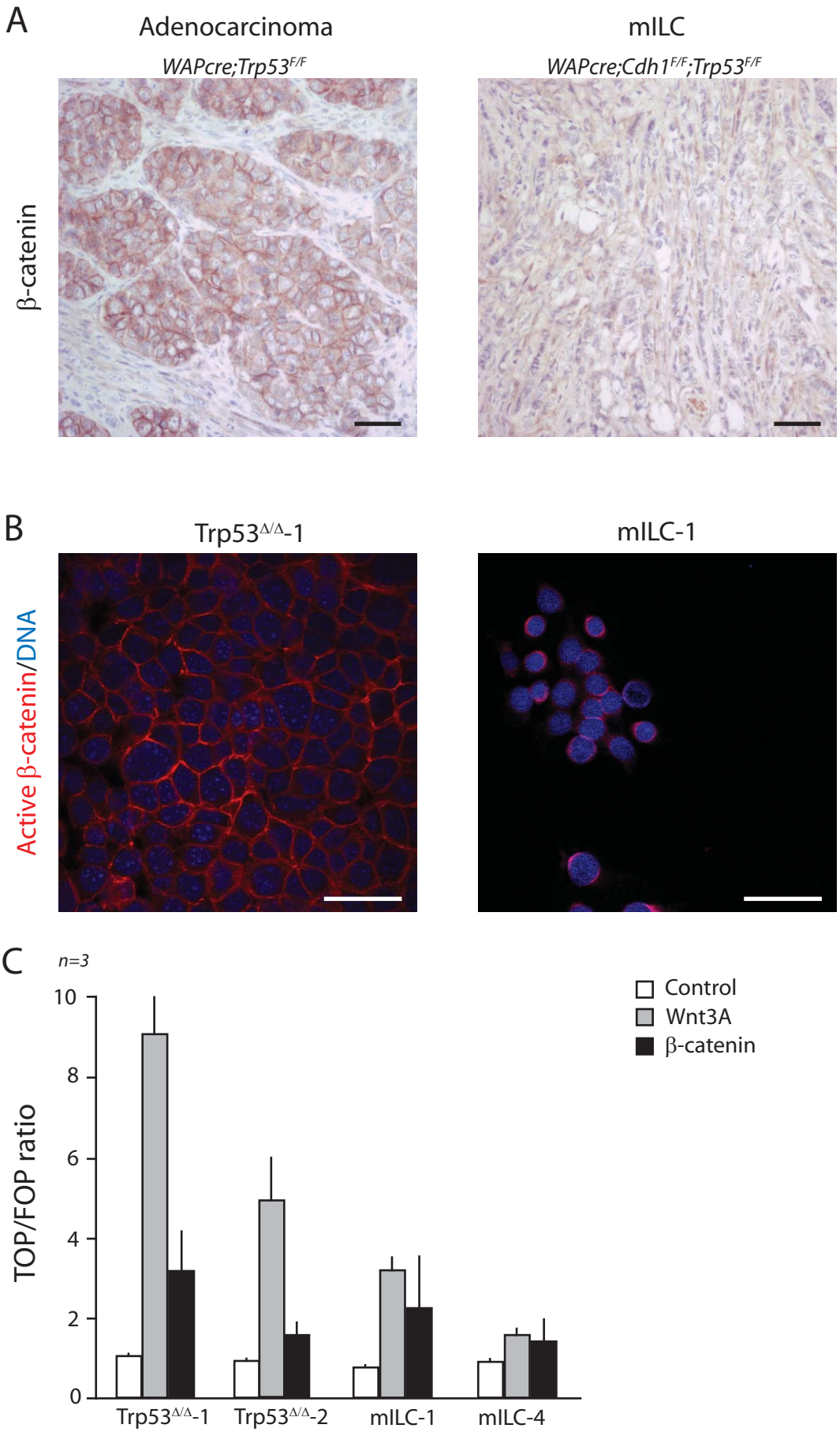
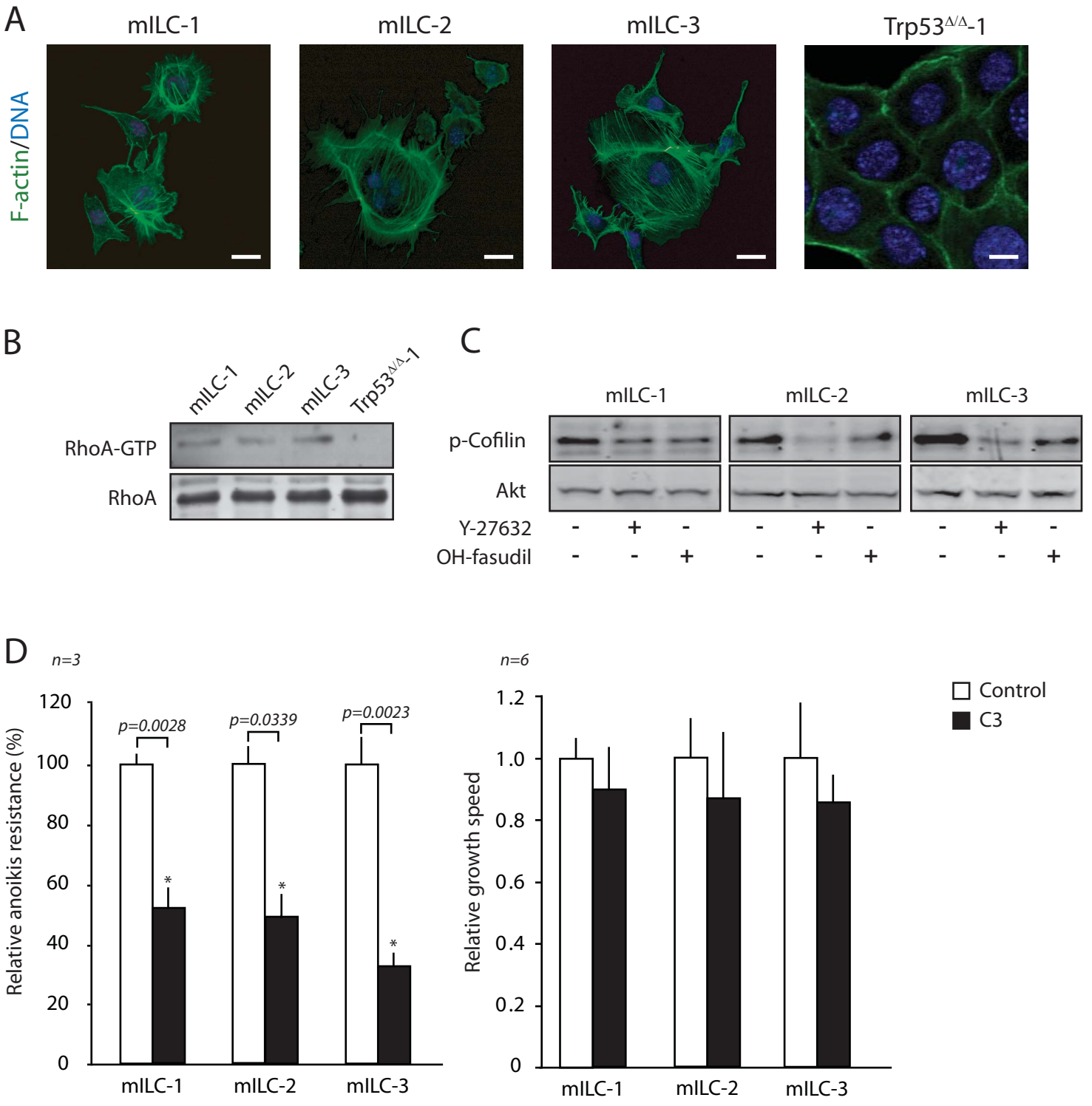
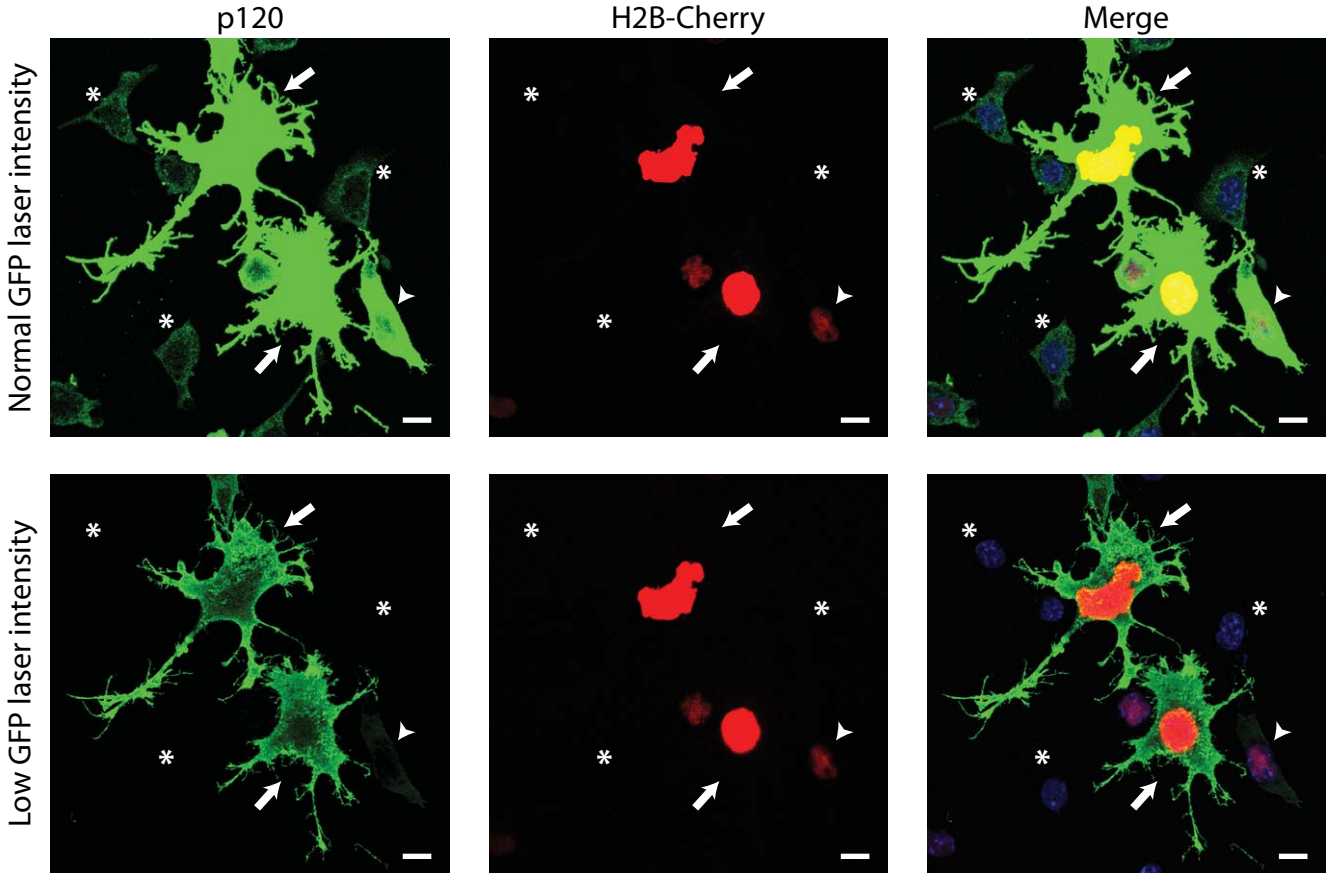


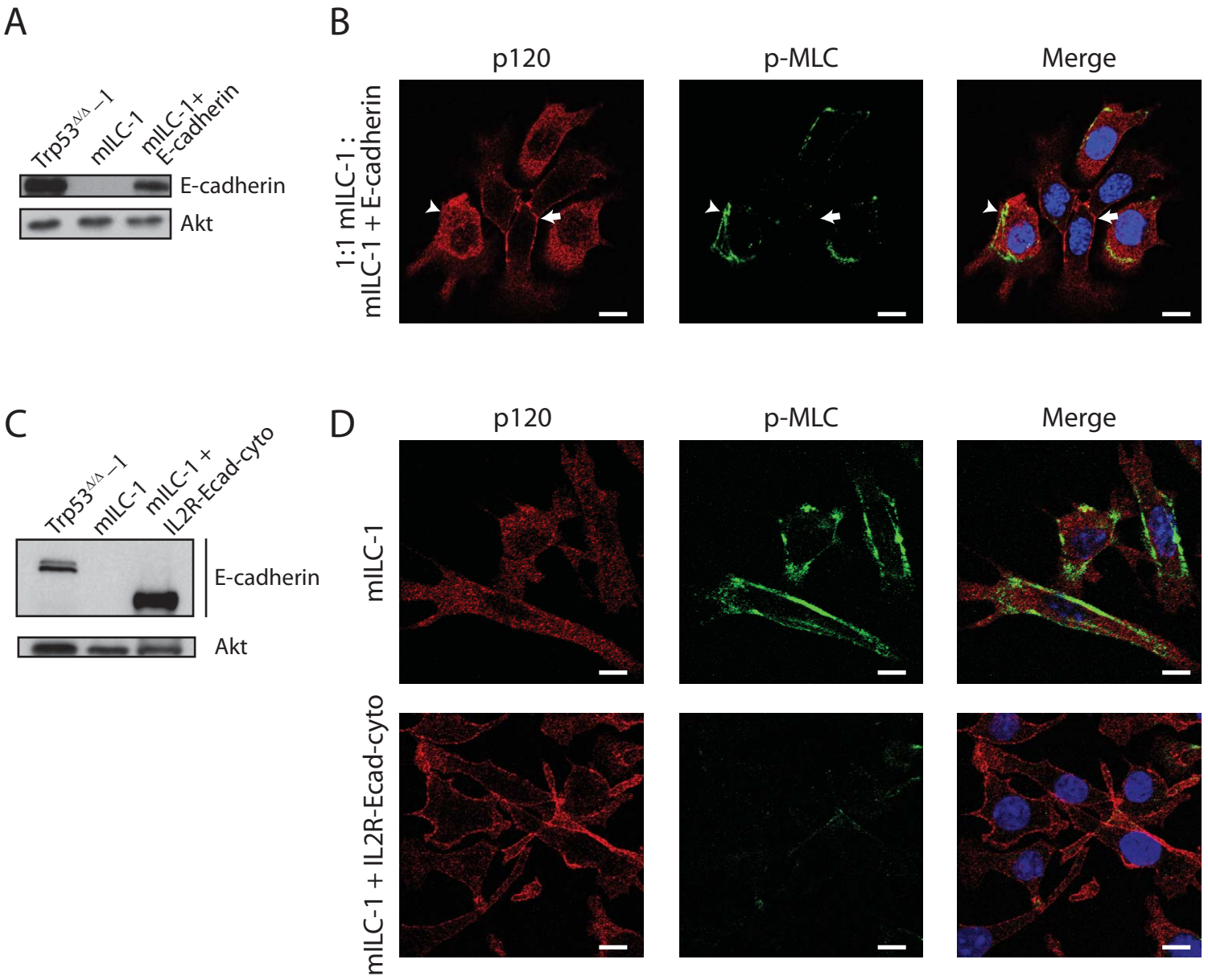
Supplementary Figure S1 Loss of the cadherin/catenin complex does not induce canonical Wnt signaling. **A**) β-catenin does not accumulate in primary mILC tumors. Adenocarcinoma (left panel) and mILC (right panel) primary tumors stained for β-catenin. Bars, 30 μm. **B**) β-catenin does not accumulate in mILC cell lines. Trp53$^{\Delta/\Delta}$-1 (left panel) and mILC-1 cells (right panel) were stained for active β-catenin (red) and DNA was visualized by ToPro3 (blue). Bars, 30 μm. **C**) Canonical Wnt signaling is not induced in mILC cells. mILC and Trp53$^{\Delta/\Delta}$ cells were transfected with TCF/LEF-luciferase reporter plasmids (TOP) or a scrambled, non responsive version thereof (FOP), and assayed for luminescence (white bars). The TOP/FOP ratio (TOP over FOP luminescence counts) is shown on the Y-axes. Also shown are the effects of administration of exogenous Wnt3a (black bars) or β-catenin transfection (grey bars).

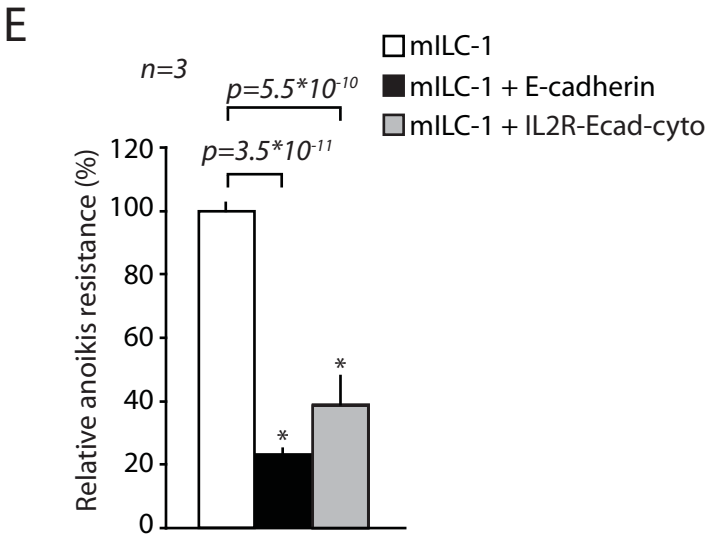


Supplementary Figure S2 mILC cells show active Rho in the presence of cytosolic p120. **A**) Rock signaling is activated in mILC. mILC cells were treated with the Rho Associated Kinase (Rock) inhibitors Y-27632 or hydroxy (OH-) fasudil and the levels of phosphorylated Cofilin were determined using western blotting. Akt served as a loading control. **B**) Hallmarks of Rho activity in mILC. Cells were stained for Filamentous (F)-actin using Alexa-488 conjugated phalloidin. Note the presence of F-actin (green) in mILC cells. DNA was visualized by DAPI (blue). Bars, 5µm. **C**) Rho activity in mILC cells. GTP-bound RhoA levels were determined using a GST-Rhotekin pulldown assay. Total RhoA levels are shown as loading control. **D**) Rho signals control anoikis resistance of mILC cells. mILC cells were grown for four days in the presence of the Rho inhibitor C3 (0,02mg/ml) and assayed for anoikis resistance (left graph), or growth speed (right graph). Error bars represent the standard deviation of triplicate measurements.

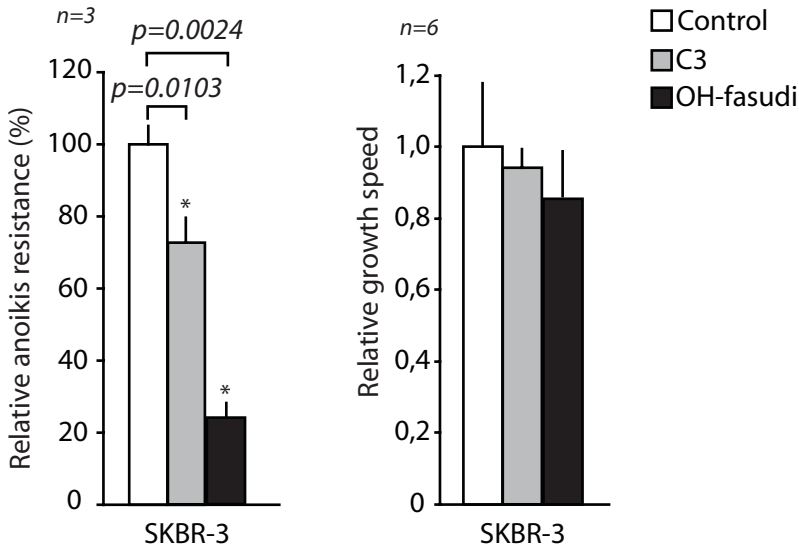


Supplementary Figure S3 Overexpression of p120 results in a branching phenotype in mILC cells, indicative of RhoA inhibition. mILC-1 cells were transfected with p120-1A and H2B-Cherry expression plasmids. Cells were stained for p120 (green) and DNA using DAPI (blue); H2B-Cherry is depicted in red. The upper panel shows normal GFP laser intensity in order to visualize endogenous p120 in the non-transfected cells; the lower panel shows low GFP laser intensity to visualize high p120 overexpressing cells. Cells with high p120 overexpression (arrows) show a branching phenotype correlated to RhoA inhibition; overexpression of lower amounts of p120 (arrow head) does not result in the branching phenotype; Non-transfected cells are marked with (*) Bars, 5µm.





Supplementary Figure S4 Localization of p120 regulates Rock-mediated anoikis resistance in mILC. **A**) mILC-1 cells were transduced with control or E-cadherin-encoding lentivirus and FACS-sorted using antibodies directed against E-cadherin. E-cadherin levels are shown by western blotting. **B**) Restoration of membranous p120 using wild-type E-cadherin leads to inhibition of Rock signaling. FACS-sorted control and E-cadherin expressing mILC-1 cells were mixed 1:1 and stained for p120 (red), p-MLC (green) and DNA using DAPI (blue). Note that cytosolic p120 coincides with expression of phosphorylated MLC (arrow head). In contrast, restoration of membrane-localized p120 leads to inhibition of phospho-MLC (arrow). Bars, 5µm. **C** and **D**) Uncoupling of E-cadherin-controlled cell-cell adhesion from the p120-mediated and localization-dependent regulation of Rock signaling. mILC-1 cells were transduced with IL2R-Ecad-cyto lentivirus. Expression levels are shown by western blotting (**C**). **D**) mILC-1 (upper panels) and IL2R-Ecad-cyto expressing mILC-1 cells were stained for p120 (red), p-MLC (green) and DNA using DAPI (blue) note the decrease of phospho-MLC upon p120 relocalization. Bars, 5µm. **E**) Re-localization of endogenous cytosolic p120 upon expression of E-cadherin restores anoikis sensitivity of mILC. FACS-sorted E-cadherin-expressing cells and IL2R-Ecad-cyto transduced cells were grown in the absence of anchorage after which anoikis resistance was analyzed.



Supplementary Figure S5 Rock signaling controls anoikis resistance of the E-cadherin mutant SKBR-3 cell line. SKBR-3 cells were cultured in the absence (left graph) and presence of anchorage (right graph), and inhibitors of Rho (C3) or Rock (OH-fasudil). After 4 days, anoikis resistance (left graph) and growth speed (right graph) were determined. Error bars represent standard deviation of triplicate measurements.