Supplemental figure legends

Figure S1

Comparative immunohistochemistry in human and mouse breast cancer. **A)** p120 expression in human IDC. A panel of 298 invasive ductal carcinomas was analyzed for p120 expression by immunohistochemistry. Depicted are four representative p120 expression patterns showing low/absent p120 expression (top panels) and medium to high expression levels (bottom panels). **B)** Epithelial cytokeratin expression in mammary carcinomas from the p120 conditional mouse model. Expression of cytokeratin (CK) 8 (left panels) and CK14 (right panels) are shown for mammary tumors that developed in, *Wcre;Trp53*$^{F/F}$ (top panels), *Wcre;Ctnnd1*$^{F/+}$;*Trp53*$^{F/F}$ (middle panels) and *Wcre;Ctnnd1*$^{F/F}$;*Trp53*$^{F/F}$ (bottom panels) conditional female mice. **C)** Loss of p120 in mouse mammary tumors leads to the development of metaplastic carcinoma. Shown are representative expression patterns of p120 and E-cadherin in mouse metaplastic carcinoma (top panels), human metaplastic carcinoma (middle panels) and mouse ILC (bottom panels). Note the absence of p120 and the punctate E-cadherin localization in the metaplastic tumors. In contrast, mouse ILC that developed in *Wcre;Cdh1*$^{F/F}$;*Trp53*$^{F/F}$ female mice is characterized by loss of E-cadherin and subsequent cytosolic localization of p120. Bars: 50μM.

Figure S2

p120 knockdown decreases AJ member expression levels and disrupts cell-cell contact in breast cancer cells. **A-D)** Dox-treated and untreated Control-iKD and Trp53$^{\Delta/\Delta}$;p120-iKD mouse mammary carcinoma cells (A and B) and human T47D;p120-iKD (C) and MCF7;p120-iKD cells (D) were subjected to western blot analysis, showing the effect of p120 knockdown on E-cadherin, β-catenin and αE-catenin expression levels. AKT was used as loading control. **E and F**) p120 controls epithelial integrity of mammary carcinoma cells. Trp53$^{\Delta/\Delta}$;p120-iKD and . Trp53$^{\Delta/\Delta}$;p120-iKD cells expressing p120-1A were stained for p120 (green) to visualize knockdown and correct relocalization. DNA was visualized

using DAPI (blue). Trp53$^{\Delta/\Delta}$ cell lines expressing inducible control (Control-iKD) or Trp53$^{\Delta/\Delta}$;p120-iKD and Trp53$^{\Delta/\Delta}$;p120-iKD cells expressing p120-1A were grown in the absence or presence of Dox for 4 days. Pictures were taken using bright field microscopy to show epithelial monolayer integrity (F). Bars: 50 µm.

Figure S3

Loss of p120 does not affect Rho GTPase activity. **A and B)** Rac1 activity in MCF7;p120-iKD and T47D;p120-IKD cells. GTP-bound Rac1 levels were determined using pulldown assays and subsequent western blotting. Total GTPγs-bound Rac1 levels are shown as loading control. Lower graph represents the quantification of triplicate experiments. Error bars represent SD. **C)** RhoA, Rac1 and Cdc42 activity was assessed in Trp53$^{\Delta/\Delta}$;Control-iKD and p120-iKD cells after Dox treatment. Western blot analysis shows the levels of GTP-bound Rho, Rac1 and Cdc42 (upper blots) and the corresponding GTPγs-bound levels as loading controls (lower blots). Lower graphs represent the quantification of triplicate experiments, normalized against untreated Control-iKD cells. Error bars represent SD of triplicate experiments.

Figure S4

Loss of AJ integrity sensitizes cells to HGF signaling. **A and B)** p120 knockdown results in sensitization to HGF-induced signaling. Two independent Trp53$^{\Delta/\Delta}$ cell lines expressing Control-iKD or p120-iKD were treated with Dox for 4 days, serum starved, stimulated with HGF and subjected to western blot analysis for phosphorylated AKT and MAPK. Total AKT and MAPK were used as loading controls. Quantification is shown in (B). **C and D)** MCF7;p120-iKD cells were cultured in the presence of Dox, serum starved, stimulated with HGF and subjected to western blot analysis as in (A). Quantification is shown in (D). **E)** HGF promotes anchorage independent survival upon p120 loss in human breast cancer cells. Dox-induced MCF7;p120-iKD cells were cultured in ultra-low cluster plates for 4 days in the presence or absence of Dox and HGF as indicated. *=$p<0.05$. Error bars in B and D represent the

standard error of the mean based on triplicate experiments. Error bars in E represent the SD of triplicate experiments.

Figure S5

Loss of p120 and subsequent AJ inactivation does not induce autocrine survival pathways or increased EGF binding. **A and B)** knockdown of p120 does not activate AKT or MAPK signaling under anchorage-dependent conditions. Two independent $Trp53^{\Delta/\Delta}$ cell lines (A) and MCF7 cells (B) expressing Control-iKD or p120-iKD constructs were serum starved, and subjected to western blot analysis for phosphorylated EGFR (upper panels), AKT (middle panels) and MAPK (lower panels) (long exposure). Total EGFR, AKT and MAPK were used as loading controls. Note the near absence of phosphorylation signal upon p120 knockdown. **C)** p120 knockdown does not increase quantitative EGF-binding. p120-iKD expressing $Trp53^{\Delta/\Delta}$ cell lines were treated with Dox for 4 days, serum-starved and trypsinized. Ice-cold cells were incubated with or without Alexa647-conjugated EGF and subjected to FACS analysis.

Figure S6

p120 knockout sensitizes tumor cells to growth factor signaling. **A**) Two independent p120 knockout cell lines ($Ctnnd1^{\Delta/\Delta}$;$Trp53^{\Delta/\Delta}$) were generated from tumors that developed in *Wcre;Ctnnd1*$^{F/F}$*;Trp53*$^{F/F}$ female mice. Cells were serum starved, stimulated with EGF and subjected to western blot analysis using phospho-specific antibodies against EGFR (upper panels), AKT (middle panels) and MAPK (lower panels). Total EGFR, AKT and MAPK were used as loading controls. **B**) EGF stimulates anoikis resistance of p120 knockout cell lines. Anoikis resistance was analyzed in $Trp53^{\Delta/\Delta}$-3 and two independent $Ctnnd1^{\Delta/\Delta}$;$Trp53^{\Delta/\Delta}$ cell lines in the presence or absence of EGF and Dox as indicated. Error bars represent the standard deviation of triplicate experiments *=$p<0.05$. **C)** Activity of downstream growth factor signaling *in vivo*. Histopathology of mammary tumors derived from *Wcre;Ctnnd1*$^{F/F}$*;Trp53*$^{F/F}$ (left panels) and *Wcre;Trp53*$^{F/F}$ (right panels) conditional mice showing p-AKT

(upper panels) and p-MAPK (lower panels). Arrows and arrowheads indicate stromal and tumor cells respectively. Bars: 50μM