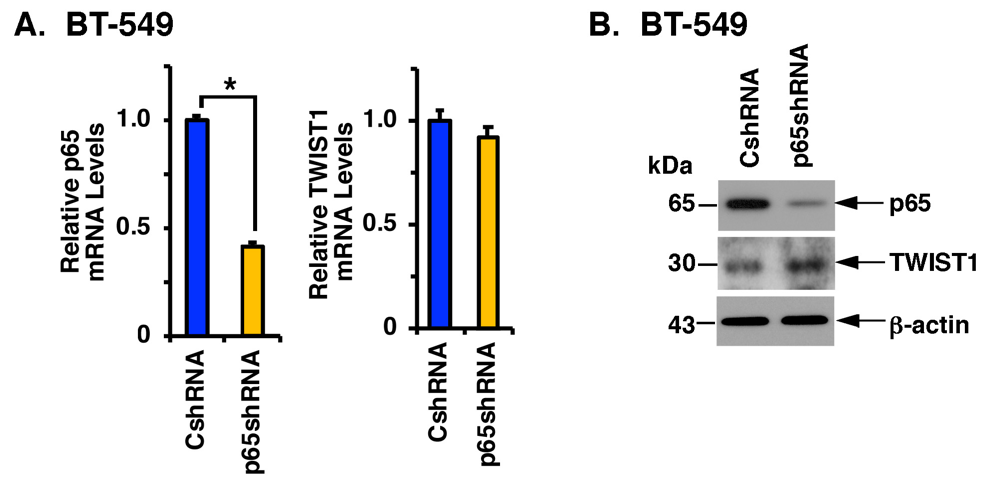
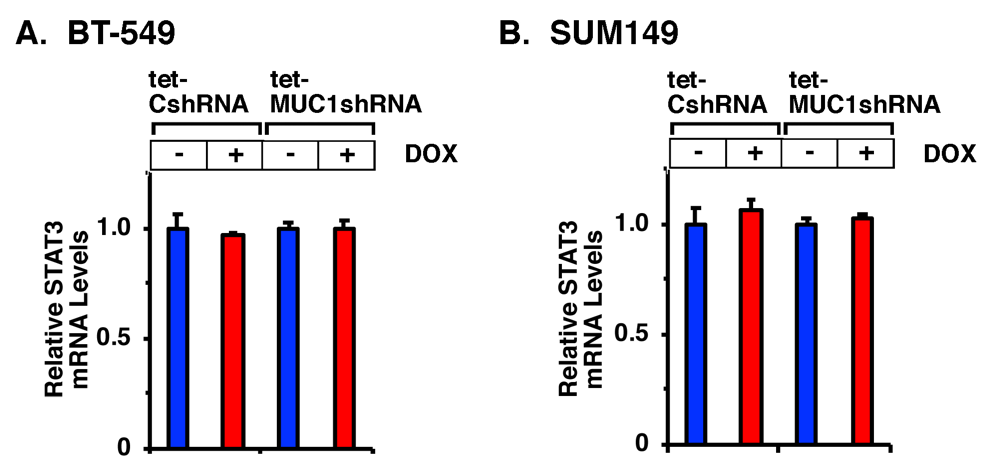
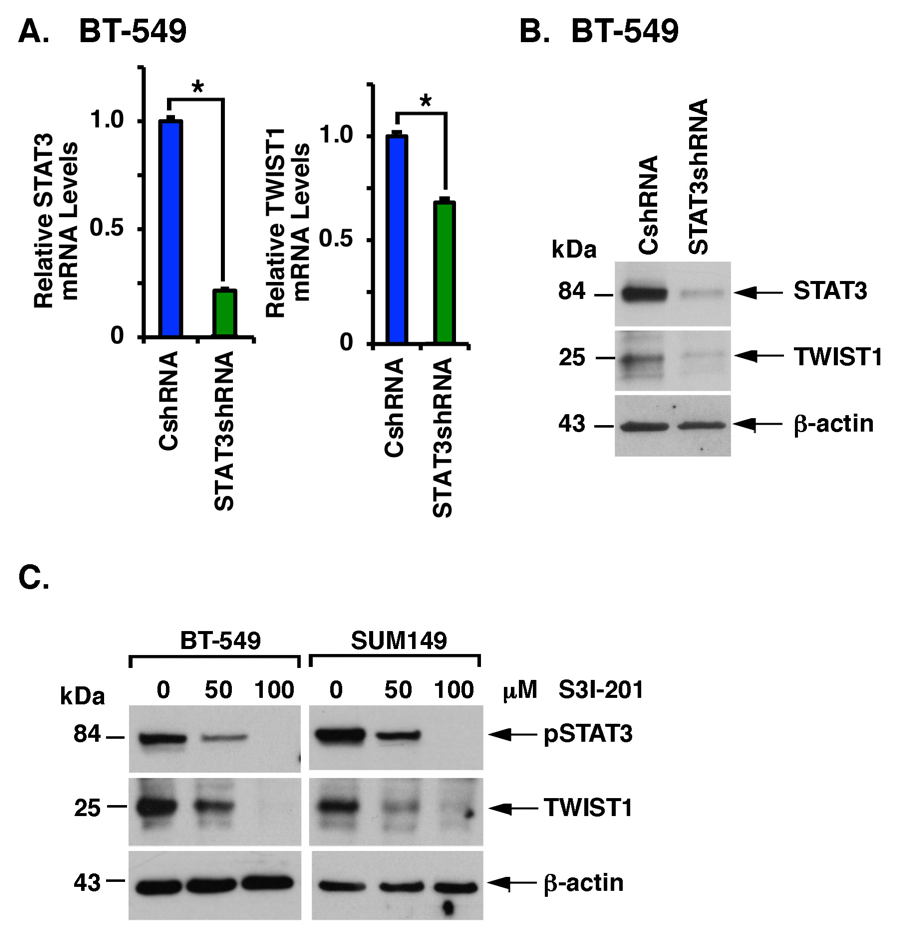
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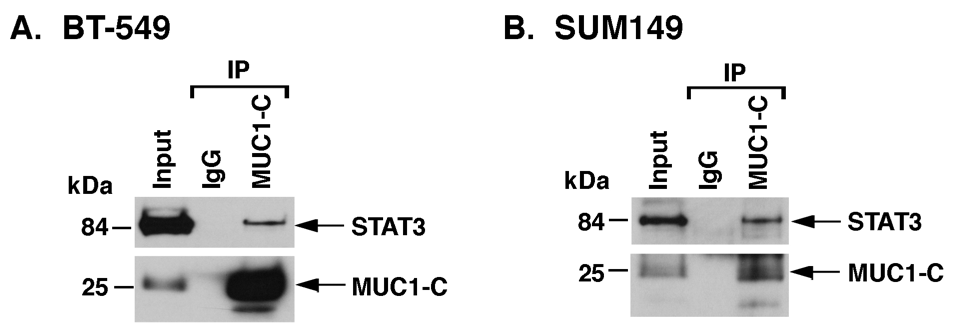
**Supplemental Figure S1. Targeting NF-κB p65 has little effect on TWIST1 expression.** A and B. BT-549 cells expressing a CshRNA or p65shRNA were analyzed for p65 and TWIST1 mRNA levels by qRT-PCR using primers listed in Supplemental Table S1. The results (mean±SD) are expressed as relative mRNA levels compared to that obtained for control cells (assigned a value of 1) (A). Lysates were immunoblotted with antibodies against the indicated proteins (B).

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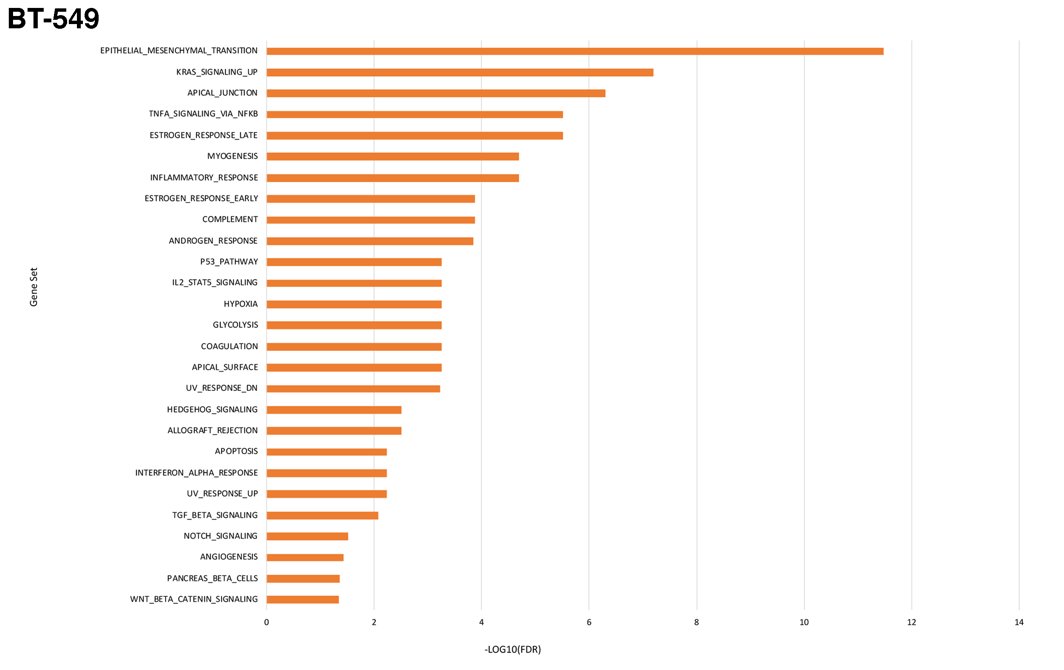
**Supplemental Figure S2. Targeting MUC1-C is not associated with regulation of STAT3 mRNA levels.** A and B. BT-549 (A) and SUM149 (B) cells expressing a tet-CshRNA or tet-MUC1shRNA were left untreated or treated with 500 ng/ml DOX for 7 days. Cells were analyzed for STAT3 mRNA levels by qRT-PCR. The results (mean±SD) are expressed as relative mRNA levels compared to that obtained for control untreated cells (assigned a value of 1).

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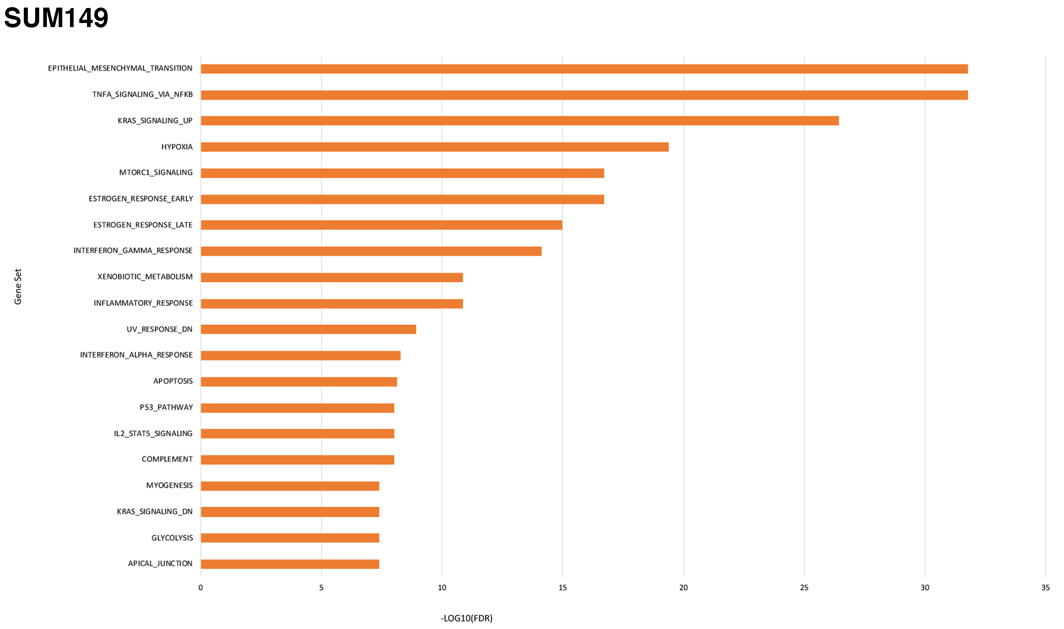
**Supplemental Figure S3. Targeting STAT3 genetically or pharmacologically decreases TWIST1 expression.** A and B. BT-549 cells expressing a CshRNA or STAT3shRNA were analyzed for STAT3 and TWIST1 mRNA levels by qRT-PCR. The results (mean±SD) are expressed as relative mRNA levels compared to that obtained for control cells (assigned a value of 1) (A). Lysates were immunoblotted with antibodies against the indicated proteins (B). C. BT-549 and SUM149 cells were treated with 0, 50 or 100 μM S3I-201 for 48 h. Lysates were immunoblotted with antibodies against the indicated proteins.

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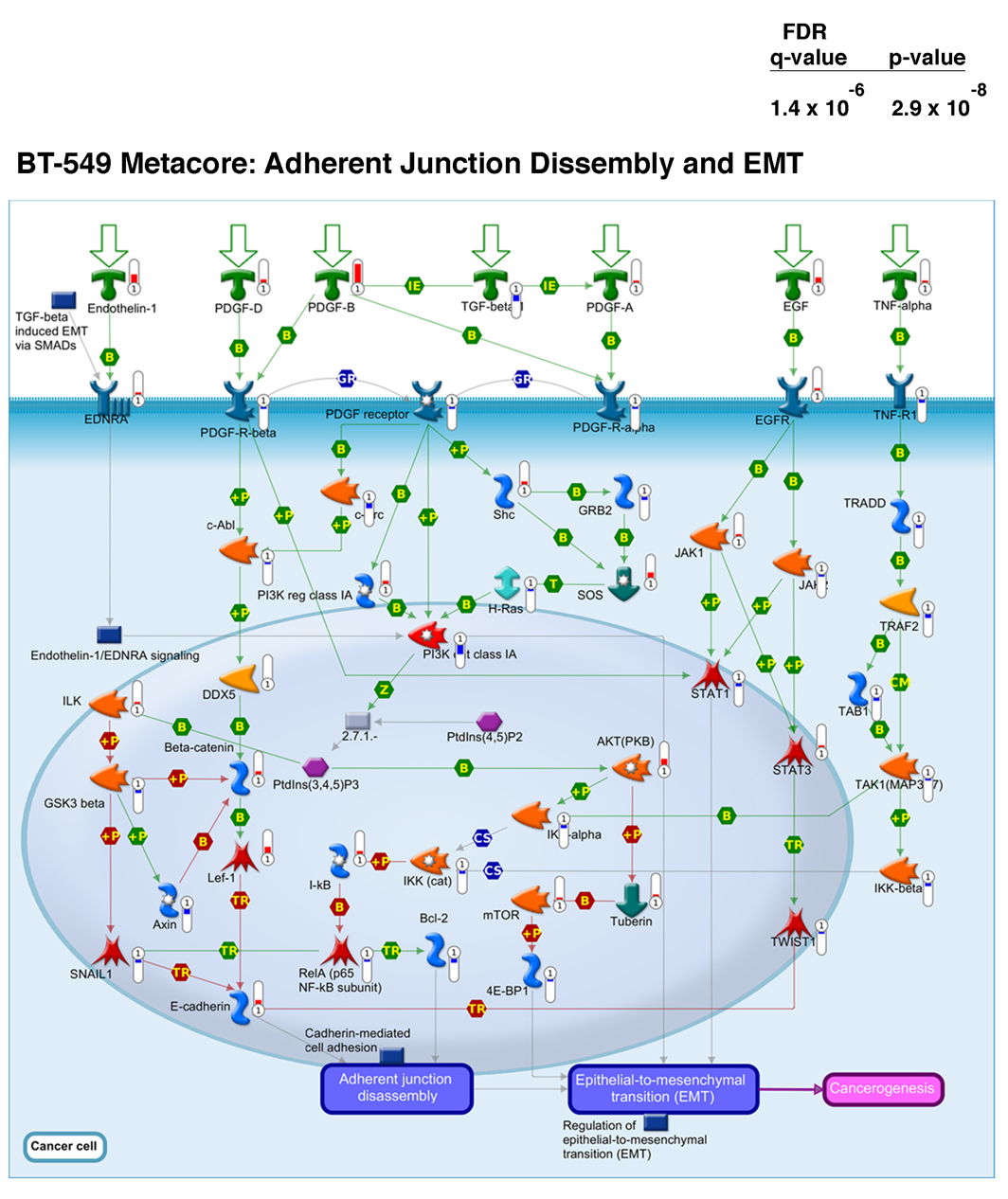
**Supplemental Figure S4. MUC1-C and STAT3 form a nuclear complex.** A and B. Nuclear lysates from BT-549 (A) and SUM149 (B) cells were incubated with anti-MUC1-C or a control IgG. The precipitates were immunoblotted with antibodies against STAT3 and MUC1-C.

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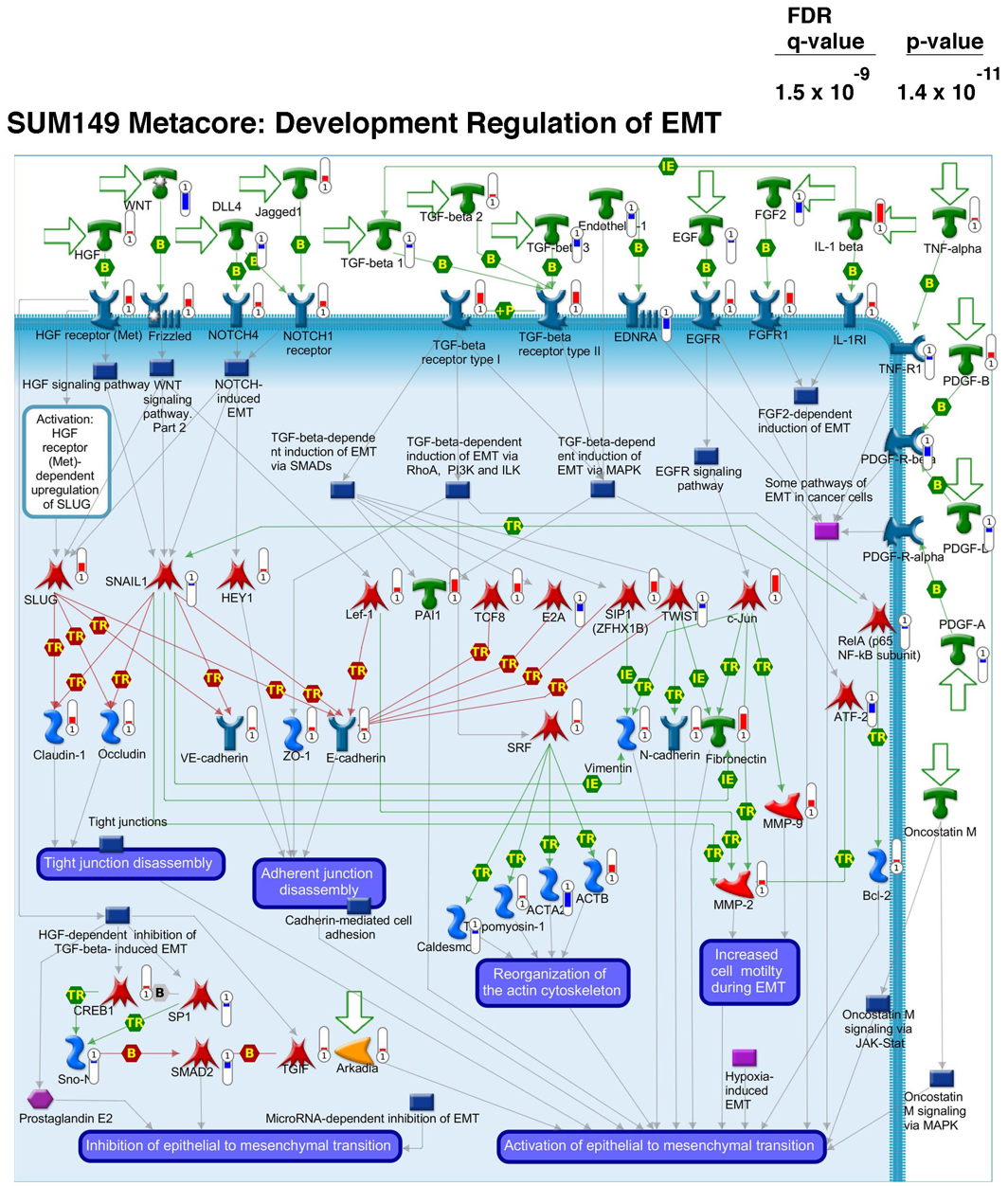
**Supplemental Figure S5. Hallmark pathway analysis for BT-549 cells.** RNA-seq was performed in triplicate on BT-549/CshRNA and BT-549/MUC1shRNA cells. The datasets were analyzed using the Hallmark gene signature collection. Results are shown for the 20 most significant pathways.

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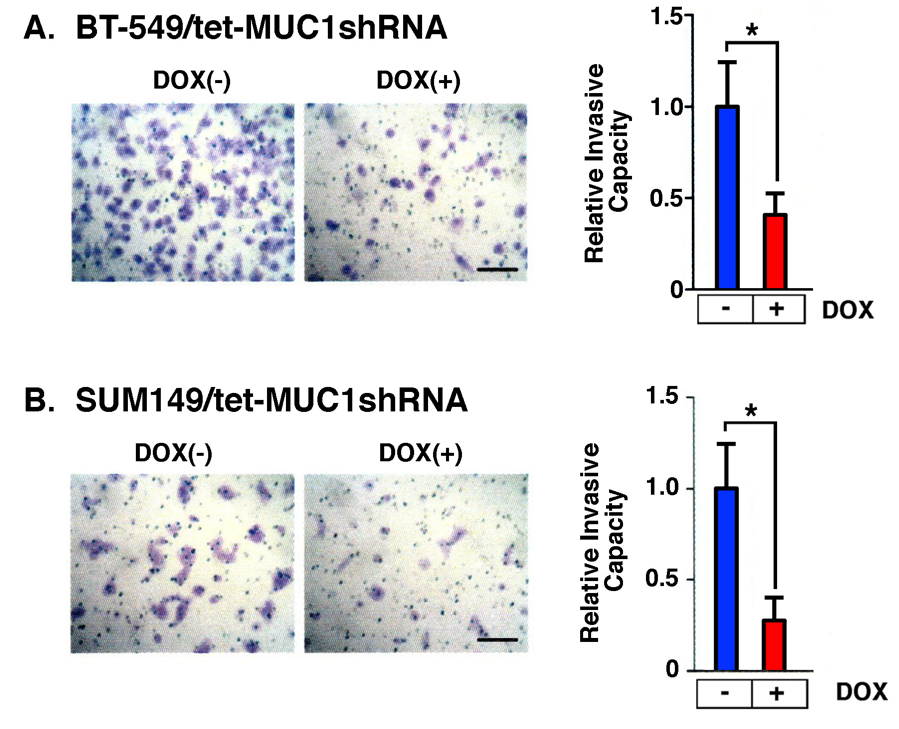
**Supplemental Figure 6. Hallmark pathway analysis for SUM149 cells.** RNA-seq was performed in triplicate on SUM149/CshRNA and SUM149/MUC1shRNA cells. The datasets were analyzed using the Hallmark gene signature collection. Results are shown for the 20 most significant pathways.

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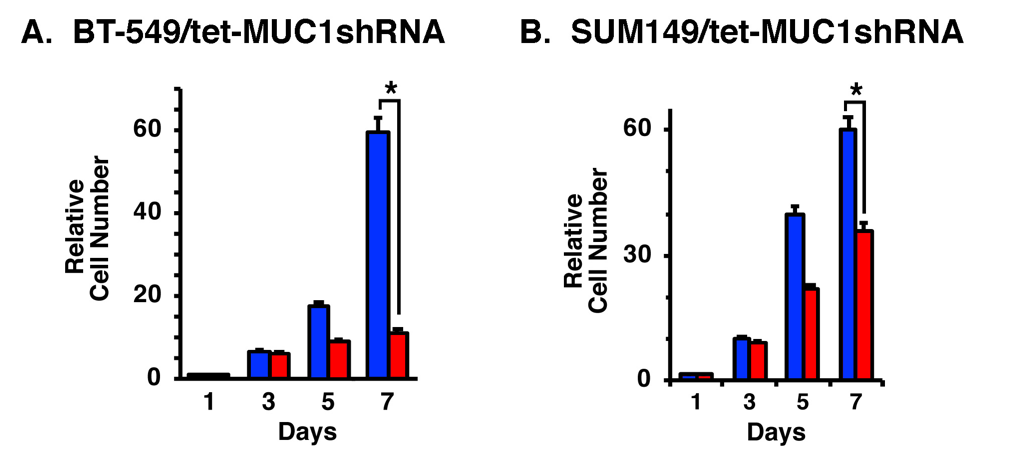
**Supplemental Figure S7. Metacore adherens junction disassembly and EMT pathway analysis for BT-549 cells.** RNA-seq data from BT-549/CshRNA and BT-549/MUC1shRNA cells was analyzed using Metacore for enrichment.

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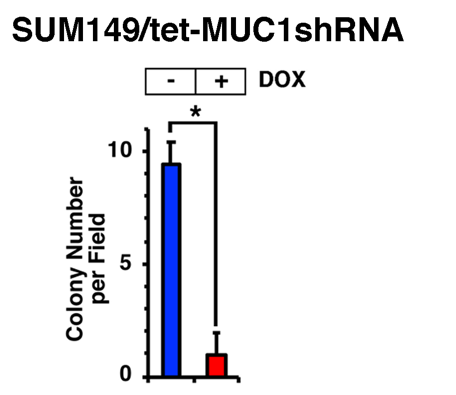
**Supplemental Figure S8. Metacore EMT pathway analysis for SUM149 cells.** RNA-seq data from SUM149/CshRNA and SUM149/MUC1shRNA cells was analyzed using Metacore for enrichment.

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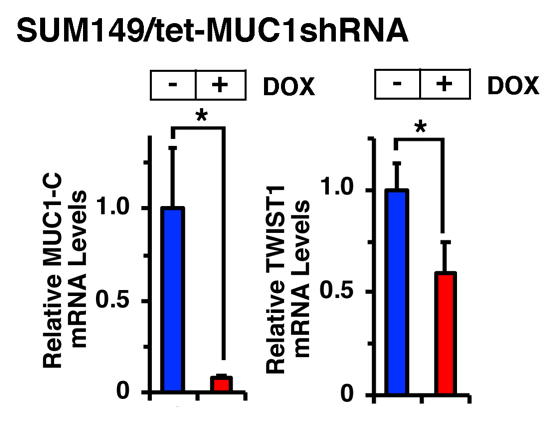
**Supplemental Figure S9. Silencing MUC1-C inhibits cell invasive capacity.** A and B. BT-549/tet-MUC1shRNA (A) and SUM149/tet-MUC1shRNA (B) cells left untreated or treated with 500 ng/ml DOX for 7 days were evaluated for invasive capacity in matrigel coated transwell chambers (left). Results are expressed as the relative invasive capacity compared to that obtained with the untreated cells (assigned a value of 1).

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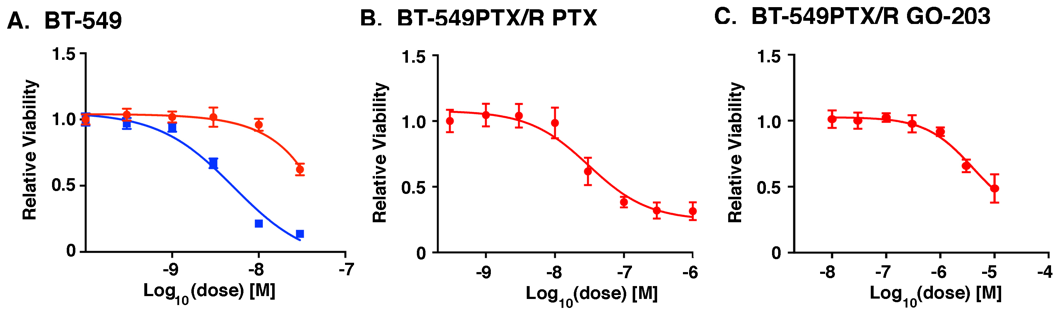
**Supplemental Figure S10. Silencing MUC1-C inhibits growth of BT-549 and SUM149 cells.** A and B. BT-549/tet-MUC1shRNA (A) and SUM149/tet-MUC1shRNA (B) cells were left untreated (red bars) or treated with 500 ng/ml DOX (blue bars) for the indicated number of days. The results are expressed as relative cell numbers (mean±SD) compared to that obtained on Day 1 (assigned a value of 1).

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**Supplemental Figure S11. Silencing MUC1-C inhibits colony formation of SUM149 cells.** SUM149/tet-MUC1shRNA cells left untreated (blue bars) or treated with 500 ng/ml DOX (red bars) for 7 days were analyzed for colony formation. The results (mean±SD of at least three determinations) are expressed as the number of colonies/field.

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**Supplemental Figure S12. Downregulation of MUC1-C and TWIST1 expression *in vivo*.** Mice bearing SUM149/tet-MUC1shRNA tumors were fed without and with DOX. Tumors harvested on day 21 were analyzed for MUC1-C and TWIST1 mRNA levels. The results (mean±SD) are expressed as relative mRNA levels compared to that obtained for control cells (assigned a value of 1).

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**Supplemental Figure S13. Selection of BT-549 cells for PTX resistance.** A. BT-549 (blue squares) and BT-549/PTX-R (red circles) cells were treated with the indicated PTX concentrations and analyzed for cell viability. B and C. BT-549/PTX-R cells treated with the indicated concentrations of PTX (B) or GO-203 (C) were analyzed for cell viability.

**Supplemental Table S1: Primers sequences for qRT-PCR.**

|  |  |  |
| --- | --- | --- |
| **Primer** | **FWD** | **REV** |
| GAPDH | CCATGGAGAAGGCTGGGG | CAAAGTTGTCATGGATGACC |
| MUC1 | TACCGATCGTAGCCCCTATG | CTCACCAGCCCAAACAGG |
| TWIST1 | CGGGAGTCCGCAGTCTTA | GCTTGAGGGTCTGAATCTTG |
| STAT3 | CAGCAGCTTGACACACGGTA | AAACACCAAAGTGGCATGTGA |
| ESR1 | GACAGGGAGCTGGTTCACAT | AGGATCTCTAGCCAGGCACA |
| GATA3 | AGCCAGGAGAGCAGGGACG | CTGTTAATATTGTGAAGCTTGTAGTAGAG |
| ZEB1 | ACCCTTGAAAGTGATCCAGC | CATTCCATTTTCTGTCTTCCGC |
| SNAIL | CGGAAGCCTAACTACAGCGA | GGACAGAGTCCCAGATGAGC |
| NF-κB p65 | CTGCAGTTTGATGATGAAGA | TAGGCGAGTTATAGCCTCAG |

**Supplemental Table S2: Primers used in ChIP assays.**

|  |  |  |
| --- | --- | --- |
| **Primer** | **FWD** | **REV** |
| TWIST1 | GCCAGGTCGTTTTTGAATGGT | CGTGAGGAGGAGGGACTTTTC |
| MUC1 | TAGTCAGGGGGTTGAGCGAT | AGCAGGTGACAGGTGACAAAA |

**Supplemental Table S3: Combination FA and CI values.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Combination** | **GO-203(μM)** | **PTX(nM)** | **FA** | **CI** |
| 1 | 0.1 | 1 | 0.470 | 0.057 |
| 2 | 0.1 | 3 | 0.488 | 0.122 |
| 3 | 0.1 | 10 | 0.484 | 0.348 |
| 4 | 0.3 | 1 | 0.560 | 0.107 |
| 5 | 0.3 | 3 | 0.556 | 0.172 |
| 6 | 0.3 | 10 | 0.595 | 0.398 |
| 7 | 1 | 1 | 0.627 | 0.281 |
| 8 | 1 | 3 | 0.624 | 0.346 |
| 9 | 1 | 10 | 0.661 | 0.572 |