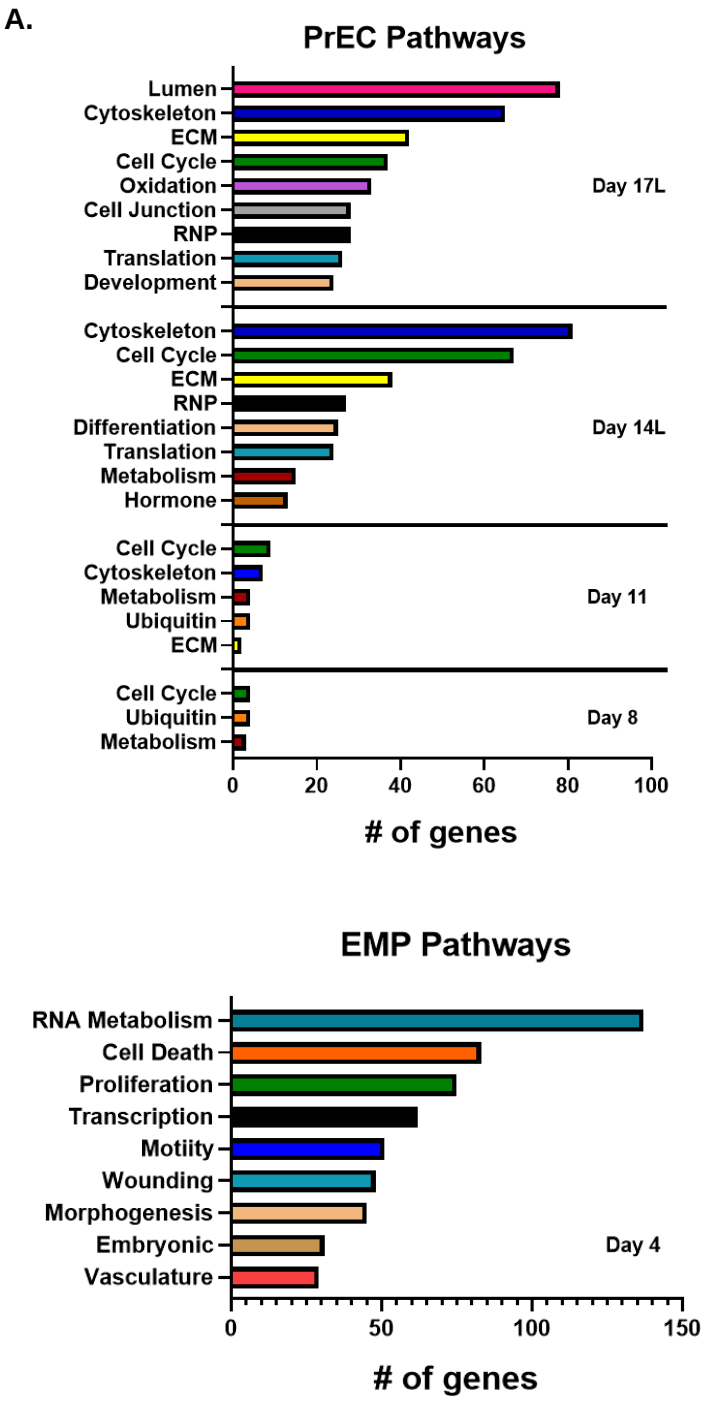
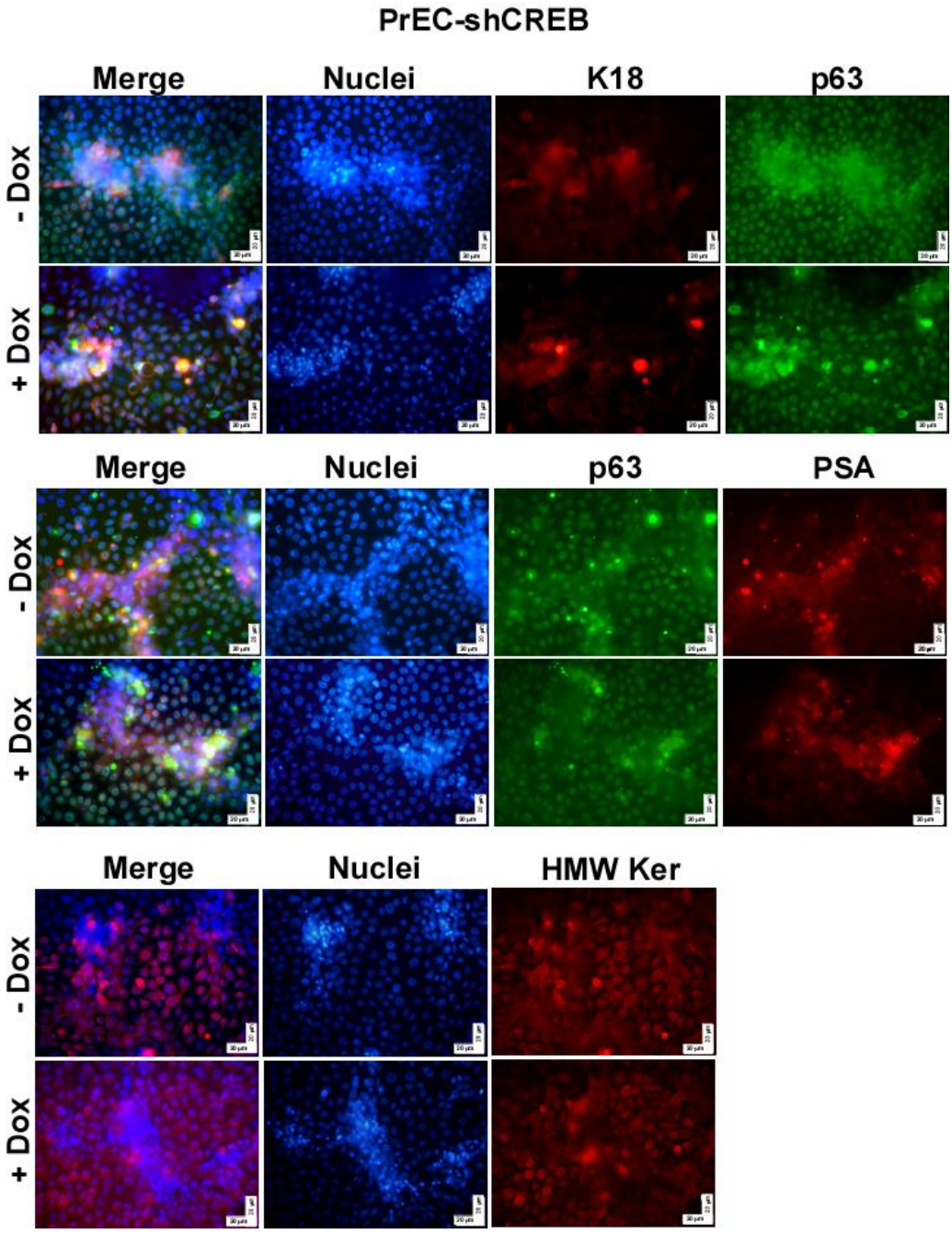
Supplementary Figure S1



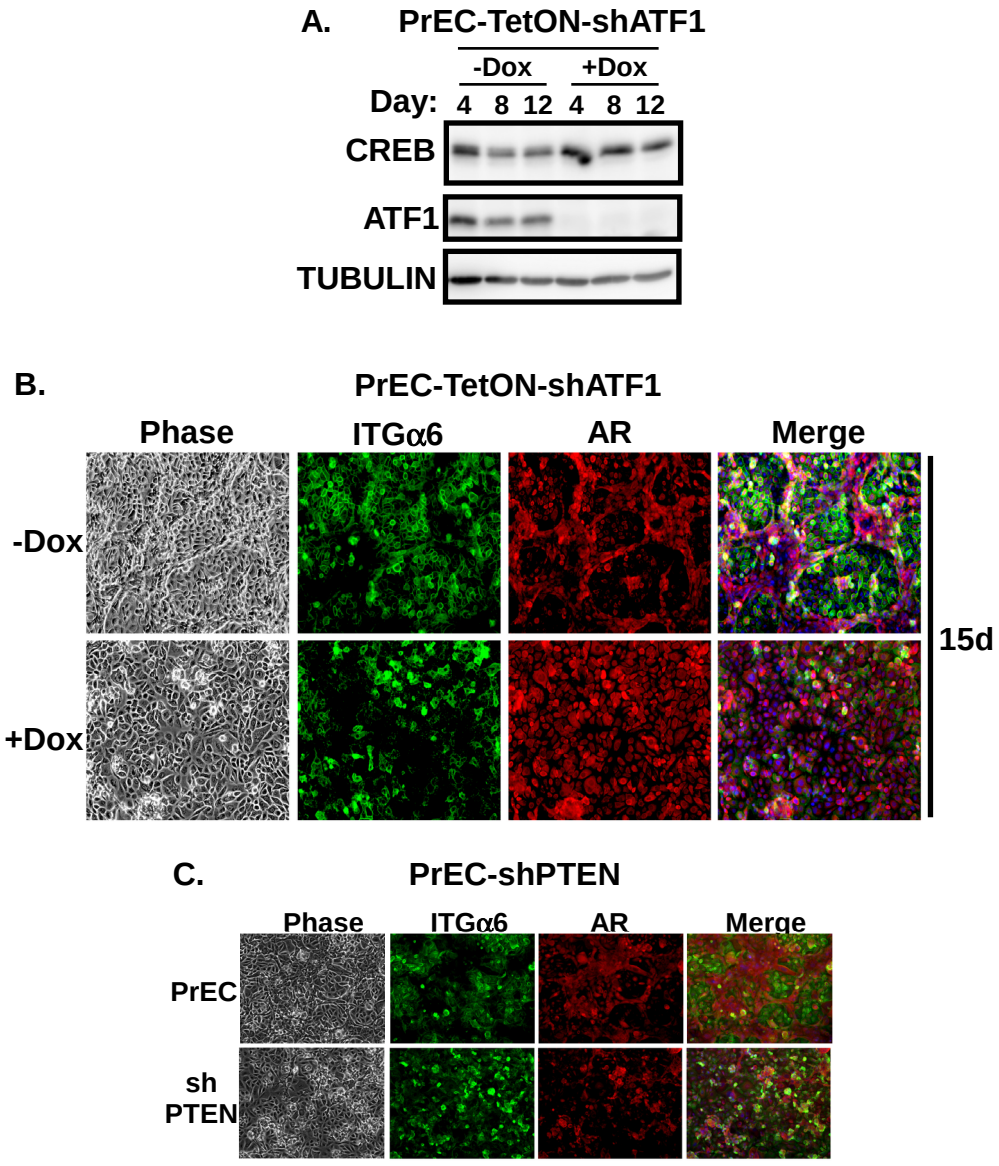
Supplementary Figure S1: A) Pathway enrichment analysis was conducted on the significantly differentially expressed genes from normal PrECs over a time course of luminal cell differentiation. At Days 14 and 17, only the luminal population (L) was assessed. **B)** Pathway enrichment analysis was conducted on the significantly differentially expressed genes in tumorigenic EMP cells compared to normal PrECs.

Supplementary Figure S2



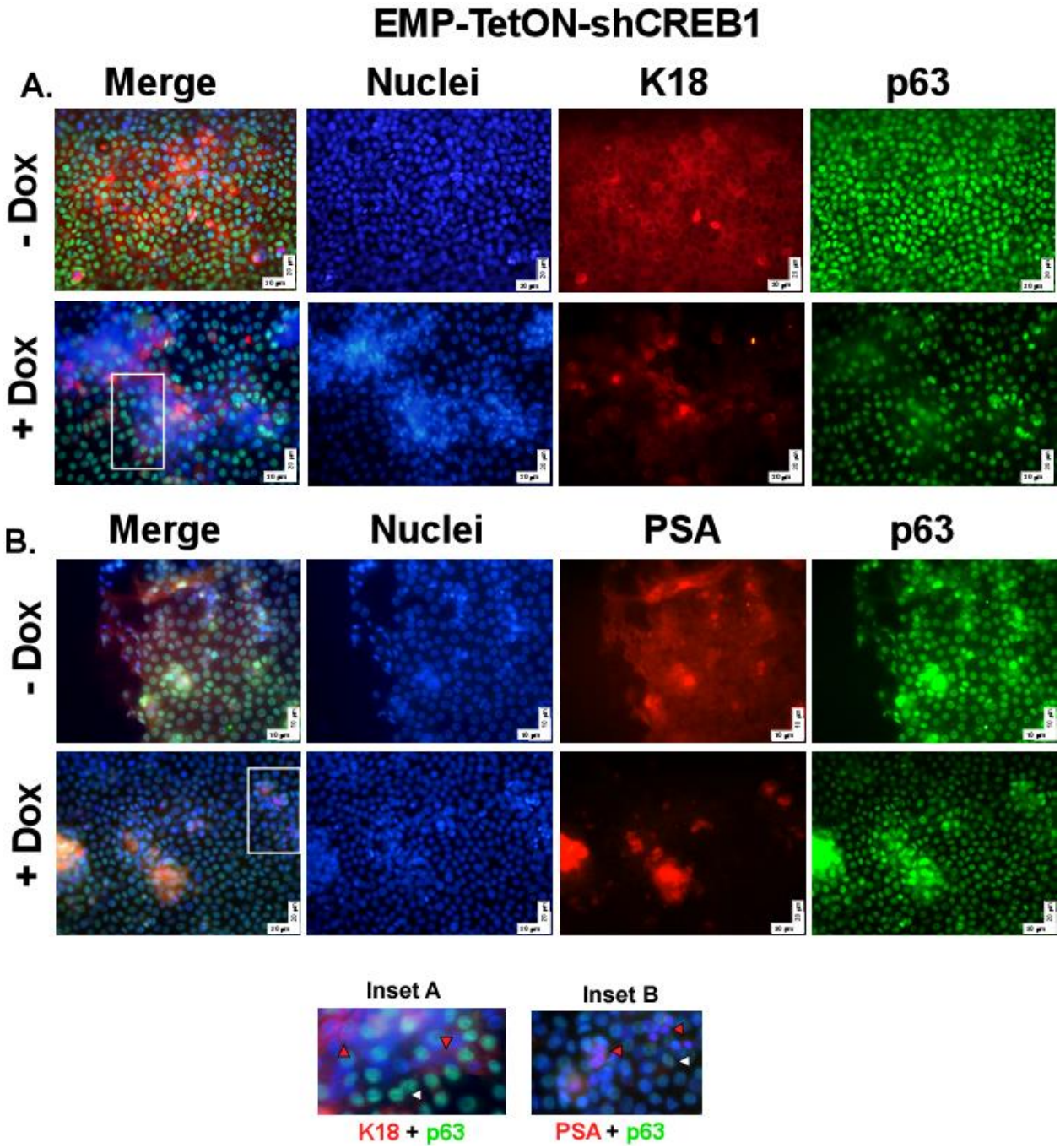
Supplementary Figure S2: PrEC-TetON-shCREB1 cells induced to differentiate for 12 days in the absence (-Dox) or presence (+Dox) of 25ng/ml doxycycline. Cultures immunostained for luminal markers K18 or PSA, basal markers p63 or HMW keratin (K5/K14), DNA counterstained with Hoescht, and imaged by fluorescence microscopy.

Supplementary Figure S3



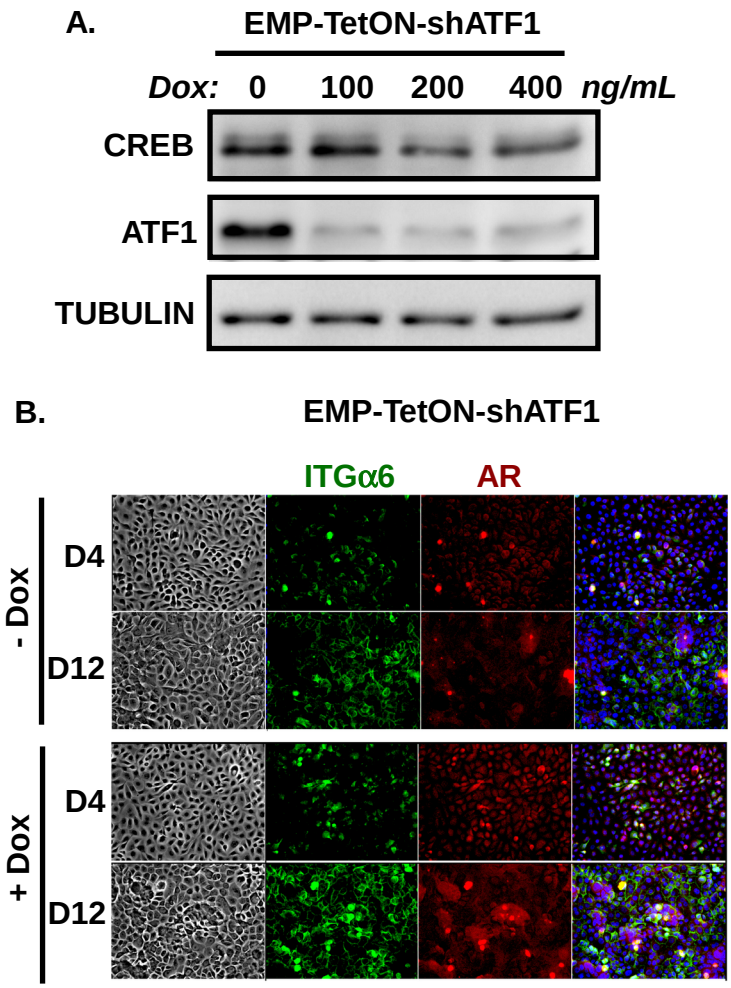
Supplementary Figure S3: ATF1 and PTEN are required for luminal cell differentiation. A) ATF1 knock-down in differentiating PrEC-TetON-shATF1 cells treated with (+Dox) or without (-Dox) 100ng/ml doxycycline measured by immunoblotting. **B)** PrEC-TetON-shATF1 cells were differentiated for 15 days with (+Dox) or without (-Dox) 100ng/ml doxycycline. Cultures were immunostained for integrin α6 (ITGα6, basal marker), AR (luminal marker), counterstained with Hoescht (Merge), and imaged by phase or fluorescence microscopy. **C)** PrEC or PrEC-shPTEN cells were differentiated for 12 days. Cultures were immunostained for integrin α6 (ITGα6, basal marker), AR (luminal marker), counterstained with Hoescht (Merge), and imaged by phase or fluorescence microscopy.

Supplementary Figure S4



Supplementary Figure S4: EMP-TetON-shCREB1 cells induced to differentiate for 12 days in the absence (-Dox) or presence (+Dox) of 25ng/ml doxycycline. Cultures co-immunostained for luminal markers **A)** K18 or **B)** PSA and basal marker p63. DNA counterstained with Hoescht and imaged by fluorescence microscopy. **Insets**: Red arrows indicate **A)** K18-positive or **B)** PSA-positive luminal cells with no basal p63. White arrows indicate p63-positive basal cells with no luminal markers.

Supplementary Figure S5



Supplementary Figure S5: Loss of ATF1 in EMP cells does not rescue differentiation. **A)** Titration of doxycycline in EMP-TetON-shATF1 cells. **B)** EMO-TetON-shATF1 cells were differentiated for 4 or 12 days with (+Dox) or without (-Dox) 200ng/ml doxycycline. Cultures were immunostained for integrin α6 (ITGα6, basal marker), AR (luminal marker), counterstained with Hoescht (Merge), and imaged by phase or fluorescence microscopy.