PAX2 maintains the differentiation of mouse oviductal epithelium and inhibits the transition to a stem cell-like state

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Recent studies have provided evidence that the secretory cells of the fallopian tube (oviduct) are a probable origin for high-grade serous ovarian carcinoma. In addition to secretory cells, the fallopian tube epithelium consists of ciliated cells and CD44+ undifferentiated stem-like cells. Loss of PAX2 expression is recognized as an early event in epithelial transformation, but the specific role of PAX2 in this transition is unknown. The aim of this study was to define the role of PAX2 in oviductal epithelial (OVE) cells and its response to transforming growth factor β1 (TGFβ), characterizing specifically its potential involvement in regulating stem cell-like behaviors that may contribute to formation of cancer-initiating cells. Treatment of primary cultures of mouse OVE cells with TGFβ induced an epithelial-mesenchymal transition (EMT) associated with decreased expression of PAX2 and an increase in the fraction of cells expressing CD44. PAX2 knockdown in OVE cells and overexpression in ovarian epithelial cells confirmed that PAX2 inhibits stem cell characteristics and regulates the degree of epithelial differentiation of OVE cells. These results suggest that loss of PAX2, as occurs in serous tubal intraepithelial carcinomas, may shift secretory cells to a more mesenchymal phenotype associated with stem-like features.

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