**ESHRE Abstract 2017 – Alison Maclean**

**Title:** The identification of epithelial cell markers contributes towards the chatacterisation of endometrial epithelial cell sub-types.

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**Study question:** Are there specific markers to define human endometrial epithelial cell (EEC) sub-types?

**Summary answer:** The expression pattern of specific markers in the three different anatomical areas of the endometrium suggests that different endometrial epithelial cell sub-types exist.

**What is known already:** The endometrial epithelial cells reside in three different anatomical locations in the endometrium: the luminal epithelium, the functionalis glands, and the basalis glands. These three areas respond differentially to the same circulating steroid hormones, suggesting the presence of functionally distinct epithelial cells. There is detailed understanding of the epithelial cell sub-types in other organs with similar regenerative capacity to the endometrium, such as the intestine and fallopian tube. This has facilitated cell specific research, which has improved the understanding of these organs in health and disease. This detailed knowledge is still lacking in the endometrium.

**Study design, size, duration:** This is a prospective observational study, analysing full-thickness, healthy human endometrial samples from a total of 21 women (n=16 pre-menopausal and n= 5 post-menopausal).

**Participants/materials, settings, methods:** Endometrium was obtained from women undergoing hysterectomy for benign conditions. The premenopausal samples were from proliferative (n=7), secretory (n=6) and menstrual (n=3) phases of the menstrual cycle. The expression of AKR1C3, CD133, CK5/6, PODXL, MUC-1, Sialylated-SSEA-1, SSEA-1, and proliferative marker, Ki-67, were examined with immunohistochemistry. We also examined the differential expression of the genes coding these proteins by interrogating the published microarray datasets using a system biology approach.

**Main results and the role of chance:** The luminal epithelial cells were marked by CK5/6 positivity and PODXL negativity, with greatest expression of CK5/6 in the secretory phase luminal epithelium (P < 0.05). The hormone-metabolising enzyme AKR1C3 was highly expressed in the epithelial cells of the functionalis during the proliferative phase (P <0.01). The surface marker sialylated-SSEA-1 was highly expressed almost exclusively on the basalis EEC’s, and the embryonic stem cell surface marker, SSEA-1, also marked the basalis epithelial cells, where expression was significantly greater than in the proliferative phase functionalis (P = < 0.05). CD133 and MUC-1 expression was present in the majority of epithelial cells throughout the endometrium. The transmembrane protein PODXL was found to express strong immunoreactivity in the cytoplasm of the epithelial cells, most notably in the basalis, and in post-menopausal endometrium. This pattern was distinct from the expected apical expression seen in the majority of EEC’s, and provides evidence that basalis EEC’s could be functionally different.

The microarray data generally confirmed the expression pattern specific to the functionalis of the genes coding for the proteins studied, highlighting the difficulties when all EEC’s are considered together.

This has provided a snapshot of differences in protein expression in EECs across the endometrium, suggesting functional dissimilarities, and the presence of EEC sub-types.

**Limitations, reasons for caution:** This is a descriptive study with a small sample size, and only protein expression of epithelial cell markers analysed.

**Wider implications of the findings:** The differential expression of these epithelial markers has provided preliminary evidence of the presence of different EEC subtypes. This warrants further investigation; with the aim of identifying the EEC subtypes that predispose to conditions such as endometriosis and endometrial carcinogenesis, and developing methods of isolation.

**Study funding/competing interests:** This work was funded by ITM/Department of Women’s Health at the University of Liverpool. There are no conflicts of interest to declare.

Trial registration number: N/a