



## CD45-Positive Blood Cells Give Rise to Uterine Epithelial Cells in Mice

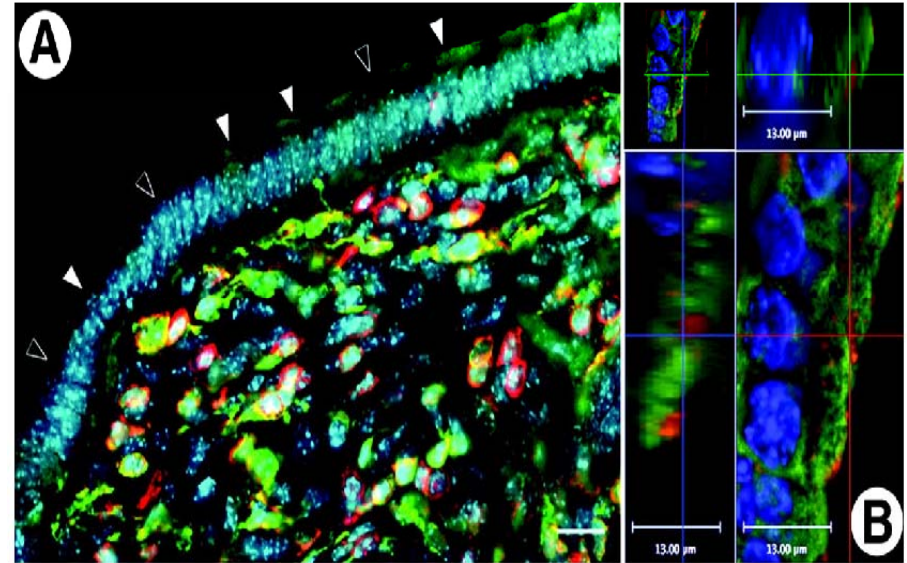
The uterine endometrium is composed of epithelial and stromal cells, which undergo extensive degeneration and regeneration in every estrous cycle. The high turnover of cells requires a correspondingly high level of cell division by progenitor cells in the uterus, but the character and source of these cells remain obscure.

Several investigators have used bone marrow (BM) transplants to show that bone marrow-derived stem cells can repopulate a variety of organs in irradiated hosts. In this study by Dr Éva Mezey and colleagues at the NIDCR, the team wanted to find out if and what kind of BM cells contribute to the uterine epithelium in healthy animals. In order to do so, they created a Cre-CD45 transgenic mouse that was crossed with EGFP-Lox mice. In the cross-bred mice all cells of hematopoietic stem cell (i.e. CD45+) origin expressed EGFP. Control mice were transplanted with EGFP positive bone marrow.

12  $\mu\text{m}$  fixed sections of endometrium were collected from mice that went through different number of cycles and the sections were viewed with an inverted microscope, and images were acquired at 0.5  $\mu\text{m}$  intervals. **Volocity Restoration** was used to deconvolve the image data and it was then viewed in **Volocity Visualization**.

The results show that CD45+ cells were present in the stromal layer, indicating that that circulating CD45+ cells provide a renewable pool of epithelial precursors in the uterus and might be involved in the development of endometriosis, a very common disease in women. The study found that in pregnancy sometimes more than 80% of the uterine epithelium can be derived from these cells.

The implications of this lead on to the question of the role that CD45+ (i.e. hematopoietic lineage) cells play in the regeneration of other tissues. Understanding the mechanisms which attract these cells to different organs and factors that drive their differentiation may prove beneficial in the wider understanding of tissue regeneration.



Endometrium of a mouse previously (10 months before) transplanted with enhanced green fluorescence protein bone marrow (BM) following irradiation. Green fluorescent protein (GFP) is shown in green, CD45 in red, and 4,6-diamidino-2-phenylindole (DAPI), the nuclear marker, in blue.

**(A):** GFP+ and CD45- uterine epithelium in the recipient endometrium shows that BM cells can contribute to the regeneration of uterine epithelial cells. CD45+/GFP+ hematopoietic cells are present in the stromal layer.

**(B):** Colocalization of a pan-cytokeratin immunostaining (in red) with GFP (in green) in epithelial cells. Viewing the data in **Volocity Visualization** allows the colocalization to be seen in XZ and YZ as well as in XY for a better understanding of the results.