Leveraging Single Cell Transcriptomics to Dissect Cellular Changes in the Late Endometrial Cycle across Primates.

Eulalie Liorzou[1, 2,*]; Axelle Brulport[1,*]; Leo Zeitler[1]; Anthony Lepelletier[1]; Camille Berthelot[1]
[1] Institut Pasteur, Université de Paris, CNRS UMR 3525, INSERM UA12, Comparative Functional Genomics group, F-75015 Paris, France.
[2] Université de Paris, BioSPC, F-75205 Paris, France
[*] Joint first authors

The mammalian uterine endometrium has developed multiple evolutionary strategies of cellular differentiation to prepare for embryo implantation and to perform its cyclic cellular renewal. In humans, the endometrium differentiates spontaneously into a decidual mucosa in response to progesterone during the window of implantation and breaks down when progesterone level decreases if implantation has not occurred. These cellular transitions have arisen during the evolution of Old World primates, but have also appeared independently in other, more distant mammalian orders. In other primates, the endometrium decidualises only in response to embryo implantation and is resorbed at the end of the cycle in the absence of fecundation through poorly described mechanisms. This phenotypic divergence between related primate clades offers opportunities to dissect the genetic mechanisms underlying the evolution of spontaneous decidualization and menstruation.
To identify gene expression changes underlying the evolution of cellular differentiation of the endometrium, we collected samples of 3 menstruating Old World primates (human, baboon, macaque) and 3 non-menstruating primates (New World primates : saimiri, marmoset – Lemurs : mouse-lemur) at two time points of the endometrial cycle: during the luteal phase when progesterone is maximal, and when the endometrium is shed or resorbed in response to progesterone withdrawal. We performed single-nucleus gene expression sequencing to assemble the first cross-species cartography of endometrial cell populations in the late endometrial cycle. Here, we report the preliminary results of this project. We identified a differentiation of both stromal and epithelial endometrial cells in menstruating species that is not shared with non-menstruating species, and are now pursuing the gene expression changes that control these cellular transitions. This first characterization of endometrial cell types aims to further dissect how endometrial gene expression has evolved in primates, and its functional impact on cellular remodelling in response to progesterone.