CSE 527 Project Proposal
Re-analysis of the Human Endometrial Cell Atlas

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Background

The acceleration of machine learning methods in the modern age has rapidly opened many doors for biomedical research, including accelerating high throughput analyses, the creation of cell atlases, and precision medicine. These methods have been applied across biomedical applications such as creating the Allen Institute Atlases, developing individualized cancer immunotherapies, and the source of the focus dataset, the Human Endometrial Cell Atlas (HECA). [**marevckova2024integrated**]

The endometrium is the innermost epithelial lining of the uterus and provides a thick granular tissue layer and prevent adhesions to the myometrium. It is composed of two layers: the functional columnar epithelium, which is built up and subsequently shed during menstruation, and the stromal basal layer, which contains the progenitors that replace the f.

The process of building up the functional columnar epithelium, decidualization, enables implantation of the embryo into the endometrial surface and coordinates the invasion of extra-embryonic trophoblast lineages. As part of decidualization, endometrial fibroblasts cells can differentiate into decidual secretory cells that have the ability to regulate trophoblast invasion, to resist oxidative stress, and to protect the placental semi-allograft against maternal immune responses. [**Gellersen˙Brosens˙Brosens˙2007**]

Hormones, such as progesterone and estradiol, have a significant role in regulating the function of the endometrium. However, undifferentiated endometrial cells have an approximately 10 day refractory period to signals of either progesterone or estradiol, indicating additional signals are required such as cAMP signaling.[**de1998hormonal**, **brar1997progesterone**, **gellersen2003cyclic**] In primary cultures, cAMP is insufficient to maintain decidualization.

Several diseases impact the endometrium, including adenomyosis, endometrial hyperplasia, endometrial cancer, asherman's syndrome, and endometriosis. Endometriosis, the growth of endometrial tissue outside the uterus, affects up to 10% of women between the ages of 15 and 44 [**Johns**] , pelvic pain, decreased fertility, and diminished quality of life. [**johnson2017world**] Improved understanding of endometrial development, regeneration, cell niches, and function can improve health outcomes for individuals with endometrial diseases and can inform practices in regenerative medicine. Additionally, this research can contribute towards reducing the well documented disparity in women's health research. [**<empty citation>**]

Method

HECA, a high-resolution single-cell reference atlas (313,527 cells) combining published and new endometrial single-cell transcriptomics datasets of 63 women with and without endometriosis. In our re-analysis of the

Challenges

- batch effects - cell cycling effects - perturbations by hormone signalling - related: uterine cycle (Phases: menstrual phase, follicular phase, luteal phase, ischemic phase) - ... ? - ground truthing results

Short-term goals

- establish comparison metrics

Resources

https://github.com/seandavi/awesome-single-cell