

Project title: Engineering collective cell dynamics during differentiation.

A full-time undergraduate co-op student/research assistant position (4-12 months) is available in the Zandstra Stem Cell Bioengineering laboratory, which is in the School of Biomedical Engineering located within the Biomedical Research Centre, and is affiliated with the Michael Smith Laboratories, at the University of British Columbia's Vancouver campus. The successful candidates will join our world-class research team **to engineer collective cell dynamics during differentiation, by investigating pluripotent stem cell differentiation in small sized colonies.** Our highly successful multidisciplinary program integrates researchers in stem cell biology, biological computation, synthetic biology, developmental biology, and regenerative medicine. Our research program is based on understanding how individual cells make developmental decisions by studying multiscale interactions between cells, their internal regulatory networks, and the external microenvironment, and then mobilizing our findings to generate therapeutically relevant blood cells from stem cells.

Details on the project and position:

Background:

In this project, through multiple steps, we will investigate the multi-scale process of human pluripotent stem cell (hPSC) differentiation on small micropatterns. Observations show differentiation of hPSCs in response to the growth factor BMP4 in small colonies (2-20 cells) results in different realms of behavior. Heterogeneity in differentiation response is seen at low initial cell numbers whereas a more coordinated and homogeneous differentiation outcome emerges as cell number increases. We will study this system to reveal collective emergent cell dynamic behavior, as outlined below.

Project description:

The candidate first will learn the basics of human pluripotent stem (hPSCs) cell culture, micropattern fabrication [1], and the basics of hPSC differentiation on micropatterns [2]. After this step they will be able to run a basic protocol of differentiation of hPSCs in small colonies with a small number of cells (<20). In the next step, they will screen for different physical factors to optimize the running protocol, namely, by changing the size and cell density followed by differentiation. A side goal of this step is to obtain an empirical distribution function of the number of cells on micropatterns based on pattern size and cell density. This will help to control the colonies more easily in the steps following. After the optimization step, the experiments will be performed in different conditions (in terms of physical and chemical conditions) to dissect the effect of different signaling pathways (BMP4, NODAL, WNT, FGF) on the observed [3] collective behavior in hPSC differentiation. Namely, they will run screening by changing the concentration of chemical signals in the medium, inhibiting the pathway's activity via small molecule inhibitors, and inhibiting the endogenous signaling activity via microRNA inhibition. All the experiments will be followed by fixing and staining of cells or live-cell confocal microscopy imaging. This work has the possibility to be combined with some computational/theoretical work, including optimizing and developing the existing image analysis platform to perform image analysis. Training will be provided if the candidate lacks some of the necessary skills.

Measurements:

Initially, the candidate will perform antibody staining on the marker genes that are expressed in response to BMP4 in small colonies (CDX2 and SOX2), E-CAD which affects pluripotency, and also perform Fluorescence In Situ Hybridization (FISH) experiments on genes related to the major diffusive signals in the system: BMP4, FGF. This is followed by imaging using confocal microscopy.

Relevant literature:

- [1] Tewary, Mukul, et al. *PLoS biology* 17.10 (2019).
- [2] Tewary, Mukul, et al. *Development* 144.23 (2017).
- [3] Nemashkalo, Anastasiia, et al. *Development* 144.17 (2017).

Notes:

- 1) This position is suitable for an independent, resourceful, highly self-motivated student candidate with relevant experience
- 2) Position will be 4-12 months duration, to start in May 2021
- 3) No vacation time is provided as vacation pay is provided in lieu; however if the candidate has any scheduling constraints please discuss with us
- 4) We encourage successful applicants to also apply for external award funding as appropriate and eligible
- 5) The salary will be \$2600/month full-time (based on 35 hours work/week). Salary will be pro-rated for any partial months worked, and is inclusive of any award funding received.

Ideal candidates would have experience in some or all of the below:

- Cell biology
- Mammalian cell culture and aseptic technique
- Stem cell biology lab experience and/or experience working with pluripotent stem cells is an asset
- Computer programming skills (working knowledge of Python or MATLAB is an asset)
- Data analysis (statistical methods are an asset)
- Fluorescence in-situ hybridization (FISH) assay
- Confocal microscopy with fluorescent proteins or fluorophore-conjugated antibodies

Individuals must also:

- Work well in a goal-oriented team environment;
- Be highly self-motivated and engaged in research
- Possess excellent communication skills – both verbal and written;
- Be open to instruction and constructive criticism on the project and their capabilities
- Have the ability to work semi-independently and organize own workload under supervision
- Keep meticulous records of experiments and data, report on research progress and outcomes openly within the team, utilize our lab's electronic lab notebook system as instructed, and maintain research confidentiality
- Demonstrate an ability to design and analyze experiments, review experimental methodologies in response to feedback
- Have the ability to acquire and update knowledge in their specialized area and implement relevant technologies to advance the project

For further information about these projects and to apply, please also send us your application package **as one PDF file** via email at zandstra.lab@ubc.ca to include

- Email subject line: “Engineering collective cell dynamics during differentiation 2021 co-op/RA student application”
- Cover letter
- Dates and duration of your availability (preferred start date, for how many months)
- CV
- Copy of all university transcripts (require English translations where applicable; originals must sent prior to acceptance of offer)
- Contact information for 3 references

For further information on our research and team, please visit our website and Twitter account:

<https://www.stemcellbioengineering.ca/>

<https://twitter.com/StemCellBioEng>

We will consider applications until the position is filled, at which time we will remove the job posting on our lab website - <https://www.stemcellbioengineering.ca/careers/>

We regret that we can only contact those applicants who are selected for further consideration.
