

Project title: Bioinformatics of PSC-derived T cell transcriptomics and epigenomics

Application deadline: Aug 31, 2022

Start date: January 2023

We are recruiting a **Master of Science student** for co-supervision in the UBC Bioinformatics Program within the Zandstra and Hirst laboratories. The Zandstra lab is in the School of Biomedical Engineering located within the Biomedical Research Centre, the Hirst lab is in the Department of Microbiology and Immunology, and both are affiliated with the Michael Smith Laboratories, at the University of British Columbia's Vancouver campus. The successful candidate will join our world-class research teams **to perform transcriptomic and epigenomic profiling on cells generated in our human pluripotent stem cell (hPSC) to T cell in vitro differentiation platform.**

Our highly successful multidisciplinary program integrates research in stem cell biology, epigenetics, biological computation, synthetic biology, developmental biology, and regenerative medicine, with the goal of developing a platform for scalable *in vitro* production of T cells and other immune cells from stem cells for eventual use as off-the-shelf cell therapies. Our research program is based on understanding how individual cells make developmental decisions by studying multiscale interactions between cells, their internal gene and epigenetic regulatory networks, and the external microenvironment, and then mobilizing our findings to generate therapeutically relevant immune cells from stem cells.

Details on the project and position:

We are looking to recruit a bioinformatics-focussed Master's student to drive forward data analyses for projects using our human pluripotent stem cell (hPSC) to T cell in vitro differentiation platform (Michaels et al. 2022), working closely with a research associate and other lab members. The candidate will perform bioinformatics analyses of datasets for gene expression, chromatin accessibility, epigenetic profiling (including histone modifications and DNA methylation), and transcription/regulatory factor binding profiling, through this cell differentiation process, which has significant cell based therapeutic connections and potential. The Zandstra lab are experts in stem cell bioengineering, therapeutics development, and computational modelling, whereas the Hirst lab are experts in cancer epigenetics and analysis of high-throughput sequencing/whole-genome epigenomics datasets; we are joining forces to collaborate on this project. Zandstra lab has developed a computational platform called IQCELL that allows prediction of effects of gene perturbations on developmental trajectories using single-cell RNA-seq data. Zandstra lab also have an ongoing collaboration with Dr. Geoff Schiebinger's group (Math Dept., UBC) on applying Optimal Transport and SCENIC computational methods to explore lineage trajectory analyses of gene expression. We aim to extend our gene regulatory analyses to include chromatin accessibility and epigenetic profiling information. There will be opportunities for the motivated candidate to further develop such computational modelling and analytical tools as applied to the hPSC to T cell differentiation platform, and learn the wet-lab techniques used in our cell differentiation platform.

Relevant literature:

Tewary, M., Shakiba, N., and Zandstra, P. W. (2018) Stem cell bioengineering: building from stem cell biology. *Nat. Rev. Genet.* 19, 595–614.

Shukla, S., Langley, M. A., Singh, J., Edgar, J. M., Mohtashami, M., Zúñiga-Pflücker, J. C., and Zandstra, P. W. (2017) Progenitor T-cell differentiation from hematopoietic stem cells using Delta-like-4 and VCAM-1. *Nat. Methods* 14, 531–538.

Michaels Y.S., Edgar J.M., Major M.C., et al. (2021) DLL4 and VCAM1 enhance the emergence of T cell competent hematopoietic progenitors from human pluripotent stem cells. *bioRxiv*. 2021:1-41. doi:10.1101/2021.11.26.470145; *Science Advances* 2022 in press

Heydari T, Langley MA, Fisher C, Aguilar-Hidalgo D, Shukla S, Yachie-Kinoshita A, Hughes M, McNagny KM, Zandstra PW. (2022). IQCELL: A platform for predicting the effect of gene perturbations on developmental trajectories using single-cell RNA-seq data. *PLOS Comp Biol* 18(2): e100990.

Kusakabe M., Sun A.C., Tyshchenko K., Wong K., et al. (2019) Synthetic modeling reveals HOXB genes are critical for the initiation and maintenance of human leukemia. *Nat. Commun.* 10, 2913. <https://doi.org/10.1038/s41467-019-10510-8>

Sloma I., Beer P., Desterke C., Bulaeva E., et al. (2021) Epigenetic and functional changes imposed by NUP98-HOXA9 in a genetically engineered model of chronic myeloid leukemia progression. *Haematologica*. Vol. 106 No. 3. <https://doi.org/10.3324/haematol.2020.249243>

Notes:

- 1) This position is suitable for an independent, resourceful, highly self-motivated bioinformatics Master's degree candidate with relevant experience
- 2) We encourage applications that will enhance the diversity in our team
- 3) Start date is early Jan 2023
- 4) If we are not able to fill this position for the Jan 2023 intake, we would consider applications for the next (May 2023) intake, please indicate in your email to us if this is relevant for you. While the position remains open, it will stay posted on the Zandstra lab website.
- 5) We encourage candidates to apply for external award funding as appropriate and eligible
- 6) Stipend support will be provided and top-ups apply for those receiving external awards
- 7) We would consider advancement to a PhD program once enrolled if the candidate is successful in their Master's program

Ideal candidates would have knowledge of and/or experience in some of the below areas:

- Computer programming (working knowledge of R and/or Python)
- Computational modelling
- Data analysis (including statistical evaluation methods)
- Strong background in undergraduate level mathematics and statistics
- Understanding of quantitative approaches used in science and/or engineering research
- Gene expression, genetics, and epigenetics analysis methods (wet-lab and/or data analysis)
- Cell biology or biochemistry (stem cell biology lab experience and/or experience working in the field of hematopoiesis research is an asset)
- Mammalian cell culture and aseptic technique
- Flow cytometry

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, training, 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, 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

All applications must be submitted **directly to the UBC Master of Science in Bioinformatics Program by August 31, 2022** through this web portal:

<https://www.bioinformatics.ubc.ca/apply/>

Please also send us an application package **as one PDF file** via email at zandstra.lab@ubc.ca by Aug 31, 2022 to include:

- Email subject line: “Bioinformatics of PSC-derived T cell transcriptomics and epigenomics – Master’s student application”
- Cover letter
- CV
- Copy of all university transcripts (require English translations where applicable)
- Contact information for 3 references

For further information on our research and teams, please email us at zandstra.lab@ubc.ca and visit these websites and Twitter account.

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

<https://twitter.com/StemCellBioEng>

<https://www.msl.ubc.ca/people/dr-martin-hirst/>

For specific information about the UBC Bioinformatics program please consult these links and contact details:

<https://www.bioinformatics.ubc.ca/>

<https://www.grad.ubc.ca/prospective-students/graduate-degree-programs/master-of-science-bioinformatics>

Applications must meet the UBC minimum academic requirements for admission to UBC Graduate Studies and the UBC Bioinformatics graduate program criteria to be considered for this opportunity.

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