

A short-term (8 months) undergraduate co-op student/research assistant position 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 **to engineer blood stem cell graft composition using high-throughput, combinatorial methods, and cell communication molecules and drugs**. Our highly successful multidisciplinary program integrates researchers in stem cell biology, biological computation, microfabrication, developmental biology, and regenerative medicine, with the goal of developing in vitro and in silico representations of complex tissue and organ development. Our research program is based on understanding how individual cells form complex functional tissues and organs 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:

Project title:

High-throughput automated bioengineering of human blood stem cell culture for clinical therapy

Successful outcomes from this project will translate into supporting ongoing clinical trials aimed at improving blood stem cell transplantation outcomes for patients suffering from a host of blood malignancies. A critical aspect of developing clinical therapies using stem cells involves accurate and robust control of stem cell behavior in controlled laboratory conditions. The expansion and production of functional blood cells is a critical step to enhancing existing bone marrow transplants, and for developing new, targeted therapies.

We anticipate that an engineered blood stem cell graft can be tuned to meet the clinical needs of specific diseases in a precise manner. A promising approach to achieve this involves identifying combinations of molecules that enhance blood stem cell expansion and immune cell production by mimicking soluble signals of the blood stem cell microenvironment, and/or reproducing signals associated with normal developmental events. A defined combination of signaling molecules offers an efficient, cost-effective, reproducible, scalable, and clinically-appropriate method to expand blood stem cells. To achieve this, we are developing and utilizing a high-throughput, automated platform capable of preparing and analyzing large numbers of culture conditions in a programmable manner, combined with modeling our cell population outputs to predict other possible conditions within the design space.

The candidate will have the opportunity to assist in developing an automated protocol for high-throughput testing of conditions to control the behaviour of cultured human blood stem cells and their differentiated progeny. They will also analyze and model this behavior over a wide range of conditions. This translational research project is in support of an ongoing clinical program in partnership with an industry collaborator, ExCellThera Inc. Specifically, the student will be involved in aspects of the project that may include:

- “Design of Experiments” approaches for screening and optimizing blood stem cell culture conditions using statistical software
- Programmed implementation of experimental designs with automated/robotic liquid handling of selected culture conditions
- Cell output data analysis and modeling using statistical methods

- Follow-up experiments testing scalability and function of cells produced in desirable conditions
- Defining new methods to improve processes

This project is funded in part by an industry collaboration with ExCellThera Inc., a Canadian clinical stage cell and molecular medicine company developing novel curative therapies for patients with hematologic malignancies.

Relevant literature:

Lipsitz, Y., Timmins, N. & Zandstra, P. Quality cell therapy manufacturing by design. *Nat Biotechnol* 34, 393–400 (2016). DOI: [10.1038/nbt.3525](https://doi.org/10.1038/nbt.3525)

Fares, I., Chagraoui, J., Gareau, Y., Gingras, S., Ruel, R., Mayotte, N., Csaszar, E., Knapp, D.J.H.F., Miller, P., Ngom, M., et al. (2014). Cord blood expansion. Pyrimidoindole derivatives are agonists of human hematopoietic stem cell self-renewal. *Science (New York, NY)* 345, 1509-1512. DOI: [10.1126/science.1256337](https://doi.org/10.1126/science.1256337)

Audet J, Miller CL, Eaves CJ, Piret JM. Common and distinct features of cytokine effects on hematopoietic stem and progenitor cells revealed by dose-response surface analysis. *Biotechnol Bioeng.* 2002 Nov 20;80(4):393-404. 10.1002/bit.10399. DOI: [10.1002/bit.10399](https://doi.org/10.1002/bit.10399)

Qiao W, Wang W, Laurenti E, Turinsky AL, Wodak SJ, Bader GD, Dick JE, Zandstra PW. Intercellular network structure and regulatory motifs in the human hematopoietic system. *Mol Syst Biol.* 2014 Jul 15;10(7):741. DOI: [10.15252/msb.20145141](https://doi.org/10.15252/msb.20145141)

Cohen S, Roy J, Lachance S, Delisle JS, Marinier A, Busque L, Roy DC, Barabé F, Ahmad I, Bambace N, Bernard L, et al. Hematopoietic stem cell transplantation using single UM171-expanded cord blood: a single-arm, phase 1-2 safety and feasibility study. *Lancet Haematol.* 2020 Feb;7(2):e134-e145. DOI: [10.1016/S2352-3026\(19\)30202-9](https://doi.org/10.1016/S2352-3026(19)30202-9)

Notes:

- 1) This position is suitable for an independent, resourceful, highly self-motivated candidate with relevant experience.
- 2) Position will be 8 months duration, to start in early January 2021.
- 3) No vacation time is provided as vacation pay is provided in lieu; however if the candidate wishes to minimally alter the start or end dates, please discuss with us
- 4) We encourage successful applicants to also apply for external award funding as appropriate e.g. an NSERC undergraduate summer research award (USRA) (<https://students.ubc.ca/career/campus-experiences/nserc-undergraduate-student-research-awards>) and/or a Centre for Blood Research-School of Biomedical Engineering USRA (<https://www.bme.ubc.ca/research/funding-opportunities/>); either one of these awards can be held at one time concurrent with a co-op position. Note that the NSERC USRA program requires a minimum 16 week continuous duration of work.
- 5) The salary will be \$2500/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 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, with 2D and/or bioreactor cultures
- Bioengineering methods (e.g. factorial Design of Experiments, bioprocess, Quality by Design)
- Computer programming skills (working knowledge of Python is an asset)
- Data analysis (statistical methods and data modeling is an asset)
- 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 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

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: “Bioengineering of human blood stem cell culture” 2021 co-op/RA student application
- cover letter
- dates of your availability
- 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 on a rolling basis until the position is filled, at which time we will note this on the job posting on our lab website here - <https://www.stemcellbioengineering.ca/careers/>

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