



StemSpecs

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Welcome to the first issue of StemSpecs, the on-line newsletter of “Mass Spectrometer-based Flow Cytometer, Methods and Applications”, a Genome Canada project launched in February 2005. This issue includes a biography of our Lead Investigator, John Dick and a list of our upcoming meetings. Future issues will include updates on our progress, a list of job opportunities within the project, and biographies of other members of the project team.

Our website, launched in June 2005, is intended to inform readers of the goals and structure of our project, and to introduce you to the multidisciplinary team that is doing this work. If you haven't seen the site, please have a look, starting from our homepage: www.uhnres.utoronto.ca/stemspec. We hope that you will find the website informative, and that you'll check back to follow our progress.

Our team is very excited that the project is underway. We have been in an intense start-up phase, including the installation of Dr. Scott Tanner's team in their new, purpose-built facility in the Chemistry Department at the University of Toronto. We are all very grateful to the people at the University of Toronto (and the University Health Network and McMaster University) who have made the Tanner team's transition to academia as smooth as possible.

We want to acknowledge all of our sources of financial support. This project was funded by Genome Canada through the Ontario Genomics Institute. Complementary funding is gratefully acknowledged from: the Ontario Cancer Research Network, the National Cancer Institute of Canada, the Leukemia and Lymphoma Society (USA), the University of Toronto (Faculties of Arts&Science, Applied Science & Engineering, and Medicine), DVS Sciences Inc. and MDS Sciex (in-kind hardware). This project can only be accomplished by an inter-disciplinary team, with the support of all of these agencies.

Thank you!
Welcome to StemSpecs; see you again soon.

Sincerely,
The Editors

Editor-in-Chief: John Dick
Contributing Editors: Scott Tanner, Amy Dambrowitz

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Biography



Dr. John Dick, the Project Leader for the Genome Canada Project “Mass Spectrometer-based Flow Cytometer, Methods and Applications”, wants to understand how normal, “healthy” hematopoietic stem cells become leukemic stem cells. He leads a research program that seeks to determine how human hematopoietic (blood) stem cells and leukemic stem cells sustain themselves, proliferate and differentiate into the many cell types in blood. His lab also characterizes changes in the

expression and function of key regulatory genes that lead to the leukemic transformation of hematopoietic stem cells.

Dr. Dick, who holds a Canada Research Chair in Stem Cell Biology, is a native of Manitoba. He grew up in Elm Creek (outside Winnipeg) and attended the University of Manitoba, where he completed a B.Sc. (Honours) in Microbiology, and a Ph.D. in Microbiology and Biochemistry under the direction of Dr. Jim Wright. In 1984, John began his work in Toronto as a post-doctoral fellow in the lab of Dr. Alan Bernstein, an internationally respected researcher in the areas of hematopoiesis and cancer.

Since then, John has been an active member of the research community in the Toronto

area, where he is presently appointed as a Senior Scientist at the University Health Network and as a Professor in the department of Medical Genetics and Microbiology at the University of Toronto. His work has produced over eighty papers in the field of hematopoiesis and has attracted many honours, including the Michael Smith Award for Excellence in 1997, and his appointment as a Fellow of the Royal Society of Canada in 2004. John is also a popular mentor, having directed over forty students, post doctoral fellows and technicians.

Research

Dr. Dick is known throughout the world for developing the NOD/SCID repopulation assay. This assay allows researchers to take stem cells from human bone marrow or cord blood, transplant them into immune-deficient mice and observe while those stem cells proliferate, differentiate and develop into all of the cellular elements of human blood. This protocol has revolutionized the study of normal and leukemic human blood systems; before the repopulation assay was developed, there was no model to study how stem cells generate the many cell types in blood.

Dr. Dick and his research team initially developed the NOD/SCID repopulation assay to study Acute Myeloid Leukemia (AML) and used it to confirm that AML is a stem cell disease. This means that only the leukemic stem cells in AML patients (which are present at a rate of one in a million cancer cells) drive the growth, immortality and malignancy of the cancer. The lab currently uses the assay to define the differences between normal hematopoietic stem cells (HSCs) and leukemic stem cells (LSCs). By comparing the developmental programs of normal and leukemic stem cells, the group characterizes the molecular transitions that give leukemic

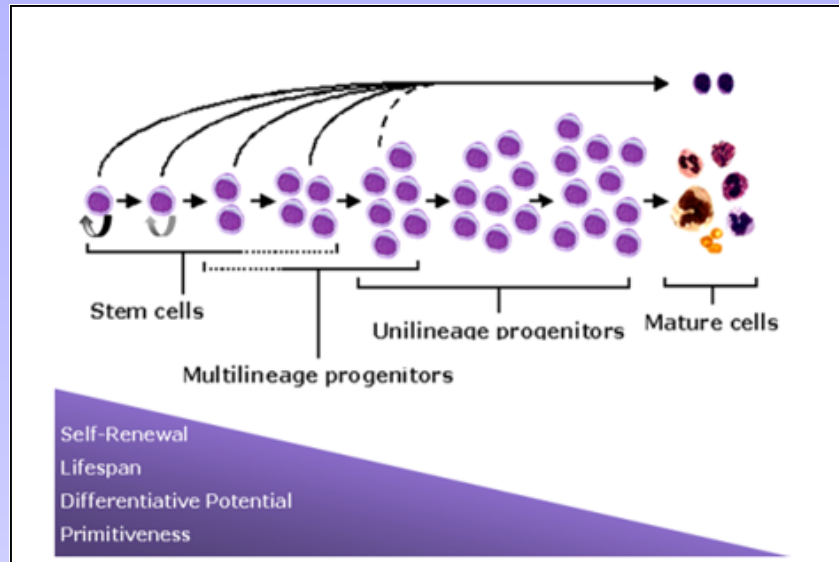
stem cells their malignant properties. Understanding how leukemic stem cells differ from normal hematopoietic stem cells should inform efforts to eradicate them in patients, which is essential to the effective treatment of leukemia.

In John’s own words: *“If cancer stem cells lie at the heart of some cancers, then being able to predict the behavior of tumors and providing effective therapies against them means understanding the abnormal growth pathways within the stem cells themselves”*.

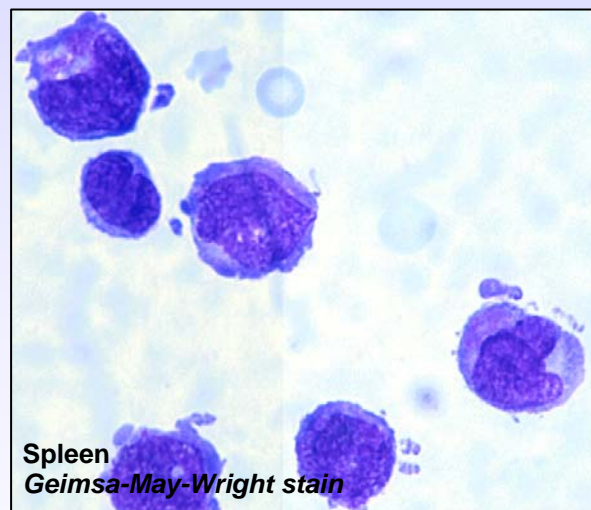
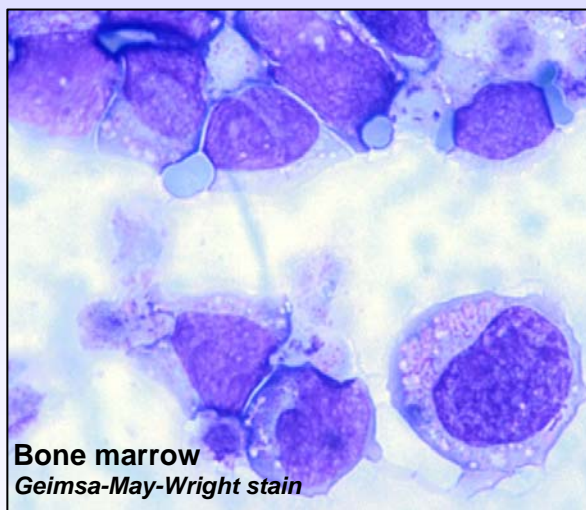
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Hematopoietic Hierarchy



Infiltration of human leukemic blasts into mouse bone marrow and spleen

Why This Project ?

Cancer Stem Cells have been poorly characterized because they are rare and difficult to isolate by conventional means, and because relevant assay methods are not available. Dr. Dick was drawn to this collaborative Genome Canada project because the new instrument that is being developed (an inductively coupled plasma mass spectrometer (ICP-MS) dedicated to discrete particle assay in a flow cytometer configuration) will allow his lab to perform more comprehensive analyses of individual cells. The new ICP-MS instrument is designed for multiplexed analysis of tens (or possibly hundreds) of different types of proteins in each individual cell in a sample.

Presently, John's research relies on the use of fluorescence-activated cell sorting (FACS) to rapidly analyze cells

and determine their molecular characteristics. FACS instruments are very popular for the analysis and sorting of single cells and populations of cells, but FACs analysis is generally limited to detecting a few (approximately 5) concurrent signals. Increased multiplex capabilities will allow Dr. Dick's lab (and other cancer research labs) to analyze the rare stem cells, to perform more thorough proteomic analyses of individual cells, and to detect the molecular differences that give stem cells their unique properties. This will extend our understanding of the proteins and protein-protein interactions that affect the function of HSCs and LSCs.

John is also excited about the rapid benchtop-to-bedside progress inherent to the design of this Genome Canada project. The instrument will have an

immediate clinical application; this high-throughput instrument, in combination with the project's suite of element-tagged affinity products, will allow the rapid detection and characterization of individual cancer cells in patient samples. This means that, once the "fingerprints" (the identifying combination of molecular markers) of leukemic stem cells have been identified, any patient's blood sample can be rapidly analyzed to determine whether or not leukemic stem cells are present, and to identify what specific type of diseased cells are represented. Identifying the unique molecular characteristics of diseased cells will allow physicians to make personalized diagnoses and deliver appropriate therapy that is specific to the patient's disease, resulting in timely, effective treatment with minimized debilitating side effects.

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