Another project brought to you by GenomeCanada

Massively Multiparametric Flow Cytometer Analyzer

Status	Current
Competition	Development of New Technologies Competition
Sector	Development of New Technologies
Genome Centre	Ontario Genomics Institute
Project Leader	Scott Tanner

Project Description

Diagnosing a disease is most difficult at the early stages, where therapeutic intervention is most effective and least devastating. A patient's sample contains many different cells, each of which can be distinguished and identified by the biomarkers (proteins, genes and small molecules) that comprise the cell's biochemical signature. Groundbreaking research in leukemia has advanced the belief that a particular disease may be sustained by only a small fraction of the diseased cells ("cancer stem cells" in the case of cancer), and is thus particularly difficult to detect and treat. The biomarker signature also reflects biochemical processes within the cells that determine cell activity and fate. Accordingly, the capability to measure the full signature of biomarkers at the same time for individual cells provides an opportunity for improved understanding of cell genesis and for the development of drugs to treat the disease.

Enormous progress is being made on the identification of diagnostic biomarker signatures and the understanding of biomarker interactions. Unfortunately, there are few analytical tools capable of recognizing these signatures, and these have serious limitations for detecting many biomarkers in a single analysis. Current single cell diagnostic technologies are based on the detection of fluorescent emission from tagged reagents that specifically recognize the biomarkers. While up to 10 detection channels can be monitored simultaneously, the approach is limited by poor resolution. This results in signal overlap and large errors when biomarkers are present over a wide range of concentrations. There is a clear need for a new technology that will provide for the simultaneous quantitative and independent determination of many (up to 100) biomarkers in individual cells, especially where that analysis can be performed at high speed so that 1000 or more cells can be analyzed per second.

The applicants are developing an innovative solution to this challenge that is receiving considerable enthusiasm from the scientific community. The approach takes advantage of the high resolution of mass spectrometry to distinguish biologically-rare metal atoms that replace the fluorescent dyes in current use. A new generation of diagnostic reagents that bind different metals to biomarkers is being developed. These “tagging metals” are detected with high sensitivity and resolution, and in a quantitative manner, by a prototype flow cytometer. This instrument introduces individual cells at a rapid rate, up to 1000 cells per second, to a multichannel mass spectrometer analyzer. In our current Genome Canada Applied Human Health (AHH) project, we were able to demonstrate the feasibility of this new technology. The present proposal seeks to transform the complex research prototype instrument (and the reagents required for its operation) into an engineering prototype that will be made available to other Genome Canada researchers and that will subsequently be converted to a commercial instrument for widespread diagnostic and research use.

In addition to enabling genomics and proteomics researchers to achieve a vast improvement in the depth and range of cellular analysis, this project will provide a diagnostic tool that will define the new standard-of-care benchmark in hospitals, clinics and research departments world-wide. The applicants bring long experience in the development of commercially successful analytical tools, and are ideally positioned to realize the project’s ambitious goals.

The success of this project will lead to healthcare savings for Canadians and others worldwide, resulting from first-time-correct diagnosis and reduction in adverse drug reactions. It will advance international awareness of Canada as a leader in bioanalytical research. The commercial development of this mass spectrometer-based flow cytometer with its unprecedented multiplexing capabilities, along with its associated reagents technology development, will lead to many new highly-skilled jobs for Canadians and create millions of dollars of new revenue, much of it derived from export sales.