

The Benjamin Pearl Memorial Fellowship

AN UPDATE ON YOUR SUPPORT

Life-saving discoveries in leukemic stem cell research

Thanks to your generosity, Dr. John Dick, world-renowned stem cell biologist at the McEwen Stem Cell Institute, together with Benjamin Pearl Memorial Fellow Dr. Sagi Abelson, are continuing their groundbreaking research in the study of blood stem cells – analyzing normal blood stem cells and leukemic stem cells – to identify ways to catch and treat leukemia early on in its development. Building on the work of previous Pearl Fellow Dr. Liran Slush, now a Principal Investigator at the Weizmann Institute of Science in Israel, Dr. Dick and his team discovered a pre-leukemic stem cell which may be a first step in triggering the cancerous disease, and also responsible for evading therapies, which triggers a relapse in patients with acute myeloid leukemia (AML).

A COMMON GENETIC ANCESTOR

The discovery of a common genetic mutation shared by normal blood stem cells and leukemic stem cells, known as DNMT3A, is driving the work of Drs. Dick and Abelson forward. This rare abnormality, known as age-related clonal hematopoiesis (ARCH), is linked to pre-leukemic patients who have a higher risk of developing AML as they get older. Dr. Abelson investigated the early evolutionary steps in the development of AML, and found that a large proportion of blood cells are being generated from a single mutated cancerous stem cell. But, which cell does



Dr. John Dick was recently awarded the 2018 ASH Mentor Award by the American Society of Hematology. He also received the 2018 Richard Hill Mentorship Award from the Princess Margaret Cancer Centre, and the 2018 Special Achievement Award at the 51st Annual Miami Winter Symposium at the University of Miami.

the first mutation come from, and how long does it take for that gene to develop? This Fellowship has enabled Dr. Abelson to delve deeper into finding answers to these questions.

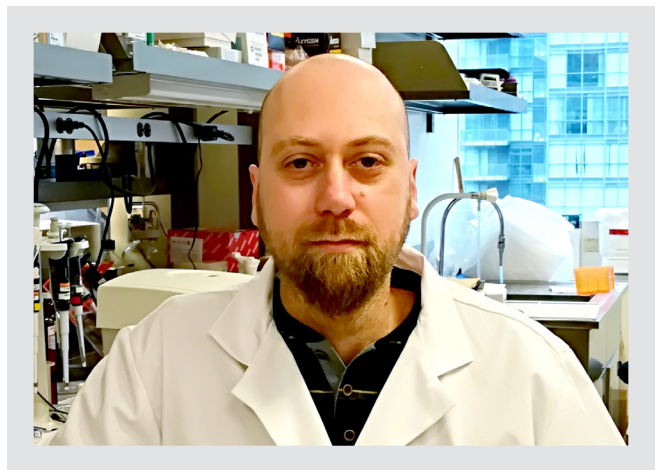
Through the genomic analysis of blood samples obtained from individuals years prior to their diagnosis with AML, Dr. Abelson identified the early genomic abnormalities in leukemia evolution and identified a population at high risk for developing AML. This proof of concept study is the first step in the design of screening a test for the early

detection of AML, and was published in the July 2018 issue of *Nature*, enclosed in this report. This was a significant milestone for Dr. Abelson, as his study proves that patients at risk of developing leukemia can be identified as early as six to 10 years before a cancer diagnosis, which has a huge impact on the ability to prevent, treat and save lives of people all over the world. His study also suggests that these early detection screenings might help identify and predict individuals at high risk for other diseases in the future.

MOVING TOWARDS PREVENTATIVE REGENERATIVE MEDICINE

Drs. Dick and Abelson are making progress in collecting blood samples from AML patients consisting of diagnosis and relapse samples, and samples taken during remission. Their team has undertaken and completed all the genome sequencing to find the relapse-specific mutations. In the coming year, they will monitor the relapse mutations in the diagnosis and remission samples to shed light on why relapse-fated leukemia cells survive therapy and remain able to regenerate leukemias.

By collaborating with researchers in Boston, it was discovered that if cancer survivors who received radiation or chemotherapy have ARCH in their blood, they have a higher risk of developing heart disease. This has enormous implications, as Dr. Dick's team can now use ARCH as a way to determine who is at risk for cardiovascular diseases, and other inflammatory conditions, linked to blood. In a follow-up to his recent paper, Dr. Abelson has refined his ARCH detection test (\$1,000 per test) to develop a rapid and highly cost-effective tool (less than \$100) that will be applied in the clinic. Dr. Dick's team is working with



Dr. Sagi Abelson, Benjamin Pearl Memorial Fellow, received the 2017 and 2018 Abstract Achievement Award at the American Society of Hematology Conference.

investigators at the Peter Munk Cardiac Centre at UHN and other hospital networks to create a cardio-oncology clinic to monitor such at-risk cancer patients. The Research Ethics Board has approved this investigation, and the final plans for patient identification and implementation are being completed with a plan to start patient monitoring in the beginning of 2019. At present, Dr. Shlush is collaborating with Dr. Abelson to test the preliminary samples for ARCH in his lab in Israel. In 2019, Dr. Abelson's test will be implemented in Dr. Dick's lab and applied to cancer patients, which they believe will lead to revolutionized patient care.

Dr. Abelson's publication is one of the first in a series of long-term studies that pioneers the amazing advances made in early AML detection. Thank you for supporting his world-leading research.

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