INTERVIEW

WITH DR. TOBIAS BERG

BATTLING ACUTE MYELOID LEUKEMIA (AML) AS BOTH A CLINICIAN AND SCIENTIST

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ABSTRACT

Acute myeloid leukemia (AML) is characterized by the accumulation of immature hematopoietic cells in the bone marrow that impair normal blood formation. Chemotherapy is always the first treatment option for AML. Patients can also be cured by allogeneic stem cell transplantation, which consists of transferring stem cells from a healthy donor to the patient after high-intensity (high-dose) chemotherapy. Many mutations found in AML affect the cells on an epigenetic level, influencing the gene expression of the cells such as influencing DNA-methylation genes and chromatin-modifying genes. Affecting these epigenetic mechanisms is therefore of great interest in the area of AML.

Dr. Tobias Berg, MD, Ph.D.

Dr. Tobias Berg is a clinician-scientist who was recently appointed the Boris Family Chair in Leukemia and Hematopoietic Stem Cell Translational Research in June 2019. Prior to joining McMaster, he specialized in Hematology and Oncology at the University of Frankfurt with a focus on epigenetics, AML, and allogeneic stem cell transplantation. After completing his doctoral project at the University of Minnesota and residency at the University of Freiburg, Dr. Berg completed a postdoctoral fellowship at the B.C. Cancer Agency. When asked about his overall experience at McMaster he stated that, "My experience here at McMaster so far has been very good. I have a clinical practice at the Juravinski Cancer Centre and have my research work at the university. I've been welcomed very warmly, and everyone was very supportive, it's great. There are certainly challenges when being a new faculty member, and they've been very helpful when starting up the lab."

► Why did you choose to work in the field of Leukemia and Hematopoietic stem cells?

So, I was fascinated by the field of hematology, generally in the field of cancer, since high school. During the early phases of my medical studies, I got more and more interested in cancer as this is probably the area in medicine where our growing understanding of underlying biological processes of disease is probably leading to the greatest improvements. Also, during my doctoral thesis, I developed a growing interest in immune tolerance which brought me in contact with the

field of allogeneic stem cell transplantation.

► Your research focus has been on adult AML and providing novel treatments. What is your approach in developing some novel treatment options?

AML treatments for a long time have been more or less the same. The treatments that are still used as the backbone of our treatments were first published before I was born! This standard regimen that we are using is called 7+3. It is seven days of cytarabine and three days of daunorubicin. That, as well as allogeneic stem cell transplantation, was developed in the early 70s. So, there was a very long gap period in which there were not many new developments. We are now in a time where we have a lot of new approval of drugs in the area of AML. When the patient is diagnosed with leukemia, the immune system has already lost the fight. So, we either have to get the immune system back on track or give them another immune system using allotransplantation. And then the epigenetic treatments can help the new immune system to fight cancer by essentially getting genes expressed that would otherwise not be expressed. I am very excited about this development and about integrating these into treatment algorithms. I am also very interested in contributing to the development of novel treatments by understanding the epigenetics of AML and interactions between genetic mutations and epigenetic regulation.

► You also work on epigenetic regulators and their interplay with genetic regulators. What is your stance on the role of genetic vs environmental factors in cancer development?

In general, both play a role. There are genetic syndromes in the area of AML that make a patient prone to the development of AML, but it is rare. And, there are obviously environmental factors that enhance the risk of acquiring spontaneous types of mutations. So, they are both important.

While I often get the question from patients about the direct cause of their disease this is often very hard to say, because mutations often arise spontaneously in rapidly dividing cells. With a bit of bad luck these mutations occur in genes that are important for the growth regulation or the differentiation of cells which can be the first step in the development of cancer.

"The treatments that are still used as the backbone of our treatments were first published before I was born!"

► What are some challenges in developing treatment options for AML?

There are two main challenges in the area of AML. Number one is treatment resistance. We have chemotherapy regimens that 60-80% of young patients respond to, while for old patients, the rate is less, maybe 40-60%. And then some patients cannot tolerate such intensive treatments. So, treatment resistance is a very important area. Number two is relapse. We need to understand what leads to the relapse of leukemia. Both treatment resistance and relapse are interconnected because if you cannot eradicate the leukemia cells, then the residual cells are the source of the relapse. This connection is a challenge and also an opportunity. Our group is therefore very interested in understanding the biological processes in these residual cells after treatment.

"Both treatment resistance and relapse are interconnected...if you cannot eradicate the leukemia cells, then the residual cells are the source of the relapse."

► What is your advice for students and researchers who want to pursue the field of stem cell research?

It is a very active area of research. Stem cell research can be connected to several things such as mechanisms in cancer and leukemia. If you want to get involved in that type of research, a strong molecular biology and biochemistry background is helpful. Also, a good background in the area of bioinformatics is helpful because a lot of studies in this area, particularly genetic studies such as single-cell sequencing, require the use of advanced analysis tools to analyze large data sets. Stem cell research is also very interdisciplinary. For someone who is more interested in stem cell research from a medical perspective, it is where people from various fields of medicine and research come together, and interdisciplinary communication is the important thing which will drive this field. So, whatever you are interested in, either more on the research side or more on the clinical side, it is essential to understand this interface and connection.