Universität Basel

Research Project

A systems medicine approach to hematopoietic stem cell diseases 'StemSysMed'

Third-party funded project

Project title A systems medicine approach to hematopoietic stem cell diseases 'StemSysMed'
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Blood cancer occurs relatively rarely in humans, despite the fact that hematopoietic stem cells divide frequently, making mutations common. The scientists involved in the StemSysMed MRD Project aim to identify the factors that contribute to an onset of rampant proliferation of mutated blood cells.

During blood formation, also called hematopoiesis, blood cells are produced from precursor or stem cells. This process features some of the highest cell formation, division and therefore mutation rates of all the cell types in our bodies. Nonetheless, blood cancer is not the most frequent type of cancer in humans. The reason for this is the presence of a fine-tuned control system. This system prevents excessive cell proliferation on various levels of blood formation, and eliminates the progeny of mutated precursor or stem cells, called malignant clones.

Numerous mutations are already known to give rise to blood cancer. However, what is not yet known, is what happens before a clone is able to proliferate sufficiently to cause blood cancer. The StemSysMed MRD Project team aims to collect data and insight pertaining to this early phase, and to model them systematically. The scientists will examine healthy individuals displaying normal or clonal blood production as well as patients suffering from myeloproliferative neoplasms. This disease serves as a model for a neoplastic disease in which blood cells begin to proliferate uncontrollably.

0.0.1 Identifying factors that enable clones to proliferate

It is already known that frequency and traceability of mutations in hematopoietic cells increase with age. Additionally, infections, inflammations and other stress factors can influence the frequency and number of mutations. The StemSysMed project will examine the influence of these additional factors on the mutation profile, as well as the presence of clones during hematopoiesis.

Using a systems biology approach, and taking myeloproliferative neoplasms as an example, the scientists will examine how the disease develops in a mouse model as well as in primary cells of affected patients. The goal is to identify the factors that enable a clone to proliferate to such an extent that disease occurs. Is it possible to explain the development of myeloproliferative neoplasms solely by the occurrence of a crucial cancer-inducing mutation in a precursor or stem cell? Or do oncogenic mutations

in fact occur quite frequently, leading to blood cancer only in the presence of additional external factors? The scientists will test these hypotheses using mathematical models.

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