2. StemSysMed – When mutated blood cells begin to multiply uncontrollably

Blood-forming cells multiply often, with mutations occurring relatively frequently. Despite this, blood cancer is a comparatively rare disease in humans. The MRD Project StemSysMed aims to find out why some mutated blood cells suddenly start to proliferate uncontrollably.


Radek Skoda

Blood cells are formed from stem cells and progenitor cells. “Every year, a person produces around 70 kg of blood in this way,” says Radek Skoda, PI of the MRD Project and professor at the University of Basel. The high rate of cell division leads to many mutations. The fact that these do not necessarily lead to blood cancer is attributed to a finely tuned control system.

Blood-forming stem cells rarely divide – it is the progenitor cells that produce most new blood cells. These progenitor cells have a short lifespan, which limits the chance of mutations being passed on. Mutations in stem cells, however, are potentially more dangerous. The offspring of a mutated stem cell carrying the same mutation are called clones. Many of these remain harmless, but malignant clones can lead to the development of blood cancer. “Stem cells are forced to divide more frequently with increasing age,” says Skoda. “And since life expectancy is always increasing, we can expect to see a sharp rise in the number of blood cancer cases.”

The StemSysMed team wants to gather quantitative data on factors influencing the occurrence of mutations as well as those determining the early stages of these clones in order to model them. To do this, the scientists are comparing blood samples from healthy individuals with those from patients with stem cell transplantations. Furthermore, using a systems biology approach, the scientists will examine how myeloproliferative neoplasm, where mutated blood cells multiply uncontrollably, develops in a mouse model as well as in primary cells of affected patients. Their questions include: Can the development of myeloproliferative neoplasm be explained solely by the occurrence of a crucial cancer-inducing mutation in a stem cell? Or do such mutations occur relatively frequently, but only lead to blood cancer under the influence of additional external factors? The scientists will employ mathematical models to test these hypotheses.

As with the other MRD Projects, interdisciplinarity plays a central role here. Researchers from five different institutes are working together on StemSysMed. “This is extraordinary and would not have been possible without SystemsX.ch,” emphasizes Skoda. “It enables mathematicians to address biological problems, and biologists to incorporate mathematics into their research. We also have extensive access to omics methods. Such a project would have otherwise been almost impossible to assemble and finance.”

StemSysMed at a glance

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StemSysMed
Systems Approach to Hematopoietic Stem Cell Diseases