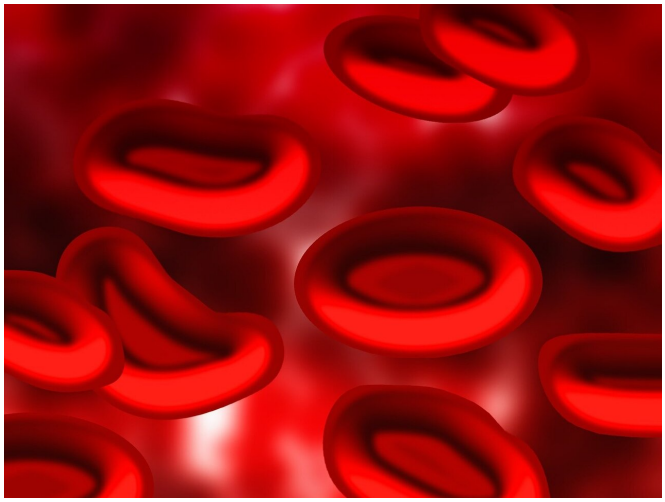
Mutation behind incurable disease mapped

12 April 2019



Credit: CC0 Public Domain

Researchers at Karolinska Institutet have mapped the genetic mutation behind the incurable disease systemic mastocytosis. The results give insights into the origin of the disease, and the researchers also discovered a protein with potential to improve disease diagnosis. The results are published in the journal *EBioMedicine*.

Systemic mastocytosis is an incurable disease characterised by accumulation of mast cells, a type of immune cell. Mild disease forms often cause severe allergy-like symptoms, whereas the advanced form, mast cell leukaemia, leads to complete organ failure and death. A common feature in most of the patients is a mutation in a gene called KIT.

Researchers at Karolinska Institutet and Uppsala University have now traced which cells in the body that harbor the KIT mutation.

Map of the mutation's propagation

Analysing more than 10,000 bone marrow cells allowed the researchers to generate a map of the mutation's propagation.

"The mutation could be traced all the way back to the blood stem cell in some patients," says Joakim Dahlin, researcher at Karolinska Institutet's Department of Medicine in Solna, and principal investigator of the study. "It was also obvious that the mutated mast cells outcompete the normal mast cells in the patients."

An incidental finding was also that mast cells in patients expressed extreme levels of a protein called CD45RA.

"There was a large difference in protein levels between patients and the control group," says Jennine Grootens, Ph.D. student at the same department and first author of the study. "We are now investigating if we can use this protein to diagnose systemic mastocytosis."

Insights into the origin of the disease

According to the researchers, the study provides deep insights into the origin of the disease. They also note that the presence of mutated blood stem cells could explain why the disease is difficult to cure.

More information: Jennine Grootens et al. Single-cell analysis reveals the KIT D816V mutation in haematopoietic stem and progenitor cells in systemic mastocytosis, *EBioMedicine* (2019). DOI: 10.1016/j.ebiom.2019.03.089

Provided by Karolinska Institutet