Two genes cooperate to trigger leukemia development

20 March 2018

An international group of researchers led by Prof. Jan Cools of the VIB-KU Leuven Center for Cancer Biology have made a breakthrough in understanding the development of acute lymphoblastic leukemia, an aggressive cancer of the blood. While scientists were already familiar with many cancer-causing genes and their separate functions, the VIB team has now illustrated how two of these cancer genes work together to trigger leukemia. Their insights are published in the scientific journal *Cancer Discovery*.

Acute lymphoblastic leukemia (ALL) is the most commonly occurring cancer in children, with 100 new cases reported in Belgium every year. Despite the efficacy of chemotherapy in treating this disease, its long and short-term side effects are considerable. The team of Prof. Jan Cools pursued this research project to learn more about how cancer genes interact with each other, with the goal of identifying alternative therapy options that don't cause severe side effects.

Characterized by specific mutations

ALL is caused by the accumulation of genetic changes (mutations) that alter the behavior of developing immune cells that transform them into aggressive leukemia cells. Recent studies have found that ALL cases are often characterized by mutations in a certain gene pathway, called JAK3/STAT5.

Prof. Jan Cools (VIB-KU Leuven): "JAK3/STAT5 mutations are important in ALL, since they stimulate the growth of the cells. However, leukemia patients have additional gene mutations, and we found that JAK3/STAT5 mutations, frequently occur together with HOXA9 mutations."

Connecting the genetic dots

In this study, Jan Cools and his team created a mouse model with cancer-associated JAK3/STAT5 and HOXA9 mutations to determine if they cooperate to drive the development of ALL. HOXA9 mutations have a well-established role in leukemia development.

Dr. Charles de Bock (VIB-KU Leuven): "We examined the cooperation between JAK3/STAT5 mutation and HOXA9. We observed that HOXA9 boosts the effects of other genes, leading to tumor development. As a result, when JAK3/STAT5 mutations and HOXA9 are both present, leukemia develops more rapidly and aggressively."

The team's identification of a direct cooperation between these two cancer genes paves the way for targeted treatments – not only in ALL, but also in other leukemias where JAK3/STAT5 could cooperate with HOXA9.

More information: Charles E. de Bock et al. HOXA9 cooperates with activated JAK/STAT signaling to drive leukemia development., *Cancer Discovery* (2018). DOI: 10.1158/2159-8290.CD-17-0583

Provided by VIB (the Flanders Institute for Biotechnology)