

CANCER SCIENCE INSTITUTE OF SINGAPORE

SEMINAR ANNOUNCEMENT

Jan Cools

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Oncogene Cooperation in Leukemia Development

Date: Monday, 26 August 2019
Time: 11.00am – 12.00pm
Venue: L1 Auditorium, Clinical Research Centre (MD11)
 10 Medical Drive, Singapore 117597
Host: Dr Takaomi Sanda

Abstract:

Leukemia is caused by the accumulation of multiple genomic lesions in hematopoietic precursor cells. However, how these events cooperate during oncogenic transformation remains poorly understood. We studied the cooperation between activated JAK3/STAT5 signaling and HOXA9 overexpression, two events identified as significantly co-occurring in T-cell acute lymphoblastic leukemia. Expression of mutant JAK3 and HOXA9 led to a rapid development of leukemia originating from multipotent or lymphoid-committed progenitors, with a significant decrease in disease latency compared with JAK3 or HOXA9 alone. Integrated RNA sequencing, chromatin immunoprecipitation sequencing, and Assay for Transposase-Accessible Chromatin using sequencing (ATAC-seq) revealed that STAT5 and HOXA9 have co-occupancy across the genome, resulting in enhanced STAT5 transcriptional activity and ectopic activation of FOS/JUN (AP1). Several STAT5 target genes, including the kinase PIM1, showed increased expression in JAK3/HOXA9 transformed cells. Similarly, we have found a similar cooperation between the oncogenic kinase NUP214-ABL1 and the transcription factor TLX1 in T-cell acute lymphoblastic leukemia. Our data suggest that oncogenic transcription factors such as HOXA9 or TLX1 provide a fertile ground for specific signaling pathways to thrive, explaining why JAK/STAT pathway mutations accumulate in HOXA9 or TLX1 expressing cells.

Biosketch:

Jan Cools completed a master in bio-engineering in 1997 at the University of Leuven (KU Leuven, Belgium). He obtained his PhD degree in 2001 from the same university with a study on chromosomal defects in leukemia. From 2001 to 2003 he continued his research on the genetic causes of leukemia in the laboratory of Dr Gary Gilliland at Harvard Medical School (Boston, USA). After return to Belgium, he was promoted to assistant professor in 2005 and to full professor in 2009 at KU Leuven. In 2008, Jan was also appointed as group leader of VIB, a life sciences institute in Flanders. The laboratory of Jan Cools studies the genetics of leukemia and the mechanisms by which oncogenic events cooperate during leukemia development. Jan has published over 120 articles, including articles in leading journals such as the New England Journal of Medicine, Cancer Cell, Nature Genetics, Molecular Cell, PNAS, Blood. He received numerous grants, including an ERC starting grant and ERC consolidator grant, as well as many awards. He was the editor-in-chief of Haematologica from 2012 to 2017 and is now editor-in-chief of a new hematology journal: HemaSphere (journal of the European Hematology Association).