Cancer Core Europe Lecture

Presented by the Education & Training Pillar

SPEAKERS

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Blood Genomics in Focus

Date: Friday September 26th – Time: 13:00 CEST / 12:00 BST

Join zoom meeting or visit **bit.ly/CCE-Cam25**

Talk 1: Genetic Reconstruction of Blood Cells in Ageing and Cancer (Nangalia)

Naturally occurring somatic mutations can be used to reconstruct the ancestral relationships between cells. Applying this to blood, we can retrace clonal relationships, population dynamics and somatic evolutionary patterns during healthy ageing as well as in blood cancers. Extending this approach, we can also reconstruct the epigenetic history of individual blood lineages, tracking changes in health and disease. We will discuss how differences in somatic mutation rates and tissue dynamics dramatically influence the normal architecture of blood in different species.

Talk 2: Deciphering the genomics of aggressive lymphoma (Hodson)

Diffuse large B cell lymphoma (DLBCL) is a clinically and genetically heterogeneous group of lymphomas that arise from the transformation of germinal centre (GC) B cells. Genomic profiling studies have catalogued nearly one thousand recurrent hotspot mutations in DLBCL. However, the functional relevance of most of these mutations remains unclear – a knowledge gap that limits the implementation of precision medicine. To address this challenge, we developed a co-culture system that mimics the GC microenvironment, enabling the *ex vivo* expansion and genetic manipulation of primary human GC B cells. We used this platform for high-throughput functional genomic screening to interrogate the oncogenic or tumour-suppressive potential of DLBCL-associated genes and mutations. This work provides a high-resolution understanding of the functional landscape of essentially every DLBCL hotspot mutation. By integrating genome-scale perturbation, base editing, and single-cell transcriptomics in a human GC B cell model, we uncover new mechanisms of lymphomagenesis and offer a framework to decipher the complex genetic heterogeneity of DLBCL.

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