CIBIO EXTERNAL seminar

9 NOVEMBER AT 1 P.M.
ROOM A 207 | POVO 1

INTERPLAY OF CODING AND NONCODING RNAS IN CANCER MECHANISMS

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The eukaryotic genome contains non-coding elements that contribute, both at RNA (lncRNAs, miRNAs) and DNA level (enhancers), to shaping the cell transcriptome in physiology and disease. A key scientific priority is to be able to understand the interplay of the coding and non-coding elements within cellular programs, providing the functional mechanisms of transcriptional and epigenetic plasticity. In cancer biology, plasticity is a key mechanism, fueling both cancer heterogeneity and evolution, which are at the basis of the most threatening aspects of tumor biology, such as the onset of tumor, the resistance to therapies and the occurrence of metastasis.

Here we present a thorough investigation of cancer heterogeneity and adaptive phenotypes, using as a model the triple-negative subtype of breast cancer (TNBC) and focusing on the transcriptional and epigenetic mechanisms at the basis of cancer plasticity.

Using single-cell multi-omics and lineage tracing, we investigated the predictive characteristics of cancer clones primed for in vivo tumour initiation and drug tolerance within the same cancer population. We identified the existence of multiple subpopulations, only minimally overlapping, that support the adaptive evolution of cancer through parallel trajectories.

We propose a technological framework that can be used to investigate the non-coding layer within such cancer complexity. Our approach combining high-resolution sequencing, including Nascent RNA sequencing and Third Generation Native RNA Sequencing by Nanopores, with functional analysis provided by CRISPR-interference (CRISPRi) tools, was used to isolate and validate lncRNAs, enhancers and miRNAs-based mechanisms involved in TNBC, revealing separate and mutual paths participating at cancer plasticity.

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