BIOTECHNOLOGY AND BIOSCIENCES SEMINARS

Dipartimento di Biotecnologie e Bioscienze – UNIMIB

Thursday, November 7, 2024, 4:30 p.m., U3-BIOS building, room U3-08

Cellular and molecular heterogeneity in human cancer

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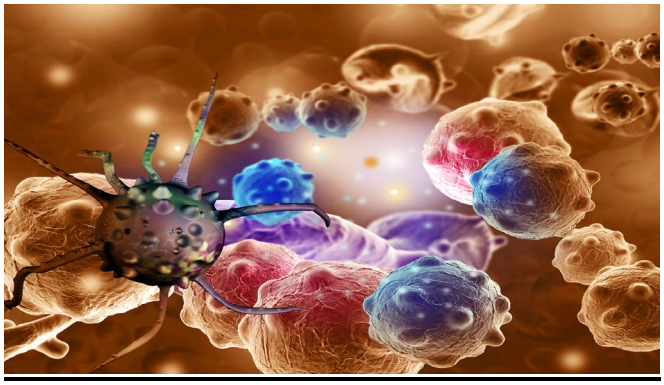

Abstract: Cancer is a highly heterogeneous disease, where phenotypically distinct subpopulations coexist and can be primed to different fates. Both genetic and epigenetic factors may drive cancer evolution, however little is known about whether and how such a process is pre-encoded in cancer clones. Using single-cell multi-omic lineage tracing and phenotypic assays, we investigate the predictive features of either tumour initiation or drug tolerance within the same cancer population. In Triple-Negative Breast Cancer models, we found that cancer evolution can be driven by a limited subset of clones within the parental population. Clones primed to tumour initiation in vivo display two distinct transcriptional states at baseline. Remarkably, these states share a distinctive DNA accessibility profile, highlighting an epigenetic basis for tumour initiation. The drug tolerant niche is also largely pre-encoded, but only partially overlaps the tumour-initiating one and evolves following two genetically and transcriptionally distinct trajectories. Our study highlights coexisting genetic, epigenetic and transcriptional determinants of cancer evolution, unravelling the molecular complexity of pre-encoded tumour phenotypes.

Host: **Mattia Pelizzola**

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