NICO Neuroscience Institute Cavalieri Ottolenghi

DBios

UNIVERSITÀ DI TORINO

SEMINAR CYCLE

of the PhD in Neuroscience of Turin

1st Appointment

Prof. Paolo Malatesta

University of Genoa and IRCCS Policlinico San Martino, Genoa.

"Tracing Clonal Evolution and Immune Evasion in Glioblastoma Progression"

30th January, 2025 h 2:00 PM

The lecture will last 1 hour and it will be followed by discussion

Host: Prof. Federico Luzzati

Seminar Room, NICO, Ospedale San Luigi Gonzaga, Regione gonzole 10, Orbassano (TO)

Link: unito.webex.com/meet/federico.luzzati

Organized by PhD in Neuroscience - Doctoral School of the University of Turin

ABSTRACT

Human Glioblastoma remains a significant challenge in oncology research, with its early progression remaining notably elusive. In a recent study, we traced the clonal dynamics of glioblastoma evolution by co-introducing PDGFB and genetic barcodes into mouse brains, observing a sustained loss of clones during the transition to a malignant state—an effect tied to shifts in c-Myc expression levels and their downstream targets.We then extended our investigation of glioblastoma evolution by transplanting multiclonal, early- stage glioma cells into multiple immunodeficient NOD-SCID mice. This approach allowed us to follow clonal behavior across serial transplants, revealing the acquisition of immune-evasive capabilities by early-stage glioma clones, which later proved able to initiate tertiary tumors in immunocompetent hosts. By combining barcode sequencing and single-cell RNA sequencing of early-stage gliomas with bulk RNA sequencing of secondary and tertiary tumors, we examined both the clonal and transcriptomic makeup of these lesions. Among the numerous clones present in the primary tumors, only a fraction persisted through subsequent passages. Moreover, the clonal configuration of secondary tumors originating from the same primary glioma demonstrated partial overlap, hinting at a degree of predetermination in the acquisition of immune-evasive features. Our intra- and inter-clonal transcriptomic analyses across different tumor stages illuminate how novel functional traits may arise in gliomas. Ongoing exploration of these data will reveal whether such traits stem from the expansion of clones already harboring them, or if they emerge through functional shifts within the clones themselves. Overall, our findings reinforce the significance of clonal competition, underscoring the central role of immune-system interactions in shaping these competitive dynamics.

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