



RESEARCH TOPIC MECM13
Dissection of neutrophils heterogeneity in glioblastoma
MECM standard

Research Area

Immunology

Laboratory name

Chemokine biology lab

Research Supervisor

Prof. Raffaella Bonecchi raffaella.bonecchi@hunimed.eu

Abstract

Diffuse gliomas are severe brain tumors accounting for 30% of central neural system malignancies. Glioblastoma multiforme (GBM) is one of the most severe form with a very poor prognosis. Its heterogeneity and immunosuppressive nature are the principal causes of failure of different therapeutic approaches, including immunotherapy. Neutrophils represent a relevant component of the tumor microenvironment. Their presence in tumor tissue and high neutrophilia has been associated with poor prognosis in different oncological contexts. However, neutrophils are not a homogeneous population, they are present in tumor patients in different maturation and activation states with both pro and anti-tumoral roles. Although most patients with glioma exhibit neutrophilia, the knowledge of the interplay of neutrophils and GBM is still limited. To address these knowledge gaps, the overall aim of this project is to elucidate the role and heterogeneity of neutrophils in glioblastoma. Understanding neutrophil heterogeneity and how to harness neutrophil antitumoral potential represent important therapeutic options to improve current cancer treatments and patient clinical outcomes. Further studies are needed to deeper elucidate the role of neutrophils in brain cancer biology to find new potential therapeutic approaches.

Main technical approaches

Genetically engineered mouse models, single cell RNA sequencing, flow cytometry, analysis of patient derived tumor explants, histology, standard immunology techniques and bioinformatics.

Scientific references

1. Albano F, Mollica Poeta V, Zotti L, Castagna A, Felicetta A, Mesaglio A, Zaghen E, Sironi M, Capucetti A, Di Donato R, Laffranchi M, Massara M, Carriero R, Condorelli G, Sozzani S, Mantovani A, Locati M, Bonecchi R. Selective expression and significance of ACKR2 in lung aerocytes. *J Immunother Cancer*. 2025 Jan 21;13(1):e009467.

2. Carezza C, Franzese S, Castagna A, Terzoli S, Simonelli M, Persico P, Bello L, Nibali MC, Pessina F, Kunderfranco P, Peano C, Balin S, Mikulak J, Calcaterra F, Bonecchi R, Savino B, Locati M, Della Bella S, Mavilio D. Perioperative corticosteroid treatment impairs tumor-infiltrating dendritic cells in patients with newly diagnosed adult-type diffuse gliomas. *Front Immunol.* 2023 Jan 10;13:1074762.
3. Simonelli M, Persico P, Capucetti A, Carezza C, Franzese S, Lorenzi E, Dipasquale A, Losurdo A, Giordano L, Pessina F, Navarra P, Politi LS, Mavilio D, Locati M, Della Bella S, Santoro A, Bonecchi R. Immunotherapeutic early-phase clinical trials and malignant gliomas: A single-center experience and comprehensive immunophenotyping of circulating leukocytes. *Neurooncol Adv.* 2021 Nov 13;3(1):vdab160.
4. Jaillon S, Ponzetta A, Di Mitri D, Santoni A, Bonecchi R, Mantovani A. Neutrophil diversity and plasticity in tumour progression and therapy. *Nat Rev Cancer.* 2020 Sep;20(9):485-503.
5. Massara M, Bonavita O, Savino B, Caronni N, Mollica Poeta V, Sironi M, Setten E, Recordati C, Crisafulli L, Ficara F, Mantovani A, Locati M, Bonecchi R. ACKR2 in hematopoietic precursors as a checkpoint of neutrophil release and anti-metastatic activity. *Nat Commun.* 2018 Feb 14;9(1):676.

Type of contract

PhD scholarship of € 21.000 gross per year awarded by Humanitas University. This sum is exempt from IRPEF income tax according to the provisions of art. 4 of Law no. 476 of 13th August 1984, and is subject to social security contributions according to the provisions of art. 2, section 26 and subsequent sections, of Law no. 335 of 8th August 1995 and subsequent modifications.

Borsa di dottorato pari a € 21.000 annui lordi erogata da Humanitas University. Importo non soggetto a tassazione IRPEF a norma dell'art. 4 della L. 13 agosto 1984 n. 476 e soggetto, in materia previdenziale, alle norme di cui all'art. 2, commi 26 e segg., della L. 8 agosto 1995, n. 335 e successive modificazioni.