# The IL-1 Decoy Receptor IL1R2 Is a Systemic-to-Tumor Biomarker of Glioblastoma Immunosuppression


## Claudia Cerella

Claudia Cerella (1,2), Andrea Scafidi (1,3), Tony Kaoma (4), Bakhtiyor Nosirov (2,5), Frank Hertel (6), Guy Berchem (6), Simone P. Niclou (3,5), Antonio Cosma (7), Petr V. Nazarov (2,4), Anna Golebiewska (5), Aurélie Poli (1), Alessandro Michelucci (1)

1) Neuro-Immunology Group (NIG), Department of Cancer Research (DoCR), Luxembourg Institute of Health (LIH), Luxembourg; 2) Multiomics Data Science Group, Department of Cancer Research, LIH, Strassen, Luxembourg; 3) Faculty of Science, Technology and Medicine, University of Luxembourg, Esch-sur-Alzette, Luxembourg; 4) Bioinformatics and AI, Department of Medical Informatics, LIH, Strassen, Luxembourg; 5) NORLUX Neuro-Oncology Laboratory, Department of Cancer Research, LIH, Luxembourg; 6) Centre Hospitalier de Luxembourg, Luxembourg; 7) National Cytometry Platform, Translational Medicine Operation Hub, LIH, Esch-sur-Alzette, Luxembourg



Glioblastoma (GBM) is characterized by profound systemic and local immunosuppression, driven by myeloid accumulation and lymphoid depletion. Despite these dysfunctions being well-established, mechanisms linking peripheral monocyte dysfunction to the tumor immune microenvironment remain incompletely defined, and no approach currently exists to monitor or target them.

Using single-cell cytometry and transcriptomics, we delineated peripheral monocyte trajectories in GBM patients and identified a coordinated IL1R2high/IL1Blow phenotype in circulating monocytes relative to healthy donors, accompanied by loss of HLA class II antigen-presentation programs (1). Integration of public transcriptomic resources spanning blood and tumor tissue validated and extended these findings across IL-1 pathway genes (IL1R1, IL1R2, IL1RAP, IL1RN, IL1A, IL1B, ADAM17). Transcriptomics analysis of matched circulating and tumor-infiltrating monocytes confirmed differential expression of IL-1 pathway genes between compartments and different immune cell subsets, confirming peripheral IL1R2high as GBM-specific.

In tumor tissue, IL1R2 gene correlated with signature scores for monocyte-derived macrophages, myeloid-derived suppressor cells, and neutrophils, while IL1R1, that antagonizes IL-1R2, prominently correlated with CD4+/CD8+ T cells, revealing an IL1R2 myeloid-restricted axis and a broader IL1R1-associated axis tracking lymphoid infiltration. Spatial mapping across laser-dissected anatomical regions localized these programs to distinct histological niches, with the perinecrotic zone emerging as a site where myeloid IL1R2 dominance and IL1R1-linked immune infiltration were most tightly coupled at the sample level.

These findings position IL1R2-mediated decoy as a candidate node linking systemic monocyte reprogramming to local immunosuppressive remodeling in GBM, with potential relevance as a biomarker or therapeutic target to restore IL-1-driven antitumor immunity.


### References


1. Scafidi A*, Kaoma T*, Cerella C*, et al. Circulating immune profiling reveals impaired monocyte states and trajectories driving immunosuppression in glioblastoma. J. Neuroinflammation. 2026 (in press). https://doi.org/10.1186/s12974-026-03964-3. *equal contribution

# Biosketch


## Claudia CERELLA, PhD, ADR

Senior Scientist
ORCID ID: 0000-0001-9308-8176


### CURRENT AND PAST POSITIONS

02/2025-present: Senior Scientist, Neuro-Immunology Group (NIG); MultiOmics Data Sciences (MODAS) Group, Department of Cancer Research (DoCR), Luxembourg Institute of Health (LIH), Luxembourg.

01/2012-01/2025: Research Scientist and Cell Death Team Leader, Laboratoire de Biologie Moléculaire et Cellulaire du Cancer (LBMCC), Fondation Recherche sur le Cancer et les Maladies du Sang, Luxembourg.

09/2016-02/2017: Researcher, Laboratory of Molecular Oncology, College of Pharmacy, Seoul National University, Seoul (KR).

02/2016-03/2016: Mobility Research, Laboratory of Drug Resistance & Oncometabolism in Acute Leukemia, CRCT, Oncopole, Toulouse (FR).

01/2007-12/2011: Post-doctoral fellow, LBMCC, Fondation Recherche sur le Cancer et les Maladies du Sang, Hôpital Kirchberg, Luxembourg.

12/2004-10/2006: Research Fellow, Department of Occupational Medicine, Tor Vergata Policlinic (PTV), Rome (IT).

### EDUCATION

2005: Ph.D. in Cellular and Molecular Biology, Department of Biological Sciences, University of Rome Tor Vergata, Rome (IT).

11/2000: Master of Science (Laurea) with honors in Biological Sciences, Department of Biological Sciences, University of Rome Tor Vergata, Rome (IT).

### AWARDS AND HONORS

2016: Outstanding Paper Award, College of Pharmacy, Seoul National University (SNU), South Korea.

2026: ADR, Doctoral Programme in Systems and Molecular Biomedicine, Doctoral School in Science and Engineering (DSSE), University of Luxembourg.

2017: Italian National Scientific Habilitation as Full Professor in Applied Biology, Italian Ministry of Education, University and Research.

### OTHER RELEVANT PROFESSIONAL ACTIVITIES AND ACCOMPLISHMENTS

Author of 101 peer-reviewed articles (99 indexed in PubMed). 14 national or international research grants awarded. Scientific board member of international journals and grant-funding schemes. Councilor for the International Society of Precision Health (ISPH), 2025-2028. Director/co-director/supervisor of 50 laboratory members at different career stages.