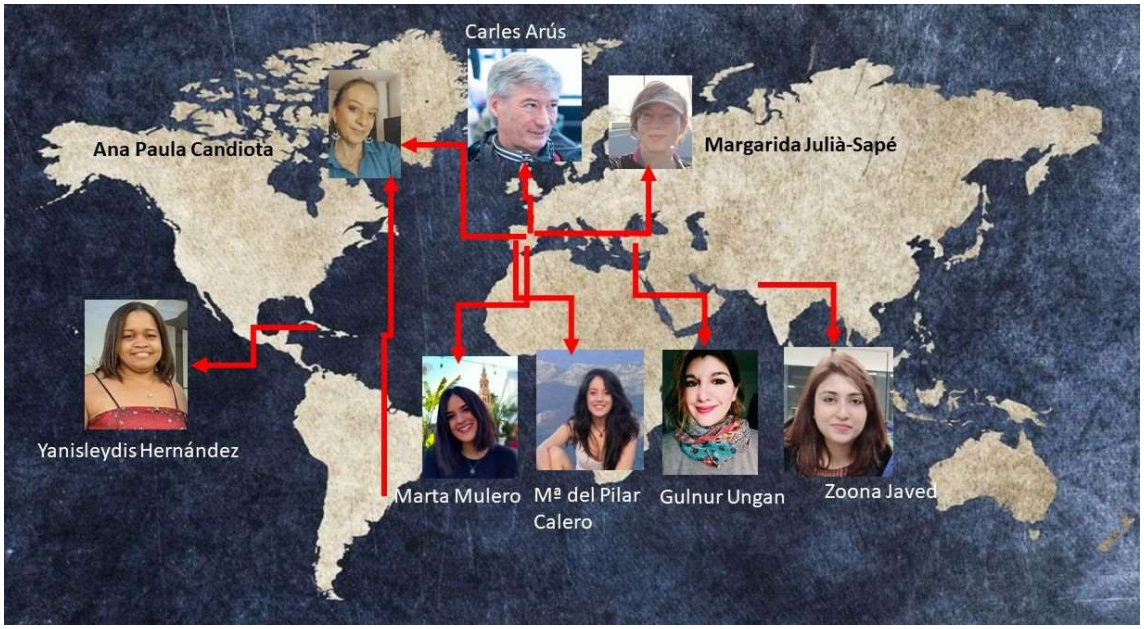
# GRUP D'APLICACIONS BIOMÈDIQUES DE LA RMN (GABRMN)

## CARLES ARÚS CARALTO




## PROFILE

Carles Arús b 1954, BSc in Biology 1976, PhD in Chemistry 1981 (Barcelona, ES). Postdoctoral in muscle NMR with Michael Bárány and John L. Markley (1982-1985, USA). Since 1985 at the Department of Biochemistry and Molecular Biology of UAB and leading GABRMN since then. About 153 publications, "h" number of 36. (http://www.researcherid.com/rid/C-2361-2009). Since 2006 director of Research group CB06-01-0010, Centro de Investigación Biomédica en Red en Bioingeniería, Nanomateriales y Nanomedicina. Director of Unit 25, NMR: Biomedical Applications I, of the Singular Scientific Technological Infrastructures (ICTS) NANBIOSIS. Present interests in the field of MR-based molecular imaging of brain tumours, for diagnosis, prognosis and therapy planning.

## RESEARCH

### RESEARCH INTERESTS

Our major research interest is the improvement of the diagnosis, treatment and therapy response follow-up of abnormal brain masses, using noninvasive monitoring tools based in Nuclear Magnetic Resonance.

The large track of GABRMN in MR-based metabolomic studies, either in vivo, ex vivo or in vitro, is supported by solid results from group and its collaborators (see chosen publications from previous 5 years at the end of this text).

Unravelling the potential of the metabolomics studies was always one of the main objectives of GABRMN. From the in vitro point of view, the group has worked with murine and human glioblastoma biopsies or cell lines, exploring high resolution approaches either through metabolite sample extraction or ex vivo analyses such as HRMAS (high resolution magic angle spinning) NMR.

The preclinical in vivo MRI/MRS/MRSI was possible from 2006-2007 onwards due to the arrival of the 7T preclinical horizontal scanner (Bruker Biospec 70/30). Preclinical models were used for the study of the diagnostic and therapeutic efficacy in vivo, both spontaneous transgenic models and ortothopic models generated through stereotactic injection.

Our group is part of the CIBER-BBN consortium since its foundation in 2006, which fostered collaborations within the CIBER collaborative network for the investigation of novel contrast agents and therapeutic compounds targeting glioblastoma. The GABRMN-UAB is the core of the CB06/01/0010 CIBER-BBN group, which also incorporates other members of the UAB community, clinical centers such as Hospital Universitari de Bellvitge, Universitat Politècnica de Catalunya and also a close relationship with members of the NMR Facility at UAB (SeRMN). The GABRMN is also in charge of the direction and scientific coordination (respectively C. Arús and AP Candiota) of the Unit 25 of NANBIOSIS ICTS, devoted to NMR Biomedical Applications.

This close collaborative work allowed the development of MRSI-based noninvasive surrogate biomarkers of response to therapy in preclinical glioblastoma (GL261), one of the main interests of our group, related to its application to other preclinical models and translation to clinical settings. The application of such biomarker to other therapeutic strategies, as well as its validation through cellular and molecular approaches is one of the main research lines of our group, reflected in the publication list at the end of this section.

Moreover, the use of metabolomics information in order to develop and refine radiomics approaches based in MRI is an important goal in the landscape of our research, which may allow to increase the translational potential of our studies

**STRATEGIC OBJECTIVES**

Our strategic objectives are mainly related to refine the translational potential of our research, with special emphasis in the improvement of treatment outcome in preclinical and clinical glioblastoma.

- Diversification of preclinical models under study, going from syngeneic glioma models described to be less responsive to treatment, and also humanized patient-derived xenografts
- Diversification of therapeutic strategies to be studied, including preclinical radiotherapy
- Inclusion of new therapeutic agents and/or administration routes
- Analysis of novel contrast agent strategies
- Translation of preclinical therapeutic schedules to clinical settings
- MR-based metabolomics characterizing response to therapy: response phenotyping, metabolic reprogramming

To achieve such strategic objectives, the GABRMN holds strong collaborations with other research groups with complementary interests, as follows:

* MIDALab (M. Julià-Sapé, UAB) – MR signal processing/postprocessing and machine learning strategies, with special emphasis on clinical data (joint paper)

* Protein Engineering and Nanomedicine (J. Lorenzo, UAB) – Development and characterization of functional nanocarriers and bioinspired nanomaterials for applications in both nanomedicine and nanotechnology (joint paper)

* BIT-UPM (A. Santos, UPM) – Biomedical signal processing, development of dedicated graphical user interfaces (joint paper)

* NANOSFUN (D. Ruiz-Molina, ICN2) - Coordination polymers for therapy and clinical imaging. (joint paper)

* NANOMOL-BIO (J.Vidal, Vega Lloveras, ICMAB-CSIC) - synthesis, characterization and development of molecular and polymeric (nano)materials for biomedical applications. (joint paper)

* Oxidoreductases in Cellular Defense and Signaling. Search of inhibitors for therapeutic purposes (J. Farrés, UAB) - Research in enzymes acting on the metabolism of signaling molecules (retinoids and prostaglandins) and associated with cancer and diabetes. Joint paper in progress. (SEBBM 2021 joint communication, page 46)

* Cell Death, Sencescence and Survival (V. Yuste, UAB) – analyses of immunogenic signals and death mechanisms in murine glioma cell lines (joint paper)

* Neuroimmunity lab (C. Barcia, UAB) – investigation of the immune landscape of murine glioblastoma under therapy using immunofluorescence. (EMIM 2020 joint communication, n.194)

* Department/Neurosurgery lab (Jörg-Walter Bartsch, Philipps-Universität Marburg, Germany) – characterization of clinical and preclinical glioblastoma tumour microenvironment during response to therapy. (SEBBM 2021 joint communication, page 24)

* Oncohematologic Diseases (M. Virtudes Céspedes, Institut de Recerca Hospital de la Santa Creu i Sant Pau). Management of preclinical solid tumour models and evaluation of novel therapeutic agents.

* Hospital São João and Instituto Português de Oncologia (R. Simões, i3S - Instituto de Investigação e Inovação em Saúde da Universidade do Porto). 3T studies (MRI, MRS, MRSI) of different preclinical models. (new scanner configuration, starting collaborative work next shortly)

* Radiotherapy/Medical Oncology (J. Balart & O. Gallego, Hospital de la Santa Creu i Sant Pau) – starting application of joint ethical protocol for preclinical glioblastoma RT

* Drug Delivery & Targeting (DDT) research group (I. Abasolo, Vall d'Hebron Institut de Recerca)- application of joint ethical protocol for MR studies of different preclinical cancer models (e.g. prostate)

* QuBiotech (SME, D. Fernández) – development and commercialization of software for advanced processing and quantification of medical images. Joint application to research projects such as ATTRACT phase II.

**MAIN RESEARCH LINES**

- Treatment with conventional or novel therapeutic agents and response follow-up of preclinical brain tumour models, using magnetic resonance imaging and spectroscopy.
- Search for molecular MR-based surrogate biomarkers of in vivo tumor therapy response, through in vitro, ex vivo and in vivo studies of cell lines, animal models and their biopsies. Correlation with molecular and cellular parameters (histopathology, genomics). Potential translation to clinical practice.
- In vivo molecular phenotyping of brain tumor progression and therapy response.
- Characterization of novel contrast agents with potential in brain tumour studies
- Molecular characterization of different murine glioma cell lines (e.g. immunogenic potential)-

Magnetic resonance imaging and spectroscopic characterization of novel glioblastoma murine models

## LAB FEATURED PUBLICATIONS:

Selected publications from previous 5 years:


1: Candiota AP, Arús C. Establishing Imaging Biomarkers of Host Immune System Efficacy during Glioblastoma Therapy Response: Challenges, Obstacles and Future Perspectives. Metabolites. 2022 Mar 14;12(3):243. doi: 10.3390/metabo12030243.

2: Mao X, Wu S, Calero-Pérez P, Candiota AP, Alfonso P, Bruna J, Yuste VJ, Lorenzo J, Novio F, Ruiz-Molina D. Synthesis and Validation of a Bioinspired Catechol-Functionalized Pt(IV) Prodrug for Preclinical Intranasal Glioblastoma Treatment. Cancers (Basel). 2022 Jan 14;14(2):410. doi: 10.3390/cancers14020410.

3: Zhang S, Lloveras V, Lope-Piedrafita S, Calero-Pérez P, Wu S, Candiota AP, Vidal-Gancedo J. Metal-Free Radical Dendrimers as MRI Contrast Agents for Glioblastoma Diagnosis: ex vivo and in vivo Approaches. Biomacromolecules. 2022 Jul 11;23(7):2767-2777. doi: 10.1021/acs.biomac.2c00088.

4: Calero-Pérez P, Wu S, Arús C, Candiota AP. Immune System-Related Changes in Preclinical GL261 Glioblastoma under TMZ Treatment: Explaining MRSI-Based Nosological Imaging Findings with RT-PCR Analyses. Cancers (Basel). 2021 May 28;13(11):2663. doi: 10.3390/cancers13112663.

5: Villamañan L, Martínez-Escardó L, Arús C, Yuste VJ, Candiota AP. Successful Partnerships: Exploring the Potential of Immunogenic Signals Triggered by TMZ, CX-4945, and Combined Treatment in GL261 Glioblastoma Cells. Int J Mol Sci. 2021 Mar 26;22(7):3453. doi: 10.3390/ijms22073453.

6: Wu S, Calero-Pérez P, Arús C, Candiota AP. Anti-PD-1 Immunotherapy in Preclinical GL261 Glioblastoma: Influence of Therapeutic Parameters and Non-Invasive Response Biomarker Assessment with MRSI-Based Approaches. Int J Mol Sci. 2020 Nov 20;21(22):8775. doi: 10.3390/ijms21228775.

7: Núñez LM, Romero E, Julià-Sapé M, Ledesma-Carbayo MJ, Santos A, Arús C, Candiota AP, Vellido A. Unraveling response to temozolomide in preclinical GL261 glioblastoma with MRI/MRSI using radiomics and signal source extraction. Sci Rep. 2020 Nov 12;10(1):19699. doi: 10.1038/s41598-020-76686-y.

8: Wu S, Calero-Pérez P, Villamañan L, Arias-Ramos N, Pumarola M, Ortega-Martorell S, Julià-Sapé M, Arús C, Candiota AP. Anti-tumour immune response in GL261 glioblastoma generated by Temozolomide Immune-Enhancing Metronomic Schedule monitored with MRSI-based nosological images. NMR Biomed. 2020 Apr;33(4):e4229. doi: 10.1002/nbm.4229.

9: Julià-Sapé M, Candiota AP, Arús C. Cancer metabolism in a snapshot: MRS(I). NMR Biomed. 2019 Oct;32(10):e4054. doi: 10.1002/nbm.4054

10: Suárez-García S, Arias-Ramos N, Frias C, Candiota AP, Arús C, Lorenzo J, Ruiz-Molina D, Novio F. Dual T1/ T2 Nanoscale Coordination Polymers as Novel Contrast Agents for MRI: A Preclinical Study for Brain Tumor. CS Appl Mater Interfaces. 2018 Nov 14;10(45):38819-38832. doi: 10.1021/acsami.8b15594.

11: Arias-Ramos N, Ferrer-Font L, Lope-Piedrafita S, Mocioiu V, Julià-Sapé M, Pumarola M, Arús C, Candiota AP. Metabolomics of Therapy Response in Preclinical Glioblastoma: A Multi-Slice MRSI-Based Volumetric Analysis for Noninvasive Assessment of Temozolomide Treatment. Metabolites. 2017 May 18;7(2):20. doi: 10.3390/metabo7020020.

12: Ferrer-Font L, Arias-Ramos N, Lope-Piedrafita S, Julià-Sapé M, Pumarola M, Arús C, Candiota AP. Metronomic treatment in immunocompetent preclinical GL261 glioblastoma: effects of cyclophosphamide and temozolomide. NMR Biomed. 2017 Sep;30(9). doi: 10.1002/nbm.3748.

13: Ferrer-Font L, Villamañan L, Arias-Ramos N, Vilardell J, Plana M, Ruzzene M, Pinna LA, Itarte E, Arús C, Candiota AP. Targeting Protein Kinase CK2: Evaluating CX-4945 Potential for GL261 Glioblastoma Therapy in Immunocompetent Mice. Pharmaceuticals (Basel). 2017 Feb 12;10(1):24. doi: 10.3390/ph10010024.