

Section A. PERSONAL DATA

Name and Surname	Marta Alonso Roldan
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A.1. Current professional situation

Institution	Clínica Universitaria de Navarra/CIMA Universidad de Navarra		
Dpt. / Centre	Pediatria / Instituto de Investigación Sanitaria de NavarraPediatria		
Professional category	Investigador Principal/Codirector Program Solid Tumors	Start date	2014
Keywords	Oncolytic virus, Pediatric Brain Tumors, Advanced Therapies		

A.2. Academic education (Degrees, institutions, dates)

Bachelor/Master/PhD	University	Year
Programa Oficial de Doctorado en Ciencias de la Salud	Universidad Pública de Navarra	2001
Licenciado en biología	Universidad de Navarra	1997
Certificado de aptitud pedagógica (CAP)	Universidad de Navarra	1996

A.3. General quality indicators of scientific production

To summarize my career, I will highlight that I have published more than 70 articles in leading magazines and that our work has been presented in national and international conferences. My work has an H factor of 43, with nearly 7.000 citations in total (Google Scholar). My contribution to the field of brain tumor research was recognized with prestigious fellowships from the American Brain Tumor Association and the Alex Lemonade Stand Foundation. In 2010, I began my career as an independent investigator thanks to a "Ramón y Cajal" and a "Marie Curie IRG grant". I have supervised more than 15 PhD students and fellows. Under my mentorship, some of the trainees have achieved relevant positions for example, Dr. Aldave is in charge of the tumor section of the Neurosurgery Dpt. at Texas Children's.

My lab now focused in developing new biological therapies for pediatric brain tumors. Since I started my independent career, I have been able to obtain extramural funding from international (such as the dept. of Defense of USA or an ERC-Consolidator grant), national (I have been funded non-stop by Institute Carlos III) and regional organizations. In 2013, I received the "Loreal- Unesco for Women in Science Award" that recognize young scientists with promising careers. In 2019, I received the "Rural Woman" and "Cadena SER_Navarra_Ciencia" awards. During this time, I have also been able to publish as last authors in prestigious journals such as Cancer Cell, N England J of Med, Lancet Oncol, JCI, Nat Commun, Clin Cancer Res, NeuroOncology and others. Moreover, our collaborative spirit has also led to numerous publications with other great scientists. I routinely serve as a reviewer for grants (ANEP, Horizon 2020, Italian Ministry of Health...etc.) and papers (JCI, Clin Cancer Res, etc). Of Clinical significance, our research led to several clinical trials in our institution implementing oncolytic viruses for pediatric and adult brain tumors. These trials are showing that the viruses are safe and efficacious for a group of patients; this is highly relevant and denotes the translation of our research. We have several patents and licenses regarding oncolytic viruses.

Section B. SUMMARY OF THE CURRICULUM

Section C. MOST RELEVANT MERITS (ordered by typology)

C.1. Publications (selected)

Scientific paper. TIM-3 blockade in diffuse intrinsic pontine glioma models promotes tumor regression and antitumor immune memory. Ausejo-Mauleon I, Labiano S, De lanava D, Laspeida V, Zalacain M, Marrodan L, Garcia-Moure M, Gonzalez-Huarriz M, Hervas-Corpion I, Dhanhapani L, Vicent S, Collante M, Peñuelas I, Becher OJ, Filbil MG, Jiang L, Labelle J, de Biagi-Juior CAO, Nazarian J, Laternser S, Phoenix NT, van der Lugt J, Kranendonk M, Hoodendijk R, Mueller S, De Andrea C, Carrizosa Anderson A, Gुरुceaga E, Koschmann C, Yadak VN, Gallego Pered-Larraya J, Patiño-García A, Pastor F and Alonso MM. **Cancer Cell** 2023 doi: 10.1016/j.ccell.2023.09.001. Online ahead of print

Scientific paper. Oncolytic DNX-2401 Virus for Pediatric Diffuse Intrinsic Pontine Glioma. Gállego Pérez-Larraya J, Garcia-Moure M, Labiano S, Patiño-García A, Dobbs J, Gonzalez-Huarriz M, Zalacain M, Marrodan L, Martinez-Velez N, [...] Jones C, Dharmadhikari G, Ruiz-Moreno C, Stunnenberg H, Hulleman E, van der Lugt J, Idoate MÁ, Diez-Valle R, Esparragosa

Vázquez I, Villalba M, de Andrea C, Núñez-Córdoba JM, Ewald B, Robbins J, Fueyo J, Gomez-Manzano C, Lang FF, Tejada S and **Alonso MM**. *N Engl J Med*. 2022 386(26):2471-2481. doi: 10.1056/NEJMoa2202028.

Editorial: Virotherapy for Brain Tumors - Defining the Path to Success. Galanis E. *N Engl J Med*. 2022 Jun 30;386(26):2520-2522. doi: 10.1056/NEJMe2205032.

Scientific paper. Exploiting 4-1BB immunecheckpoint to enhance the efficacy of oncolytic virotherapy for diffuse intrinsic pontine gliomas. Laspidea V, Puigdelloses M, Labiano S, Marrodan L, Garcia-Moure M, Zalacain M, Gonzalez-Huarriz M, Martinez-Vélez N, Ausejo-Mauleon I, de la Nava D, Herrado-Cañete G, Marco-Sanz J, Guruceaga E, de Andrea CE, Villalba M, Becher O, Squatrito M, Matía V, Gallego Perez-Larraya J, Patiño-García A, Gupta S, Patiño-García A, Gomez-Manzano C, Fueyo J, Gallego Pérez-Larraya J and Alonso MM. *J Clin Invest* 2022 7(7):e154812. doi: 10.1172/jci.insight.15481

Scientific paper. Local treatment of a pediatric osteosarcoma model with a 4-1BBL armed oncolytic adenovirus results in an antitumor effect and leads to immune memory. Martínez-Vélez N, Laspidea V, Zalacain M, Labiano S, Garcia-Moure M, Puigdelloses M, Marrodan L, Gonzalez-Huarriz M, Herrador G, de la Nava D, Ausejo-Mauleon I, Fueyo J, Gomez-Manzano C, Patiño-García A, Alonso MM. *Mol Cancer Ther*. 2021; 21(3):471-480. doi: 10.1158/1535-7163.MCT-21-0565. **Highlighted in the issue.**

Scientific paper. Puigdelloses M, Garcia-Moure M, Labiano S, Laspidea V, Gonzalez-Huarriz M, Zalacain M, Marrodan L, Martinez-Vélez N, de la Nava D, Ausejo-Mauleon I, Hervás-Stubbs S, Herrador G, Chen Z, Hambardzumyan D, Patiño-García A, Jiang H, Gomez-Manzano C, Fueyo J, Gallego Pérez-Larraya J and Alonso MM. *J Immunother Cancer*. 2021;9(7):e002644. doi: 10.1136/jitc-2021-002644. Jul;9(7):e002644

Scientific paper. García-Moure M, Gonzalez-Huarriz M, Labiano S, Guruceaga E, Bandres E, Zalacain M, Marrodan L, de Andrea C, Villalba M, Maritnez-Velez N, Laspidea V, Puigdelloses M, Gallego Perez-Larraya J, Iñigo-Marco I, Stripecke R, Chan JA, Raabe EH, Kool M, Gomze-Manzano C, Fueyo J, Patiño-García A and Alonso MM (22/22) (AC)Delta-24-RGD increases survival and promotes proinflammatory immune landscape remodeling in AT/RT and CNS-PNET models. *Clin Can Res* 2021 27:1807-18209. doi: 10.1158/1078-0432.CCR-20-3313

Scientific paper. Local administration of interleukin-12 with a high-capacity vector results in local and metastatic tumor control in pediatric osteosarcoma. Zalacain M, Bunuales M, Marrodan L, Gonzalez-Huarriz M, Martinez-Velez, Laspidea V, Puigdelloses M, Garcia-Moure M, Gonzalez-Aparicio, Hernandez-Alcoceba R, Patiño-García A, Alonso MM. *Mol Ther-Oncolytics* 2020 20:23-33. doi: 10.1016/j.omto.2020.11.00

Scientific paper. Puigdelloses M, Gonzalez-Huarriz, Garcia-Moure, Martinez-Velez N, Esparragosa Vazquez I, Bruna J, Zandio B, Agirre, Marigil M, Petirena G, Nunez-Cordoba J, Tejada-Solis S, Díez-Valle R Gallego-Culleré J, Martinez-Vila E, Patiño-García A, Alonso MM* and Gallego Perez-Larraya J* (18/19) (AC) RNU6-1 in circulating exosomes differentiates GBM from non-neoplastic brain lesions and PCNSL but not from brain metastases. *Neuro-Oncology Advances*, 2020; 2(1):vdz010.

Scientific paper. Martinez-Velez N, García-Moure M, Marigil M, Gonzalez-Huarriz M, Puigdelloses M, Gallego-Larraya J, Zalacain M, Marrodan L, Varela-Guruceaga M, Laspidea V, Aristu JJ, Ramos L, Tejada-Solis S, Díez-Valle R, Jones C, MacKay A, Climent JA, García Barchino MJ, Raabe E, Monje M, Becher OJ, Junier MP, Chneiweis H, Aldave G, Jiang H, Gomez-Manzano C, Fueyo J, Patiño-García A and Alonso MM. (29/29) (AC)Oncolytic virus Delta-24-RGD elicits a potent antitumor effect in pediatric high-grade glioma and diffuse intrinsic pontine glioma models. *Nat Commun* (2019) *Nat Commun*. 2019 10(1):2235. doi: 10.1186/s40478-019-0714-6. This paper was highlighted in the issue.

Scientific paper. Martinez-Velez N, García-Moure M, Marigil M, Gonzalez-Huarriz M, Aristu JJ, Ramos L, Tejada-Solis S, Díez-Valle R, Patiño-García A, Gomez-Manzano C, Fueyo J, and Alonso MM. (12/12) (AC) Delta-24-RGD combined with radiotherapy exerts a potent antitumor effect in diffuse intrinsic pontine glioma and pediatric high grade glioma models. *Acta Neuropathol Commun*. (2019); 7(1):64 doi: 10.1186/s40478-019-0714-6.

Scientific paper. Tejada S, Díez-Valle R, Patiño-García A, González-Huarriz M, Fueyo J, Gomez-Manzano C, Idoate MA, Peterkin J, Alonso MM. (9/9) (AC) *Front Oncol*. 2018 Mar 12;8:61. Doi 10.3389/fonc.2018.00061. eCollection 2018.DNX-2401, an oncolytic virus, for the treatment of newly diagnosed diffuse intrinsic pontine gliomas: a case report.

Scientific paper. García-Moure M, Martínez-Vélez N, Gonzalez-Huarriz M, Cascallo M, Alemany R, Patiño-García A and Alonso MM. (7/7) (AC). The oncolytic adenovirus VCN-01 promotes anti-tumor effect in primitive neuroectodermal tumor models. *Scientific Reports*, 2019 9(1):14368. doi:

10.1038/s41598-019-51014-1

Scientific paper. Aldave G, Gonzalez-Huarriz, M, Rubio A, Romero JP, Ravi D, Miñana B, Cuadrado-Tejedor M, García-Osta A, Verhaak R, Xipell E, Martínez-Vélez N, Acanda de la Rocha A, Puigdelloses M, García-Moure M, Marigil M, Gállego Pérez-Larraya J, Marín-Bejar O, Huarte M, Carro MS, Ferrarese R, Belda-Iniesta C, Ayuso A, Prat-Acín R, Pastor F, Díez-Valle R, Tejada-Solis S and Alonso MM. (29/29) (AC) The aberrant splicing of BAF45d links splicing regulation and transcription in glioblastoma. *NeuroOncol* 2018 20(7):930-941 doi: 10.1093/neuonc/now007.

Scientific paper. Xipell E, Aragón T, Martínez-Vélez N, Vera B, Idoate MA, Martínez-Irujo JJ, García-Garzón A, Gonzalez-Huarriz M, Acanda AM, Jones C, Lang FF, Fueyo J, mez-Manzano C and Alonso MM. (14/14) (AC) ER-stress inducing drugs sensitize glioma cells to temozolomide through downregulation of MGMT, MPG and Rad51. *NeuroOncology* 2016 18(8):1109-19. doi: 10.1093/neuonc/now022.

Scientific paper. Martínez-Vélez N, Xipell E, Vera B, de la Rocha A, Zalacain M, Marrodán L, Gonzalez-Huarriz M, Toledo G, Cascallo M, Alemany R, Patiño A, Alonso MM. (2/12) (AC). *Clin Cancer Res* 2015 Nov 24. pii: clincanres.1899.2015.

Scientific paper. Manterola L, Guruceaga E, Gállego Pérez-Larraya J, Gonzalez-Huarriz M, Jauregui P, Segura V, Sampron N, Barrena C, Ruiz I, Tejada S, Díez-Valle R, Agirre A, Ayuso A, Rodríguez J, Gonzalez A, Matheu A, Tuñón T, Zazpe I, Xipell E, Lopez de Munain A, García-Foncillas J, Paris S, Delattre JY, Alonso MM. (23/23) (AC). A snRNA signature found in microvesicles of GBM patient serum serves as a diagnostic marker. *Neuro Oncol.* 2014 16:520-7. *Highlighted in Nature Reviews Neurology (2014) doi:10.1038/nrneuro.2014.21.*

Scientific paper. Marigil M, Martínez-Vélez N, Domínguez PD, Idoate MA, Xipell E, Patiño-García A, Gonzalez-Huarriz M, García-Moure M, Junier MP, Chneiweiss H, El-Habr E, Díez-Valle R, Tejada-Solis S, Alonso MM. (14/14) (AC) Development of a DIPG orthotopic model in mice using an implantable guide-screw system. *PLoS One* 2017 Jan 20;12(1):e0170501. doi: 10.1371/journal.pone.0170501

Scientific paper. Vera B, Martínez-Vélez N, Xipell E, de la Rocha A, Patiño A, Castresana JS, Gonzalez-Huarriz M, Cascallo M, Alemany R, Alonso MM (10/10) (AC) Characterization of the antiglioma effect of the oncolytic adenovirus VCN-01. *V. Plos One* 2016 11(1):e0147211.

Scientific paper. Martínez-Vélez N, Xipell E, Vera B, de la Rocha A, Zalacain M, Marrodán L, Gonzalez-Huarriz M, Toledo G, Cascallo M, Alemany R, Patiño A, Alonso MM. (12/12) (AC). The oncolytic adenovirus VCN-01 as therapeutic approach against pediatric osteosarcoma. *M Clin Cancer Res* 2015 Nov 24. pii: clincanres.1899.2015.

Scientific paper. Lang FF, Conrad C, Gomez-Manzano C, Yung WKA, Sawaya RE, Weinberg JS, Prabhu SS, Rao G, Fuller GN, Aldape KD, Gumin J, Vence L, Wistuba I, Rodríguez-Canales J, Villalobos PA, Dirven C, Tejada S, Díez Valle R, Alonso MM, Ewald B, Peterkin JJ, Tufaro F, and Fueyo J. (19/23) Phase 1 Study of DNX-2401 (Delta-24-RGD) Oncolytic Adenovirus: Replication and Immunotherapeutic Effects in Recurrent Malignant Glioma. *J Clin Oncol.* 2018 36(14):1419-1427.

Scientific paper. Grasso CS, Tang Y, Truffaux N, Berlow NE, Liu L, Debily MA, Quist MJ, Davis LE, Huang EC, Woo PJ, Ponnuswami A, Chen S, Johung TB, Sun W, Kogiso M, Du Y, Lin Q, Huang Y, Hütt-Cabezas M, Warren KE, Le Dret L, Meltzer PS, Hua Mao10, Quezado M, van Vuurden DG, Abraham J, Fouladi M, Svalina MN, Wang N, Hawkins C, Nazarian J, **Alonso MM**, Raabe E, Hulleman E, Spellman PT, Li XN, Keller C, Pal R, Grill J, Monje M. (32/39) **Functionally-defined Therapeutic Targets in Diffuse Intrinsic Pontine Glioma. A Report of the Children's Oncology Group DIPG Preclinical Consortium.** *Nature Medicine* 2015 21(7):827 doi: 10.1038/nm.3855.

Commentary Fueyo J, Gomez-Manzano C, Lang FF, Alonso MM. **Hitchhiking to brain tumors: Stem cell delivery of oncolytic viruses.** *Commentary in Lancet Oncology.* Jun 29:S1470-2045(21)00296-5. doi: 10.1016/S1470-2045(21)00296-5..

Commentary. Iñigo I and MM Alonso; (AC). (2/2). 2019. Destress and do not suppress: targeting adrenergic signaling in tumor immunosuppression *J Clin Inv* 2019 129(12):5086-5088.

Bibliographic review Grünewald GPT, Alonso MM, Avnet S, Banito A, Burdach S L, Grigoriadis AE, Kas M, Koelsche C, Krumbholz M, Lecanda F, Lemma S, Longo DL, Madrigal-Esquivel L, Morales-Molina A, Musa J, Zalacain M, [et al], Baldini N and Heymann D (2/41) Sarcoma treatment in the era of molecular medicine. *EMBO Mol Med* (2020)

C.2. Participation in R&D and Innovation projects

Selection of 10 research and innovation research

- 1 **Defeat DIPG Grant:** “Targeting the DIPG tumor microenvironment” July 2021-August 2023. **PI: Marta M Alonso; 600.000\$ PI: Marta M. Alonso**
- 2 **AECC_Proyectos** “Combinatorial biotherapies for the treatment of pediatric diffuse midline gliomas” PRYGN21937ALON December 2021-November 2024. **PI: Marta M Alonso; 300.000€**
- 3 **Instituto Carlos III; PI19/01896** “Phase I clinical trial with oncolytic virus VCN01 for recurrent pediatric brain tumors” 186.000 € January 2020-December 2022. **PI: Marta M. Alonso**
- 4 **European Research Council (ERC) Consolidator Grant 2018;** “Oncolytic viruses for the treatment of pediatric brain tumors: An integrated clinical and lab approach” ERC-2018-COG (817884)- 2.000.000€ March 2019-Feb 2024; **PI: Marta M Alonso**
- 5 **La Marató-** Targeting calcium channels against primary and resistant glioblastoma. PI: Carles Cantí; co-PIs: Judit Herreros and Marta M Alonso. 300.000€ (117.500€ subgroup) 01/03/2020-28/02/2022. 297.875 €.
- 6 **Department of Defense of USA (DOD);** Peer Reviewed Cancer Research Program 2016 Translational Team Science Award “Oncolytic Immunotherapy for Diffuse Intrinsic Pontine Gliomas” GRANT12248417- 1.343.263\$ August 2017-July 2019; **PI: Marta M Alonso;** co-PIs: Juan Fueyo and Candelaria Gomez-Manzano
- 7 **Marie Curie International Reintegration Grant (IRG) FP7-274059.** New therapeutic strategies for the treatment of pediatric brain tumors. 100.000€. *February 2011-February 2015.* PI: Marta M Alonso
- 8 **Ramon y Cajal 2009 (RYC-2009-05571)** Contract from the Spanish Ministry of Science and Innovation: “Oncolytic virus for the treatment of brain tumors” 265.000 € *January 2010-December 2014.* PI: Marta M. Alonso

C.3. Participation in R&D and Innovation contracts

Evaluation of the immune response of GBM recurrent patients to the treatment with DNX2440 12/12/2018-12/12/2022.

Evaluation of the antitumor effect of novel immunomodulatory agents in pediatric solid tumors. AstraZena-Medimmune 20/02/2022 to 19/02/2023

C.4. Patents

Licensed patents:

MDA04-004, MDA04-005, MDA03-119, MDA10-128, MDA12-062, MDA13-050

C.5. Clinical Trials generated directly from our research

- 1 “**Combination of Delta-24-RGD with TMZ for the treatment of recurrent GBM**”. Number EudraCT: 2011-005935-21. Role: Co-PI
- 2-“**Phase I trial of DNX-2401 for Diffuse Intrinsic Pontine Glioma newly diagnosed in pediatric patients**” Number EudraCT: 2016-001577-33. Role: Co-PI
- 3-“**Phase I trial DNX-2440 oncolytic adenovirus for the treatment of recurrent gliomas**» Number EudraCT: 2018-001214-15; NCT03714334 Role: Co-PI
- 4-“**Phase I “ Phase I study for pediatric recurrent malignant brain tumors treated with oncolytic adenovirus DNX-2440**” Eudra CT: 2019-001192-36; coPI: Marta M Alonso