

Part A. PERSONAL INFORMATION

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CV date:		Nov 6 2025	
First name:	Xosé Ramón		
Family name:	García Bustelo		
Gender:	Male	Birth date:	07/11/1962
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ORCID ID:	0000-0001-9398-6072		

A.1. Current position

Position:	CSIC Research Professor / Profesor Investigación CSIC		
Initial date:	30/05/2005		
Institution:	Spanish National Research Council (CSIC)		
Department/Center:	Molecular Mechanisms of Cancer Program	Centro de Investigación del Cáncer de Salamanca	
Country:	Spain	Teleph. number:	+34 663 194 634
Key words:	Signal transduction, RHO and RAS GTPases, VAV proteins, oncogenes, cancer, mouse models, omics		

A.2. Previous positions

Period	Position/Institution/Country
2004–2005	Staff Scientist (Investigador Científico), CSIC, Spain
1999–2004	Tenured Scientist (Científico Titular), CSIC, Spain
1996–2000	Assistant Professor, Dep. Pathology, State Univ. of New York at Stony Brook, USA
1993–1996	Staff Scientist, Bristol Myers Squibb Pharmaceutical Research Institute, USA
1990–1993	Postdoctoral fellow, Bristol Myers Squibb Pharmaceutical Research Institute, USA
1989–1990	Research Faculty Assistant (Profesor Ayudante), Univ. Santiago de Compostela, Spain

A.3. Education

Degree	University/Country	Year
Ph.D.	Univ. of Santiago de Compostela, Spain	1990
Biology	Univ. of Santiago de Compostela, Spain	1985

Part B. CV SUMMARY

B.1. Research. My group has been traditionally focused on signal transduction processes initiated by RHO GTPases during both physiological and pathological conditions. In this context, my group has made key findings on the regulation of these proteins, the isolation of upstream regulators, and the elucidation of the role that these proteins play in normal physiological contexts and high-incidence pathologies. Related areas of research include the functional analysis of RAS and closely related proteins (e.g., R-RAS2). Key contributions in those areas include: **(i)** the discovery of oncogenes of the *VAV* family (*Oncogene* 1996, *Mol Cell Biol* 1999); **(ii)** the finding that VAV proteins acted as downstream signaling elements of protein tyrosine kinases and as tyrosine phosphorylated-regulated RHO activators. This included the elucidation of the main intramolecular regulatory mechanisms associated with the normal and oncogenic activation of these proteins (*Nature* 1992, *Science* 1992, *Nature* 1997, *EMBO J* 1998, *Sci Sig* 2014); **(iii)** the discovery of key roles of VAV proteins in cardiovascular-, sympathetic-, limbic nervous system-, muscle-, and metabolic-related pathways (first case ever for any RHO GEF in most cases; *Nat Med* 2006, *J Clin Inv* 2010, *Cell Metab* 2013, *Nat Neurosci* 2015, *Nat Commun* 2020); **(iv)** new VAV-dependent pathobiological programs in breast, skin, head and neck cancer, and B cell leukemia (*Sci Sig* 2012, *PLoS Biol* 2013, *Nat Commun* 2020, *Nat Commun* 2022, *Mol Oncol* 2025); **(v)** the cataloguing of 51 cancer associated somatic *VAV1* mutations and the demonstration that they can act as *bona fide* oncogenic drivers (*EMBO J* 2021, *Mol Oncol* 2022); **(vi)** the discovery of a totally unexpected tumor suppression function for VAV1 in T cell acute lymphoblastic leukemia (*Cancer Cell* 2017); **(vii)** the identification of a cytoskeletal-based feedback loop involved in generation and propagation of RAC1 activation waves during cell signaling (*EMBO J* 2011); **(viii)** the discovery of cardiovascular defects in RASopathies and upon the catalytic inactivation of PLK1 (*J Clin Inv* 2008, *PNAS* 2011, 2014, *Nat Med* 2017); and **(ix)** the discovery of the implication of the R-RAS2 GTPase in

key signaling programs in cancer (*Nat Comm* 2014, *Cell Rep* 2022, *Oncogene* 2023). This work also allowed us to unveil new biological programs, drug targets, and diagnostic signatures of clinical interest for patients.

My current scientific output includes so far 179 scientific articles, 16 book chapters, 1 book, 5 patents, and 4 commercial agreements. According to [Google Scholar](#), my published work has a *h* factor of 68 ($i_{10}=151$) and more than 17,400 citations. Currently, I stand in the top 0.5% of most influential scientists according to the 2021, 2022, 2023, and 2024 [Stanford Univ/Elsevier](#) lists. My work has been recognized by several Spanish (9) and international (4) scientific awards.

B.2. Academic leadership. I have been actively involved in management activities during all my PI period. Currently, I hold the following leadership positions: (i) Director of our research Center (since 2024); (ii) coordinatorship of the CIBERONC Cancer Molecular Mechanisms Program (since 2017); (iii) membership in the CIBERONC Executive Committee (since 2017); (iv) the presidency of two External Scientific Advisory Committees (ESABs) for health research institutes (La Princesa and Hospital del Mar Research Institute), and membership in 3 ESABs (CINBIO, IDIVAL, IIB); (v) memberships in the Royal Galician Academy of Sciences and the Royal Academy of Pharmacy of Galicia; and (vi) member of the EACR grants committee and the *Curr Opin Cell Biol* editorial board. I am also regularly invited to evaluation committees by national and international research agencies and centers (e.g., AEI, Cancer Research UK, Czech GACR, ERC, ICREA). Previous leadership positions include the CSIC Cancer-HUB network (2021-2024), all the *Redes Temáticas de Investigación Cooperativa en Cáncer* (2003-2016), and in my own Center (Deputy Directorships, 2000-2005 and 2014-2023).

B.3. Society-related actions. I have been President-Elect (2017-18), President (2019-2020), Past-President (2021-2022), Senate President (2023-2024), and Senate member (since 2025) of the [Spanish Association for Cancer Research](#) (ASEICA; 1,800 members). I have been also Vice-President (2021-2022) and President (2023-2024) of the [Spanish Federation of Oncology Societies](#) (FESEO; 6,900 members). I participate quite actively in scientific and patient-oriented activities of several organizations (e.g., AECC, [CrisCancer](#), [FERO](#)). Other actions in this area, among many others, include the participation in the committee that set up the 2021 Strategy in Cancer for the Spanish National Health System of the Spanish Health Ministry.

B.4. Mentorship. I have trained a total of 21 postdocs, 15 Ph.D. (plus 3 currently ongoing), 12 master students, and 15 technologists so far. People with subsequent leadership roles include 12 as PIs in academia either in Spain or elsewhere, 11 with leadership biotech positions, 3 as core facility directors, and 1 journal editor (*Cell Press*). I participate in the [cancer-related master](#) and [Ph.D. programs](#) organized by the CIC and the Univ. Salamanca. Finally, I also carry out mentorship activities (for grad students, postdoc, and junior PIs) associated with the activities of the CIC Training Program. In this context, it is worth noting that I have been a recipient of the [Best Tutor Archimedes Award](#) in 2014 (Spanish Ministry of Education).

Part C. RELEVANT MERITS

C.1. Publications

(10 examples of recent publications as corresponding author. Total publications: 70 in 2015-2025; 179 in whole career). Please, see complete list of our publications by clicking on [this link](#).

- Conde, J., Fernández-Pisonero, I., Lorenzo-Martín, L.F. [3 authors] & [Bustelo, X.R.](#) (CA, 7/7) (2025). The mevalonate pathway contributes to breast primary tumorigenesis and lung metastasis. *Mol Oncol* 19: 56-80 (published online in August 2024). Q1.
- Clavaín, L., Fernández-Pisonero, I., Movilla, N. [11 authors] & [Bustelo, X.R.](#) (CA, 15/15) (2023). Characterization of mutant versions of the R-RAS2/TC21 GTPase found in tumors. *Oncogene* 42: 389-405. Q1.
- Fernández-Pisonero, I., Clavaín, L., Robles-Valero, J. [12 authors] & [Bustelo, X.R.](#) (CA, 16/16) (2022). A hotspot mutation targeting the R-RAS2 GTPase acts as a potent oncogenic driver in a wide spectrum of tumors. *Cell Rep* 38: 110522. Q1.
- Robles-Valero, J., Fernández-Nevado, L., Lorenzo-Martín, L.F. [6 authors] & [Bustelo, X.R.](#) (CA, 10/10) (2021). Cancer-associated mutations in *VAV1* trigger variegated signaling outputs and T cell lymphomagenesis. *EMBO J* 40: e108125. D1.
- Rodríguez-Fdez, S., Lorenzo-Martín, L.F., Fernández-Pisonero, I. [8 authors] & [Bustelo, X.R.](#) (CA, 12/12) (2020). Vav2 catalysis-dependent pathways contribute to skeletal muscle growth and metabolic

homeostasis. *Nat Commun* **11**: 5808. D1.

- Lorenzo-Martín, L.F., Fernández-Parejo, N., Menacho-Márquez, M. [18 authors] & **Bustelo, X.R.** (CA, **22/22**) (2020). VAV2 signaling promotes regenerative proliferation in both cutaneous and head and neck squamous cell carcinoma. *Nat Commun* **11**: 4788. D1.
- Robles-Valero, J., Lorenzo-Martín, L.F., Menacho-Márquez, M. [6 authors], & **Bustelo, X.R.** (CA, **10/10**) (2017). A paradoxical tumor-suppressor role for the Rac1 exchange factor Vav1 in T cell acute lymphoblastic leukemia. *Cancer Cell* **32**: 608-623. D1.
- Larive, R.M., Moriggi, G., Menacho-Márquez, M. [4 authors] & **Bustelo, X.R.** (CA, **8/8**) (2014). Contribution of the R-Ras2 GTP-binding protein to primary breast tumorigenesis and late-stage metastatic disease. *Nat Commun* **5**: 3881. D1.
- Barreira, M., Fabbiano, S., Couceiro, J.R. [2 authors] & **Bustelo, X.R.** (CA, **6/6**) (2014). The C-terminal SH3 domain contributes to the intramolecular inhibition of Vav family proteins. *Science Sig* **7**: ra35. Q1.
- Menacho-Márquez, M., Nogueiras, R., Fabbiano, S. [3 authors] & **Bustelo, X.R.** (CA, **7/7**) (2013). Chronic sympathoexcitation through loss of Vav3, a Rac1 activator, results in divergent effects on metabolic syndrome and obesity depending on diet. *Cell Metab* **18**:199-211. D1.

C.2. Congresses

C.2.1. Organized (10 selected out of 18 in total): • **2023**: 40th Anniversary ASEICA Congress (A Coruña, Nov 14-16). • **2023**: III ASPIC-ASEICA International Symposium (Porto, PT, Oct 26-27). • **2022**: International Symposium on Cancer Genomics and Epitranscriptomics: from the bench to the clinic. Centro de Investigación del Cáncer (Salamanca, Nov 30-Dec 2). • **2021**: XXIV Cycle of Advances in Science and Technology on “Recent advances in the understanding of cancer: molecular basis and clinical applications”. Royal Academy of Sciences of Galicia (Santiago, July 6-9). • **2021**: Current Trends in Precision Medicine in Cancer ASEICA-ASPIC International Symposium (online, October 14-15). • **2021**: III ASEICA Educational Symposium (online, Nov 23-25). • **2020**: 17th ASEICA International Congress (online, Nov 4-6). • **2019**: II ASEICA Educational Symposium (online, Nov 28-29). • **2019**: Current Trends in Immunotherapy ASEICA-ASPIC International Symposium (Salamanca, Sept 12-13). • **2019**: The RAS Superfamily and Related Pathways in Health and Disease. R. Areces Foundation International Symposium (Santander, Spain, May 16-18).

C.2.2. Invited talks and chairmanships (10 selected out of >226 in whole career): • **2024**: Fifth RAS Initiative Symposium (NCI-NIH, Frederick, MD, US, speaker). • **2022**: Biochemical Society Meeting on “Small G proteins in cellular signaling and disease” (Liverpool, UK, speaker). • **2022**: 2nd OncoBell Symposium (IDIBELL, Barcelona, speaker). • **2021**: 3rd RAS Initiative Symposium (online, NIH-NCI, Frederick, MD, US, speaker). • **2018**: UK Biochemical Society Meeting on “Small G proteins in cellular signaling and disease” (Cambridge, UK, speaker). • **2018**: 3rd International Congress of the Portuguese Association for Cancer Research (ASPIC) (Lisbon, PT, plenary session speaker). • **2017**: Distinguished speaker’s lecture, Sylvester Comprehensive Cancer Center (University of Miami, FL, US, speaker). • **2016**: 61st Annual Meeting of the Argentinian Society of Clinical Investigation (Mar del Plata, ARG, plenary session speaker). • **2015**: FASEB Meeting on “Regulation and Function of Small GTPases” (Palm Beach, FL, US, speaker). • **2013**: FASEB Meeting on “Regulation and Function of Small GTPases” (Steamboat Springs, CO, US, speaker).

C.3. Selected research projects (10 selected out of a total of 22)

- **Reference**: RETOS24577LLOV (active) **Related with present call**: No
Title: Neoadjuvant-adjuvant immunotherapy to improve survival in hepatocellular carcinoma
Funding agency: AECC **Call**: AECC 70% Survivorship Challenge (2024)
PI: J.M. Llovet & X.R. Bustelo **Managed by**: Clinic Hospital
Period: 15/07/24-14/07/30 **Role**: Co-Coordinator **Funding**: €8M (€900K for lab)
- **Reference**: PLEC2022-009217 (active) **Related with present call**: No
Title: Encapsulation of CART cells in bioactive nanostructured porous systems for targeted delivery in solid tumors
Funding agency: AEI **Call**: Programa Líneas Estratégicas (2022)
PI: J. Rivas Rey **Managed by**: Univ. Santiago and CSIC
Period: 1/12/22-30/11/25 **Role**: co-PI **Funding**: €280K
- **Reference**: PID2021-122666OB-I00 (active) **Related with present call**: Yes

Title: Dissecting the pathobiological and therapeutic role of a new oncogenic driver on T cell lymphomagenesis

Funding agency: AEI

PI: X.R. Bustelo

Period: 1/9/22-31/8/25

Call: Programa «Retos investigación» (2021)

Managed by: CSIC

Role: PI

Funding: 484K

- **Reference:** PDC2022-133027-I00 (finished)

Related with present call: No

Title: Market-oriented optimization of inhibitors against the catalytic activity of the VAV1 oncoprotein

Funding agency: AEI

PI: X.R. Bustelo

Period: 1/12/22-30/11/24

Call: Proof-of-Concept Program (2022)

Managed by: CSIC

Role: PI

Funding: €132.7K

- **Reference:** HR20-00164 (finished)

Related with present call: Yes

Title: A new functional paradigm for *RHOA* gene mutations in peripheral T cell lymphoma: functional and clinical implications

Funding agency: La Caixa Found.

PI: X.R. Bustelo

Period: 1/1/21-31/12/24

Call: La Caixa Health Projects (2020)

Managed by: Fund. Inv. Cancer Univ Salamanca (FICUS)

Role: PI

Funding: €500K

- **Reference:** CB16/12/00351 (active)

Related with present call: No

Title: Centro de Investigación Biomédica en Red de Cáncer (CIBERONC)

Funding agency: ISCIII

PI: X.R. Bustelo

Period: 1/1/17-No ending

Call: Centros Investigación Biomédica en Red (CIBER, 2016)

Managed by: CIBER

Role: PI

Funding: ≈€70K/year

- **Reference:** RTI2018-096481-B-I00 (finished)

Related with present call: No

Title: Exchange factors for RHO GTPases: friends or foes in cancer?

Funding agency: AEI

PI: X.R. Bustelo

Period: 1/1/19-30/9/22

Call: Programa «Retos investigación» (2018)

Managed by: CSIC

Role: PI

Funding: 375K

- **Reference:** GC16173472GARC (finished)

Related with present call: No

Title: Function, diagnostic value and pharmacological inhibition of R-RAS2, a new oncogenic driver

Funding agency: AECC

PI: X.R. Bustelo

Funding period: 1/11/16-31/7/22

Call: Coordinated Cancer Research Groups (2016)

Managed by: FICUS

Role: Coordinator

Funding: €1.5M (€400K for lab)

- **Reference:** 14-1248 (finished)

Related with present call: No

Title: VAV proteins: catalytic role in skin tumorigenesis and tumor fate reprogramming

Funding agency: WWCRC (UK)

PI: X.R. Bustelo

Period: 1/6/14-31/5/17

Call: 2013 WCR Research Projects

Managed by: FICUS

Role: PI

Funding: €232K

- **Reference:** RO1CA7373509 (finished)

Related with present call: No

Title: Role of VAV family proteins in cell signaling and cancer

Funding agency: NIH (US)

PI: X.R. Bustelo

Period: 1/7/00-30/6/11

Call: NIH RO1 call (2 competitive renewals, 1999 and 2004)

Managed by: FICUS

Role: PI

Funding: \$1.8M

C.4. Contracts, technological or transfer merits

C.4.1. Patents

- **Bustelo, X.R.**, Ruiz, S., Santos, E., Univ. Salamanca & CSIC (2010). Ref: [WO2010070170](#) (not licensed)
- Alarcón, B., Cañaveras, P., Delgado, P., **Bustelo, X.R.**, [3 authors] & CSIC (2010). Ref: [WO2010139838A1](#) (not licensed)
- **Bustelo, X.R.**, Sauzeau, V. & CSIC (2010). Ref: [ES 2 318 921 B1](#) (not licensed)
- **Bustelo, X.R.**, Sauzeau, V., Univ. Salamanca & CSIC (2008). Ref: [ES 2303454 A1](#) (not licensed)
- **Bustelo, X.R.**, Sauzeau, V., Univ. Salamanca & CSIC (2008). Ref: [WO2008062091](#) (not licensed)

C.4.2. Current commercial agreements

- Applied Biological Materials Inc. (Richmond, BC, Canada, 2023)
- BridgeBio Oncology Therapeutics (San Francisco, CA, US, 2024)