

CURRICULUM VITAE ABREVIADO (CVA)

Part A. PERSONAL INFORMATION

First name	Santos		
Family name	Mañes Brotón		
Gender (*)	Male	Birth date (dd/mm/yyyy)	13/07/1961
Social Security, Passport, ID number	50049748T		
e-mail	smanes@cnb.csic.es	URL Web	
Open Researcher and Contributor ID (ORCID)	0000-0001-8023-957X		

(*) *Mandatory*

A.1. Current position

Position	Research Professor		
Initial date	2009		
Institution	Consejo Superior de Investigaciones Científicas		
Department/Center	Immunology/Oncology	Centro Nacional de Biotecnología	
Country	Spain	Teleph. number	915854840
Key words	Molecular Immunology, Cancer Immunotherapy, Vasculature, Inflammation, Cell Signaling, Chemokines, Migration		

A.2. Previous positions (research activity interruptions, indicate total months)

Period	Position/Institution/Country/Interruption cause
03/09/1987-27/06/1990	Researcher/ Fassel Diagnostics/Sweden-Spain/End of contract
16/07/1990-16/07/1993	Researcher/ Kabi-Fides SA/Spain/ End of contract
17/07/1993-16/12/2003	Project leader-Group leader/Pharmacia Spain SA/Spain/End Contr
23/01/2004-30/06/2005	Group leader/Department immunology&Oncology SL/Spain/ CSIC
01/07/2005-24/04/2009	Scientific Researcher/Spanish Research Council (CSIC)/Promotion

A.3. Education

PhD, Licensed, Graduate	University/Country	Year
PhD in Molecular Biology	Universidad Autónoma de Madrid	1999
Bsc. degree in Biology	Universidad Complutense de Madrid	1986
Bsc. in Biology	Universidad Complutense de Madrid	1985

Part B. CV SUMMARY (*max. 5000 characters, including spaces*)

Santos Mañes is a molecular and cellular biologist who directs the "Signaling Networks in Inflammation and Cancer" research group in the Department of Immunology and Oncology at the CNB-CSIC. He began his career as a predoctoral fellow at INIA's Department of Animal Reproduction, and later joined a small Swedish-based biotech company (Fassel Diagnostics). In 1990 he was hired by the R&D department of Pharmacia Spain and later Pfizer, directing various projects related to the relationship between the immune system and cancer. In 2005 he obtained a position of Scientific Researcher in the Spanish Council for Scientific Research (CSIC), and promoted to Full Professor in 2009. Throughout his career, his research has focused on 3 interrelated topics: (i) the identification of signaling pathways that allow cell migration and their spatial and temporal coordination, with a special focus on immune cells, (ii) the analysis of molecular elements that regulate the activation, differentiation and dysfunction of immune cells, especially T lymphocytes, and their pathological implications, and (iii) the understanding of the molecular bases that regulate the interaction between the different cells that make up the tumor microenvironment, in order to identify vulnerabilities in neoplastic cells that allow increasing protective immunity against tumors. His achievements throughout his career have been varied and include, among others, the demonstration of the key role of membrane microdomains in the spatio-temporal organization of signaling during migration of

tumor and immune cells, the function of these microdomains in cell infection by pathogens, the non-chemotactic role of the chemokine receptor CCR5 in the functionality of CD4+T lymphocytes and anti-tumor responses, and the identification of new effects of different chemokines on shaping the inflammatory infiltrate and its influence on the promotion and progression of cancer. In recent years, he has also made relevant contributions in understanding the association between “normalization” of the tumor vasculature and lymphocyte infiltration. He has collaborated with oncologist to analyze the relevance of vascular normalization for improving breast cancer immunotherapy. His laboratory has also identified new molecular mechanisms by which PD-1 causes the dysfunction of cytotoxic lymphocytes that infiltrate tumors. These investigations led to the discovery of calpain-12 as novel mediator of T cell dysfunction and its possible use as an immunotherapeutic target. His leadership in the cancer immunotherapy field is further endorsed by his role as Coordinator of the Immunothercan Program, an Excellence Consortium formed by clinical oncologists and basic researchers, during the period 2012-2022 and funded with ~2M€ by Comunidad de Madrid. In addition, he is regularly invited to participate as speaker in different national and international symposia on the field. In addition to his academic achievements, reflected in 82 ISI articles with more than 7,500 citations, he has been the director or co-director of 10 PhD Theses, and most of the doctors egressed has follow a research career in the academia or the industry. Dr. Mañes’ research has also a translational orientation demonstrated by multiple R&D contracts with biotechnological companies. One of the active contracts deals with the development of inhibitors against calpain-12 and their clinical testing in phase I, funded by Next Generation program with ~2.7 M€. His contributions in the fields of cell biology, immunology and oncology have been recognized with various awards, including “the best pharmaceutical initiative” (Correo Farmacéutico), “Best paper award” (Society for Experimental Biology and Medicine; Maywood, NJ, USA), First Prize for projects in Biomedicine and Health (Fundación Domingo Martínez), First prize in ImmunoOncology (Fundación Merck Salud) and General projects AECC2021 (Asociación Española contra el Cáncer), as well as the invitation to serve on the Editorial Boards of international journals such as Cell Adhesion and Migration (since 2006), Frontiers in Immunology (since 2010), Frontiers in Molecular and Cellular Oncology (since 2011), The Scientific World Journal (2011-2014), World Journal of Immunology (since 2012), Advances in Medicine (since 2013) and Cancers (since 2020). He has also participated as an expert for the National Science Foundation (USA), Institute National du Cancer (France) and Barts and the London Charity (UK), among others.

Part C. RELEVANT MERITS (sorted by typology)

C.1. Publications (Selected)

- 1 Carmona-Rodríguez L; Martínez-Rey D; Martín-González P; Franch M; Sorokin L; Mira E*; **Mañes S* (AC)** (7/7). 2022. Superoxide dismutase-3 downregulates laminin α 5 expression in tumor endothelial cells via the inhibition of nuclear factor kappa B signaling. *Cancers*. 14:1226
- 2 Carmona L; Martínez-Rey D; Fernández-Aceñero MJ; et al; **Mañes S (AC)**(11/11). 2020. SOD3 induces a HIF-2 α -dependent program in endothelial cells that provides a selective signal for tumor infiltration by T cells. *J Immunother Cancer*. 8:e000432
- 3 Martín-Leal A; Blanco R; Casas J; et al; **Mañes S (AC)** (15/15). 2020. CCR5 deficiency impairs CD4+ T-cell memory responses and antigenic sensitivity through increased ceramide synthesis. *EMBO J*. 39:e104749.
- 4 Quintela-Fandino M; Holgado E; Manso L; et al; **Mañes S* (AC)**. (22/22) 2020. Immunoprimering durvalumab with bevacizumab in HER2-negative advanced breast cancer: a pilot clinical trial. *Breast Cancer Res*. 22:124.
- 5 Ogando J; Sáez ME; Santos J; et al; **Mañes S (AC)** (11/11). 2019. PD-1 signaling affects cristae morphology and leads to mitochondrial dysfunction in human CD8+ T lymphocytes *J Immunother Cancer*. 7:151. IF:13.751
- 6 Mira E; Carmona-Rodríguez L; Pérez-Villamil B; et al; **Mañes S (AC)** (16/16). 2018. SOD3

- improves the tumor response to chemotherapy by stabilizing endothelial HIF-2 α . *Nat Commun.* 9:575.
- 7 Gómez-Moutón C; Fischer T; Peregil RM; Jiménez-Baranda S; Stossel TP; Nakamura F; **Mañes S (AC)** (7/7). 2015. Filamin A interaction with the CXCR4 third intracellular loop regulates endocytosis and signaling of WT and WHIM-like receptors. *Blood.* 125:1116.
 - 8 Jiménez-Baranda, S.; Gómez-Moutón, C.; Rojas, A.M.; et al; **Mañes, S. (AC)**. (12/12). 2007. Filamin-A regulates actin-dependent clustering of HIV receptors. *Nat Cell Biol.* 9, pp.838-846.
 - 9 Molon, B.; Gri, G.; Bettella, M.; et al; **Mañes, S.* (AC)**; Viola A*. (7/8). 2005. T cell costimulation by chemokine receptors. *Nat Immunol.* 6, pp.465-471
 - 10 **Mañes, S.* (AC)**; del Real, G.; Martínez-A., C.(1/3). 2003. Pathogens: Raft hijackers. *Nat Rev Immunol.* 3, pp.557-568. IF:26.96

C.2. Congresses (Selected 2018-2022)

- 1 XII BcnPitt Bienial Conference on Alzheimer. Barcelona. June 2022. Chairman of the Neuroinflammation session.
- 2 Targeting tumor hypoxia by the superoxide dismutase-3". Invited speaker. 50th Anniversary Domingo Martínez Foundation. 26/11/2021. Madrid. Spain.
- 3 Metabolismo y respuesta inmune". Invited speaker. Simposio Educativo. SEOM2021VIRTUAL. 18-22/10/2021.
- 4 Non-chemotactic functions of the chemokine receptor CCR5. Implications in immunity and cancer". Invited speaker. Translational Oncology Seminars. CNIO. 12/07/2021. Madrid. Spain
- 5 Targeting the tumor endothelium to boost selective infiltration by T cells". Invited speaker. 4th European Congress on Immunotherapies in Cancer (ECIC). 15-16/11/2019. Barcelona. Spain
- 6 Addition of durvalumab (Dur) upon progression to bevacizumab (Bev) maintenance in advanced HER2-negative breast cancer". Quintela-Fandino M, Manso-Sanchez LM, et al., Mañes S. Oral presentation. ESMO Asia 2018 Congress. 23-25/11/2018. Singapore. Singapore Republic.
- 7 Nanoscale organisation of the T cell antigen receptor by the chemokine receptor CCR5". Martín-Leal et al.// Mañes S. Oral presentation. 5th European Congress of Immunology. 2-5/09/2018. Amsterdam. Holland.
- 8 Debate Omnitalk: Immunoterapia en Oncología. Ponente. Real Academia Nacional Medicina (2018)
- 9 Metabolic dysregulation and immune response in cancer". Invited speaker. IV forum of Translational Immunology and Cancer Immunotherapy. 8-10/03/2018. Madrid. Spain
- 10 Immunoediting and immune response against tumors. Invited Speaker. 1st Translational Forum of Cancer Immunotherapy (GETICA). 13-14-Marzo 2015. Sevilla

C.3. Research projects. (Selected)

- 1 CAPN12-IO: Preclínical development and first-in-human study with a selective inhibitor for Calpain-12 as a novel strategy for cancer immunotherapy (CPP2021-009090). Proyectos de Colaboración Público-Privada 2021. Coordinator: Landsteiner Genmed SL. Participant groups participantes: CNB/CSIC (Santos Mañes), Hospital 12 de Octubre (Luis Paz-Ares), CIQUS Univ. Santiago de Compostela (Eddy Sotelo). Budget total 2.761.578 €.
- 2 Divergent effects of vascular laminins in the differentiation of regulatory T-cells and its role in resistance to immunotherapy (PRYGN211240MAÑE). Asociación Española Contra el Cancer 01/12/2021-30/11/2024. 300.000 €. Santos Mañes Brotón. Principal investigator.
- 3 Nuevos actores con potencial para regular la diferenciación, activación y migración linfocitaria en el microambiente tumoral (PID2020-116303RB-I00). Ministerio Ciencia e Innovación. 01/09/2021-31/08/2024. 332.750,00 € Santos Mañes. Principal investigator.

- 4 B2017/BMD-3733, Tumor Immunity and Immunotherapy of Cancer (IMMUNOTHERCAN) Consejería de Sanidad de la Comunidad de Madrid. Biomedicina. Santos Mañes Brotón. (Centro Nacional de Biotecnología). 01/01/2017- 31/12/2021. 952.472,28 €. Co-ordinator.
- 5 SAF2017-83732-R, Reprogramming the tumor microenvironment to increase the effectiveness of Cancer Immunotherapy (TME-REP) Ministerio de Economía y Competitividad. Santos Mañes Brotón. (Centro Nacional de Biotecnología). 01/01/2018-31/12/2020. 338.600 €. Principal investigator.
- 6 H2020-PPP-JTI-IMI2/0232, Alzheimer's Disease Apolipoprotein Pathology for Treatment Elucidation and Development (ADAPTED) European Union. Innovative Medicines Initiative. Santos Mañes Brotón. (Centro Nacional de Biotecnología). 01/10/2016-31/10/2020. 371.608,25 €. Principal investigator.
- 7 Determination of PD-1-induced molecular signature in human CD8+ T lymphocytes. First Prize InmunoOncología. Merck Salud Foundation. Santos Mañes Brotón. (Centro Nacional de Biotecnología). 01/10/2018-31/07/2019. 30.000 €. Principal investigator.
- 8 SAF2014-54475-R, Migration, activation and dysfunction of T lymphocytes in cancer Ministerio de Economía y Competitividad. (Centro Nacional de Biotecnología). 01/01/2015-31/12/2017. 399.300 €
- 9 S2010/BMD-2326. Inmunidad tumoral e inmunoterapia del cáncer -IMMUNOTHERCAN. Comunidad de Madrid. Biomedicina. Entidades participantes: CSIC, CNIC, UCM, Fundación Hospital Infanta Sofia, Hospital 12 de Octubre, Clínico San Carlos. Santos Mañes Brotón- Co-ordinador. 01/01/2012-31/12/2015. Total: 991.200 €/Grupo: 188.000 €
- 10 RD08/0075/0007. Red de Investigación en inflamación y enfermedades reumáticas (RIER). Instituto de Salud Carlos III. IP. Santos Mañes Brotón. 01/01/2009-31/12/2014. 65.528 €/año

C.4. Contracts, technological or transfer merits (Selected)

- 1 Effect of inhibitors of Calpain 12 in experimental tumorigenesis. Landsteiner GenMed SL. Santos Mañes Broton. 15/01/2022-Present. Estimated budget: 104,295.60 €
- 2 Search for Calpain 12 inhibitors as enhancers of CD8 lymphocyte cytotoxic activity. I+D Contract. Landsteiner GenMed SL. Santos Mañes. 28/07/2017-Present. 192,888.15 €.
- 3 Human CAPNS. Material transfer. Tokyo Metropolitan Institute of Medical Science
- 4 Effect of the inhibitor NPO-2237 on tumorigenesis in mice. Technological support. Landsteiner GenMed SL. Santos Mañes Broton. 15/11/2017-15/01/2018. 4,725.13 €.
- 5 Immunophenotyping of patients with breast cancer. Fundación CRIS contra el cancer. Santos Mañes Broton. 09/03/2016-31/12/2018. 43,493.45 €.
- 6 Identification of new therapeutic targets for cancer treatment using functional genomics. Technological support. NeoPharm Obesity SL. Santos Mañes Broton. 01/01/2015-01/05/2017. 78,650 €.
- 7 Identification of new therapeutic targets for cancer treatment using functional genomics NeoPharm Obesity SL. Principal Investigator. 01/01/2015-01/05/2015. 78,650 €.
- 8 Non-exclusive license anti-IGF-I antibodies "DD9F3, KM9F6" MEDIAGNOST Gesellschaft fuer Forschung und Herstellung von Diagnostika GmbH. Santos Mañes Broton. 06/11/2012-present. 5,800€. Upfront payment + Royalties (10% net sales/year).
- 9 Investigación científica dirigida al desarrollo de una nueva generación de alimentos para el control de peso y prevención de la obesidad – PRONAOS-. CENIT-2008-1004 (I+D). (2008-2011) Coordinador: Neocodex SL. Principal Investigator. 234.559 €.
- 10 Molecular and cellular mechanisms in chronic inflammatory and autoimmune diseases (MEICA). Fundación Genoma España. PI: Santos Mañes. Coordinator: Dr. F Sánchez-Madrid. Participant entities: ALK Abelló, Sistemas Genómicos, CSIC, CNIC, HUP, UCM, BIOMAC-RB. 119.485,80€ (total budget: €3,000,000)