CV: Francisco Sánchez-Madrid

PERSONAL INFORMATION

First and Family name	Francisco Sánchez Madrid		
ID number	30409868G	Age	70
Researcher numbers	Researcher ID	M-7889-2016	
	Orcid code	0000-0001-5303-0762	

A.1. Current position

Name of University/Institution	Hospital Universitario de la Princesa. Universidad Autónoma de Madrid.		
Department	Dpt of Medicine. School of Medicine. Universidad Autónoma de Madrid. Hospital de la Princesa.		
Address and Country	Diego de León, nº 62 – 28006 Madrid		
Phone number	+34915202307	E-mail	fsmadrid@salud.madrid.org
Current position	Professor of Immunology	From	March 1990
Espec. cód. UNESCO	2412		
KeyWords	Immunology/Inflammation/Activation receptors /Immunological Synapse/Mechanisms of Intercellular Communication		

A.2. Education

PhD	University	Year
Licenciate Biology	Universidad de Sevilla	1976
Ph. D. Biochemistry	Universidad Autónoma de Madrid	1980

Francisco Sánchez-Madrid is Professor of Immunology at University Autónoma of Madrid since 1990. Over the last 15 years, he has directed the Immunology Department of Hospital Universitario de la Princesa, and has served as Scientific Director of the Health Research Institute of University Hospital Princesa in Madrid.

Major achievements: During his scientific career to date he has made leading contributions to knowledge about the mechanisms of **leukocyte adhesion, polarity, migration and activation**. This contribution has pioneered the identification and **characterization of the first families of leukocyte adhesion molecules**, their physiological **role in** the control of **migration and cellular traffic**, and their **immense relevance to chronic inflammatory pathologies**. These contributions have formed the **basis for novel anti-adhesion therapies that are being used** to treat diseases such as **multiple sclerosis, and Crohn's** (granulomatous colitis).

His main achievements are the following:

i) Identification, biochemical characterization and functional regulation of the first family of leukocyte adhesion receptors (β2 integrins and CD2/LFA-3 pair) and the β1 integrin VLA-4 (α4β1), and their implications in leucocyte interactions, mainly in cell migration and infiltration in inflammatory diseases.

ii) Mechanisms of chemokine-induced leukocyte polarity: Identification of the molecular components involved and the function of two subcellular compartments: "leading edge" and "trailing edge" or uropod.

iii) Dynamic interactions of adhesion molecules (ICAMs, tetraspanin/integrin complexes) with cytoskeleton components that regulate leucocyte-endothelium interactions and early stages of the T cell-antigen presenting cell (APC) interaction during the immune synapse.

iv) His group identified the Early Lymphocyte Activation Antigen CD69, cloned the gene, generated the first CD69-deficient mice and described the CD69 *in vivo* function as a negative immuno-modulator in autoimmune diseases mainly by regulating Th17 expansion. Galectin-1 and oxLDL have been identified as CD69 cellular ligands. The role of CD69 as a new metabolic gatekeeper in inflammation through the control of amino-acid transporter CD98/LAT1.

v) During the last decade, his research group has made key contributions to understanding the functional relevance and mechanisms of genetic transfer of miRNAs from T cell to APC during the immune synapse. He has also addressed the composition and sorting mechanisms into exosomes of proteins, miRNA, mitochondrial DNA and their role in cell-cell communication in the immune response by epigenetically instructing dendritic cells to become more protected to infectious pathogens.

Sánchez-Madrid's laboratory research on the role of adhesion, migration and activation receptors of human leukocytes in intercellular immune interaction and communication is documented in more than **530 publications** in international journals**, including many recent articles in highly prestigious journals;** for example, several articles in Nature journals**,** in Immunity**,** and many others in journals such as J. Clin. Invest. J. Exp. Med., J. Cell Biol, EMBO J, NEJM, Science Advances. This track record has given him ample experience in the **creation of a high-quality research team, collaboration in translational biomedical research programmes and training of researchers. As** many as 30 alumni from his group are now university teachers and research leaders in national and international centers, including **several ERC Grant awardees.** In parallel with his research activity, he has also carried out an intense **teaching activity since 1990** in the Faculties of Medicine and Biological Sciences at the *Universidad Autónoma de Madrid*. As part of this activity, **he has supervised 46 doctoral theses** and presented more than 214 lectures and seminars at diverse research centres and universities in Spain and abroad. **He has been invited to give Plenary and Keynote Lectures** in numerous international scientific Workshops, Meetings and Congresses (Keystone Meetings, Gordon Conferences, FASEB and EFIS Meetings, etc).

B. Positions and Honors

Positions and Employment

2009-to date	Head of Immunology Service. Hospital de la Princesa.
1990-to date	Full Professor Immunology. Universidad Autónoma de Madrid (UAM), Madrid
2009-2023	Scientific Director, Instituto de Investigación Sanitaria Princesa (IIS-IP). UAM.
1992-2009	Associate Professor Immunology, Service of Immunology.
1984-1991	Assistant Professor Immunology, Service of Immunology. Hospital de la Princesa. Madrid.
1980-1983	Research Fellow, Harvard Medical School, Harvard University, Boston, MA.
1977-1980	Ph. D. Student, Centro de Biología Molecular (CSIC-UAM), Madrid.

Other Experience and Professional Memberships

Current — Member of the Scientific Advisory Board of the following scientific institutions:

- Health Research Institute IDIBAPS-Hospital Clínico, Barcelona, Spain
- Cancer Research Center, Salamanca, Spain
- Center for Cancer Research (CRCM). Marseille. Francia
- Health Research Institute Maimónides. Hospital Reina Sofía-Universidad de Córdoba, Spain
- Health Research Institute IDIVAL. Hospital Universitario "Marqués de Valdecilla". Santander.
- Health Research Institute INIBIC. Hospital Universitario A Coruña.
- Center for Research in Molecular Medicine (CIMA). Pamplona, Navarra.
- Promotion Committee for evaluation of ICREA Investigators. ICREA. Barcelona.

2007-2010	Member, Evaluation Panel LS6 of European Research Council for Young Investigator Grants.
2001-2005	Coordinator of the National Biomedicine Plan (Plan Nacional de Biomedicina).
1998-2000	President, Immunology Commission of the Spanish Health Research Fund (FIS)

Honors and Awards

2023	Robert Koch Award.
2020	National Prize in Biology Research "Santiago Ramón y Cajal".
2019	Invested "Doctor Honoris Causa". Universidad de Córdoba.
2018	Award Biomedicine Career "Constantes y Vitales". Atresmedia/La Sexta.
2018	Recipient of a Health Research Grant from "La Caixa"
2012	Recipient of an ERC Advanced Grant

2009 Science Prize from the Community of Madrid "Miguel Catalán"
2008 National Society of Neurology. "Multiple Sclerosis" award.
2005 Basic Research award from Foundation Pfizer.
2005 Lilly Foundation. Pre-clinical Research award.
2004 "Severo Ochoa" award from Foundation Ferrer.
2002 Award, Francisco Cobos Foundation-CSIC
2001 Award, CEOE Biomedicine.
2001 Award, Life Sciences Foundation.
2002 Grant for Basic Research from Juan March Foundation.
1996 Elected member of EMBO

C. Contribution to Science

During his scientific career, Sánchez-Madrid has defined several key lines of research in human immunology through leading contributions regarding the molecular and cellular mechanisms of **leukocyte adhesion, polarity, migration and activation**, and their **crucial relevance in chronic inflammatory pathologies, leading to basic and translational breakthroughs.** His publications have to date received more than **51.500 citations** (ISI-WOS), and his **H Factor is 109 (H:128 in google scholar; 66.500 citations).**

The most important achievements during my scientific career are:

- Novel modes of cell-to-cell communication and transfer of genetic information through the immune synapse (2011-Now). His group has recently addressed novel forms of cell-to-cell communication in the immune system, including the transfer of genetic information through antigen-dependent contacts. A major breakthrough was the demonstration that **genetic information is transferred between T cells and antigen-presenting cells contained in exosomes** harbouring specific repertoires of proteins, miRNAs and Mitochondrial DNA. For this activity, he was awarded an Advanced ERC Grant in 2012, and the Health Research Grant from La Caixa (2019-2022).

1. *Mittelbrunn et al., 2011 Nature Commun*
2. *Baixauli et al., 2011 EMBO J.*
3. *Martin-Cófreces et al., 2012 EMBO J.*
4. *Mittelbrunn et al., 2012 Nat Rev Mol Cell Biol.*
5. *Villarroya-Beltrí et al., 2013 Nature Commun.*
6. *Blas-Rus et al., 2016 Nature Commun*
7. *Villarroya-Beltrí et al., 2016 Nature Commun.*
8. *Cruz-Adalia et al., 2017. Nature Commun*
9. *Torralba et al., 2018. Nature Commun.*
10. *Fernandez-Messina et al., 2020 EMBO Rep.*
11. *Martín-Cófreces et al., 2020 Science Advances*
12. *Alcaraz-Serna et al., 2021 Science Advances*
13. *Céspedes et al., 2022 Nature Commun*
14. *Dosil et al., 2022 Elife.*
15. *Calzada-Fraile et al., 2023. Nature Commun*

-T-lymphocyte activation receptors and the regulation of the inflammatory response (1988- Presently). A long-term research line pioneered by Sánchez-Madrid's group was the identification of CD69 as the earliest activation antigen expressed by lymphocytes. During last 30 years, his group characterized the functional role of CD69, cloned and localized the gene and characterized the molecular regulation of its expression. They generated genetically-modified mice deficient for CD69, which were used to **demonstrate that CD69 is a physiological negative regulator of the inflammatory immune response** through the control of differentiation and expansion of the pro-inflammatory Th17 cells. Recently, Sánchez-Madrid has identified CD69 physiologic ligands, and discovered the regulatory mechanism by which CD69 governs the immune inflammatory response, acting as a metabolic gatekeeper, controlling amino acid transporter LAT-1 in T cell activation and inflammation.

1. *Cebrián et al., 1988 J. Exp. Med.*
2. *López-Cabrera et al., 1993 J. Exp. Med.*
3. *Esplugues et al., 2003, J. Exp. Med.*
4. *Sancho et al., 2003, J Clin Invest.*
5. *Martin et al., 2010 Mol Cell Biol.*
6. *Cruz-Adalia et al., 2010, Circulation.*
7. *Cibrián et al., 2016 Nat Immunol.*
8. *Tsilingiri et al., 2020. Circulation*
9. *Cibrian et al., 2020 J Allergy Clin Immunol*
10. *Cibrian et al., 2020 Trends Mol Med*
11. *Castillo-González et al., 2021 J Allergy Clin Immunol*
12. *Martin and Sánchez-Madrid J Clin Invest 2025*

- Protein microdomains that facilitate cell-to-cell communication (2004-2010). These studies include breakthroughs in understanding how cells generate finely regulated molecular subdomains that facilitate cell-to-cell communication in connection to the cellular cytoskeleton.

1. *Vicente-Manzanares et al, 2004 Nat Rev Immunol.*
2. *Mittelbrunn et al., 2004. Proc Natl Acad Sci.*
3. *Barreiro et al., 2005. Blood.*
4. *Ibiza et al., 2006 Immunity.*
5. *Martin-Cófreces et al., 2008 J Cell Biol.*
6. *Barreiro et al., 2008 J Cell Biol.*
7. *Yañez-Mo et al., 2008. Blood.*
8. *Yañez-Mo et al., 2009 Trends Cell Biol.*
9. *Sánchez-Madrid and Serrador. 2009 Nat Rev Mol Cell Biol.*

-Molecular mechanisms of leukocyte migration, orientation and cell polarity in the inflammatory immune response (1995-2003). His group made pivotal contributions to unravel the mechanisms underlying leukocyte orientation during directional migration, which is a cornerstone of inflammation, as well as the process of antigenic presentation established between T cells and antigen presenting cells. **These contributions have led to a new model of molecular polarity in leukocytes and endothelium that guides migration and facilitates cell-to-cell communication during antigenic and inflammatory contacts.** These discoveries have been reported in many studies published in leading journals in the fields of Immunology and Cell and Molecular Biology.

1. *del Pozo et al., 1995 J Cell Biol*
2. *del Pozo et al., 1997 J Cell Biol*
3. *Nieto et al., 1997 J Exp Med*
4. *Serrador et al., 1997 J Cell Biol*
5. *Yáñez-Mó et al., 1998 J Cell Biol*
6. *Sánchez-Madrid et al, 1999 EMBO J*
7. *Sancho et al., 2000 J Cell Biol*
8. *Montoya et al., 2002 Nature Immunol.*
9. *Barreiro et al., 2002 J. Cell Biol*
10. *Urzainqui et al., 2002 Immunity*
11. *Gil et al., 2002 Cell*
12. *Serrador et al., 2004 Immunity*

-Leukocyte adhesion and its relevance in inflammatory diseases (1985-1994). In 1985, Francisco Sánchez-Madrid began a career as an independent researcher in the *Servicio de Inmunología* at the *Hospital Universitario de la Princesa* in Madrid. His research comprised seminal studies characterizing the molecular mechanisms that regulate leukocyte adhesion, polarity and activation. Some examples include the characterization of several receptors essential for leukocyte migration and trafficking, for example the beta1 integrin VLA-4 and the receptor ICAM-3. These studies, both *in vitro* and *in vivo,* using models of inflammatory diseases are the conceptual foundation of novel anti-adhesion therapies for the treatment of human chronic inflammatory diseases such as multiple sclerosis, and Crohn's disease.

1. *Campanero et al., 1990, J. Cell Biol.*
2. *Campanero et al., 1993, J. Cell Biol.*
3. *Campanero et al., 1994, J Cell Biol.*
4. *Arroyo et al., 1992, J. Cell Biol.*
5. *Arroyo et al., 1994 J Cell Biol.*
6. *Yednock et al., 1992 Nature.*
7. *Laffón et al., 1992 J. Clin. Invest.*
8. *Postigo et al., 1993 J. Clin. Invest.*
9. *Gonzalez-Amaro et al., 1994 J Exp. Med*

-Identification of the first families of leukocyte adhesion molecules (1980-1983). In 1980, Dr Sánchez-Madrid joined the Pathology Department at Harvard Medical School, where he worked under the supervisiom of Drs. B. Benacerraf (Nobel Laureate in Medicine, 1980) and T. A. Springer on the molecular mechanisms of the cytotoxic T lymphocytes and the cell receptors implicated in their function. The most important discoveries during this period were the identification and functional characterization of the first family of human leukocyte adhesion receptors, including LFA-1/Mac- 1, and the family of beta 2 integrins, which are crucial mediators of inflammatory processes.

1. *Sánchez-Madrid et al., 1982, Proc Natl. Acad Sci..*
2. *Sánchez-Madrid et al., 1983a, J. Exp. Med.*
3. *Sánchez-Madrid et al., 1983b, J. Exp. Med.*

-Collaboration in translational biomedical research programmes in mechanisms of Chronic Inflammatory Diseases. Sánchez-Madrid has also been a staunch proponent of the interaction between basic and translational research. The translational activity involved specialists in rheumatology, nephrology, gastroenterology, dermatology and pathological anatomy working on various clinical aspects of inflammatory processes. These collaborations have borne fruit in numerous publications in prestigious clinical journals. Some key examples include studies published in journals of maximum impact **on the pathophysiological mechanisms of inflammatory and infectious diseases**.

1. *García-Monzon et al., 1990 Gastroenterology*
2. *Garcia-Monzon et al., 1992 Gastroenterology*
3. *Díaz-González et al., 1995 J Clin Invest*
4. *García-Monzon et al., 1995 Gastroenterology*
5. *Yánez-Mó et al., 2003 New Engl. J Med.*
6. *González-Álvaro et al., 2009 Ann. Rheum. Dis.*
7. *Riol-Blanco et al. 2009 Nat. Immunol.*
8. *Barreiro et al., 2010 Cardiovasc. Res.*
9. *Martín et al., 2010 J. Allergy Clin. Immunol.*
10. *Cruz-Adalia et al., 2014 Cell Host Microbe.*
11. *Borroto et al., 2016 Sci Transl Med.*
12. *Moreno-Gonzalo et al., 2017. PLOS Pathogens*
13. *García-Peydró et al., 2018 J Clin. Invest.*
14. *Sánchez-Cerrillo et al., 2020 J Clin. Invest,*
15. *Castillo-González et al., 2021. J Invest Dermatol*
16. *Blanco-Dominguez et al., 2021. New Engl. J. Med.*
17. *Blanco-Dominguez et al., 2023. J Clin Invest.*
18. *Esparcia-Pinedo et al., 2023 Clin Infect Dis.*
19. *Sánchez-Cerrillo et al., 2023 EMBO J*
20. *Tsukalov et al., 2024 Nature Commun*

D. Granted Patents: The candidate has participated in the invention of **15 Patents and Licenses;** some of these are being exploited by Biogen, Pharma-Mar, Millipore, Becton Dickinson, Immunostep, Immunotech, Pharmingen, and Coulter through contracts and licensing agreements with the Technology Transfer Office of the Universidad Autónoma Madrid.

(Selected patents within the last years)

- Electrochemical biosensors for diagnosing acute myocarditis. P Martín, R Blanco Domínguez, R Sánchez Díaz, **F Sánchez Madrid.** EPI17382324. Entidad titular: Canaan R&D and CNIC
- CD81 as therapeutic target for control of intracellular levels of DNTPs. M Yañez-Mó, H Suárez Montero, **F Sánchez Madrid**, V Rocha Perugini. N: P201700345. Institution: UAM
- Transinfected lymphocytes for anti-tumor therapy. E Veiga Chacón, A Cruz Adalia, G Ramírez Santiago, B Alarcón **F Sánchez-Madrid.** PCT/ES2016/070597WO2017/025657.Institutions.: CSIC and UAM
- Antibody Drug Conjugates. M Garranzo García-Ibarrola, A Francesch Solloso, JM Domínguez Correa, MJ Muñoz Alonso, **F Sánchez Madrid**, JM Zapata, AG Arroyo, MA Ursa, C Cuevas Marchante. PCT/EP2014/061392. Company PharmaMar. European Patent Office. The Hague.
- Therapeutic application of inhibitory agents for CD44 against human acute lymphoblastoic leukemia (ALL) humana. M Luisa Toribio, M García Peydró, **F Sánchez Madrid.** (Patent ES201231274): PCT/ES2013/070576.

E. Mentoring the Early Careers of Excellent Researchers (PhD students and Postdocs)

Sánchez-Madrid is involved in teaching and mentoring activities at multiple levels. Accordingly, many of his former pre- and post-doctoral fellows are currently directing their own laboratories. Among them:

Ph. D. Students: Rafael Pulido. Ikerbasque Professor. Hospital Cruces Bilbao; **Miguel R Campanero.** Associate Professor. Center for Molecular Biology UAM-CSIC. Madrid; **Paloma Sánchez-Mateos.** Professor Dpt. Immunology, University Complutense, and Hospital Gregorio Marañón, Madrid; **Alicia G Arroyo.** Associate Professor. Center for Biology Research. CSIC. Madrid; **Rosario Garcia-Vicuña**. Chief. Service of Rheumatology and Assistant Professor Clinical Research Rheumatology Service Hospital Universitario de la Princesa. UAM; **Federico Díaz González.** Chief Unit of Rheumatology and Full Professor Clinical Research Rheumatology Service Hospital Clínico-Universidad de la Laguna. Tenerife; **Miguel A. del Pozo.** Full Professor- National Center for Cardiovascular Research (CNIC) Madrid. ***EURYI Awardee 2005;*** **Marta Nieto** Associate Professor. National Center of Biotechnology (CSIC) Madrid; **JM Serrador.** Associate Professor. Center for Molecular Biology UAM-CSIC. Madrid; **David Sancho.** Associate Professor (CNIC). Madrid. ***Starting ERC Awardee 2010, and Consolidator ERC Awardee 2016;*** **Maria Yáñez-Mó*:*** Assistant Professor. Center for Molecular Biology UAM-CSIC **Miguel Vicente-Manzanares.** Associate Professor. Center for Cancer Research, CSIC. Salamanca; **María Mittelbrunn.** Associate Professor. Center for Molecular Biology UAM-CSIC. Madrid. ***Starting ERC Awardee 2016; and Consolidator ERC Awardee 2022.***

Posdoctoral Fellows: **Angel L Corbi.** Professor. Center for Biological Research CSIC. Madrid; **Joaquin Teixidó.** Professor. Center for Biological Research CSIC. Madrid; **Manuel López- Cabrera.** Associate Professor. Center for Molecular Biology. CBM-UAM. Madrid; **Agustín Valenzuela**. Assistant Professor. Dpt Pharmacology. Facultad de Medicina. Universidad de La Laguna; **Pilar Martín** Assistant Professor. (CNIC) Madrid; **Esteban Veiga.** Associate Professor. National Center of Biotechnology (CSIC). Madrid, **Noa Martín-Cófreces,** I3 Researcher, Hospital Universitario de la Princesa**; Danay Cibrián,** Miguel Servet Researcher, Hospital Universitario de la Princesa; **Hortensia de la Fuente,** Independent researcher, Hospital Universitario de la Princesa**.**

F. Invited Presentations to Conferences (Selection of 12)

1. "*Intercellular communication: transfer of genetic information and reprogramming of dendritic cells during synapsis"*. Inaugural Lecture. **DC2024: International Meeting on Dendritic Cells. Barcelona 2024. 2.** *"Intercellular communication in the immune response: Transfer of genetic information during synapsis"*. **Institute Pasteur. Paris, November 2021**. **3.** *"Intercellular communication in the immune response: Transfer of genetic information by EVs during synapsis"*. **III AICC international exosome meeting. Roma. October, 2021**. **4.** *"Microtubule Dynamics in the Control of T cell Activation and Immune Synapse Organization***". Microtubules: From Atoms to Complex Systems – EMBO Meeting. Heidelberg. June 2020. 5**."*Centrosomes and Exosomes: Pacemakers of T cell activation". "* Plenary Lecture. ECI

Meeting, **Amsterdam 2018. 6. "***Centrosomes in T cell activation".* **"Lecture "Severo Ochoa" Center Molecular Biology. Madrid. 2017. 7. "***Circulating miRNAs: Biomarkers for Inflammatory diseases"***. NIH Strategic Workshop on Extracellular RNA Transport. Washington DC, USA 2017. 8.** *"Immune cell-to-cell communication: Mechanisms of genetic and protein transfer"***. Distinguished Ludwig Lecture Series in Cancer Research. Ludwig Cancer Institute. Lausanne, Switzerland 2017. 9.** *"The role of the leukocyte activation receptor in the immune Inflammatory response: its ligands and associated molecules"* **Plenary Lecture. 7th EMBO Meeting, Mannheim 2016. 10.** *"New modes of Cell-Cell Communication in the Immune System"***. Invited Lecture. University of Manchester, UK 2016. 11. "***Immune Cell-to-Cell communication: Mechanisms of miRNA and proteins sorting into exosomes"* Plenary Lecture. 5th Annual Meeting ISEV, **Rotterdam 2016. 12. "***Immune cell-to-cell communication: Mechanisms of miRNA and proteins sorting into exosomes".* **Invited Lecturer Symposia. 4th ECI Vienna 2015.**