

LÍNEA DE INVESTIGACIÓN:

Study of the molecular basis of alterations in the signaling of T and B lymphocytes in autoimmune diseases, Systemic Lupus Erythematosus (SLE), and Psoriasis.

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FREE SUMMARY OF CV

My scientific background is in biochemistry, cellular, molecular biology, and immunology. My Doctoral Thesis, 1978-81, was done at Jiménez Diaz Foundation, Madrid with Dr. D. José Miguel López-Novoa. My post-doctoral training was done in several Research Institutes: In Spain, at the Cajal Institute-CSIC-Madrid, with Dr. D. José Borrell and Dr. D^a Carmen Guaza. In the USA, I worked in three laboratories, at the Cardiovascular Division, Harvard Medical School (HMS), Boston, with Dr. Eva J Neer; at the Cancer Research Center, Boston Univ., with Dr. Douglas V Faller; and at HMS-Boston, Immunology Dept., with Dr. Cox Terhorst. I have a long standing research interest in cellular signaling and protein interactions to study the functional relationship between the CD38 receptor, the TCR and protein kinases in the cellular behavior of T and B lymphocytes. I characterized CD38 associated molecules purified from different cell districts in B cells. We reported that extracellular vesicles and exosomes released from B cells were enriched in CD38 enzymatically active and we characterized the specific interactions between CD38 and other well-characterized exosome and lipid rafts associated signaling proteins. Based on these interactions, we postulated that exosomal CD38 was a signaling molecule that may provide an alternative route for context-dependent signal delivery or for the transmission of materials relevant for immune responses. I have long term research interest in the study of the molecular basis of alterations in the signaling of T and B lymphocytes in autoimmune diseases, Systemic Lupus Erythematosus (SLE), and Psoriasis. I studied CD38-deficient mice (CD38KO) for phenotypic, functional and proteomic studies in animal models of autoimmune diseases (arthritis rheumatoid and lupus) to search for potential biomarkers of the disease using proteomics and gene expression methodologies. Results of these studies have been presented to national and international scientific meetings, and published in peer-reviewed biochemistry, immunology, proteomic and dermatology journals. These results were the basis for doctoral thesis. I collaborated with basic and clinical scientists. Dr. J. Sancho, IPBLN-CSIC; Dr. A.L. Corbí, CIB-CSIC; Dr. R. Merino, and Dr. J. Merino, CSIC-UC; Dr. M. Carrascal and Dr. J. Abian CSIC-UAB; Dr. JA Barcenas, UCO; Dr. F. Malavasi and Dr. A. Funaro, Torino University, Italy; Dr. F. Lund and Dr. E. Zumaquero, from Alabama University, USA; Dr. C. Terhorst, Harvard Univ., USA; Dr. N. Ortego, Dr. J. Salmeron, and Dr. FJ Blanco from the University of Granada.

PUBLICACIONES RECIENTES

1. Burlock B, et al.,(MZ,position:5/6). The Role of CD38 on the Function of Regulatory B Cells in a Murine Model of Lupus.2018 Int J Mol Sci.,19(10). pii: E2906. doi: 10.3390/ijms19102906.
2. García-Rodríguez, S., et al, (MZ, 17/19).CD38 promotes pristane-induced chronic inflammation and increases susceptibility to experimental lupus by an apoptosis-driven and TRPM2-dependent mechanism. 2018 Scientific Reports 8(1),3357. Q1. doi: 10.1038/s41598-018-21337-6.
3. Ferrero, E., (..),et al, (MZ,11 /14) Human canonical CD157/Bst1 is an alternatively spliced isoform masking a previously unidentified primate-specific exon included in a novel transcript. 2017. Scientific Reports 7(1),15923. Q1. doi: 10.1038/s41598-017-16184-w.
4. García-Rodríguez S, et al., (last author: MZ). Increased expression of microRNA-155 in peripheral blood mononuclear cells from psoriasis patients is related to disease activity. J Eur Acad Dermatol Venereol.(2017)Feb;31(2):312-322. doi: 10.1111/jdv.13861. Q1
5. Rosal-Vela A, et al., (MZ, 11/13) Supporting data for the MS identification of distinct transferrin glycopeptide glycoforms and citrullinated peptides associated with inflammation or autoimmunity. Data Brief. (2016) Jan 11;6:587-602. doi: 10.1016/j.dib.2015.12.045.
6. Rosal-Vela A, et al. (MZ,11/13) Identification of multiple transferrin species in the spleen and serum from mice with collagen-induced arthritis which may reflect changes in transferrin glycosylation associated with disease activity: The role of CD38. (2016). J Proteomics.134:127-37. Q1
7. Rosal-Vela A, et al. (MZ, 9/10) Distinct serum proteome profiles associated with collagen-induced arthritis and complete Freund's adjuvant-induced inflammation in CD38^{-/-} mice: The discriminative power of protein species or proteoforms. (2015). Proteomics. 15(19):3382-93. Q1
8. Rios-Fernández R, et al.,(MZ, 5/6) Tocilizumab as an Adjuvant Therapy for Hemophagocytic Lymphohistiocytosis Associated With Visceral Leishmaniasis. (2016) Am J Ther. 23(5), E1193-E1196. Q3
9. García-Rodríguez, S., et al, (last author: MZ). Abnormal levels of expression of plasma MicroRNA-33 in patients with psoriasis. (2014) Actas Dermo-Sifiliograficas, 105 (5), 497-503...Q2.
10. García-Rodríguez, S. et al., (last author: MZ). Decreased plasma levels of clusterin in patients with psoriasis. (2013) Actas Dermo-Sifiliograficas, 104 (6), 497-503. Q2
11. Pavón, E.J., et al.,(MZ, 13/14) Increased CD38 expression in T cells and circulating anti-CD38 IgG autoantibodies differentially correlate with distinct cytokine profiles and disease activity in systemic lupus erythematosus patients. (2013) Cytokine, 62 (2), 232-243. Q2.
12. Garcia-Rodriguez S, et al., (last author: MZ). Increased gene expression of Toll-like receptor 4 on peripheral blood mononuclear cells in patients with psoriasis. (2013) J Eur Acad Dermatol Venereol., 27(2):242-250. Q1.
13. Garcia-Rodriguez, S., et al., (last author: MZ). Altered AKT1 and MAPK1 gene expression on peripheral blood mononuclear cells and correlation with T-helper-transcription factors in Systemic Lupus Erythematosus patients (2012) Mediators of Inflammation, 2012, art. no. 495934. Q2.

14. Arias-Santiago, S., et al.,(MZ, 9/11). Atheroma plaque, metabolic syndrome and inflammation in patients with psoriasis. (2012) *European Journal of Dermatology*, 22 (3), 337-344. Q2.
15. Pavón, E.J., et al.,(MZ, 12/13). Increased expression and phosphorylation of the two S100A9 isoforms in mononuclear cells from patients with systemic lupus erythematosus: A proteomic signature for circulating low-density granulocytes. (2012) *J. Proteomics*, 75 (6), 1778-1791. Q1.
16. Postigo, J., et al.,(MZ, 6/9) Mice deficient in CD38 develop an attenuated form of collagen type II-induced arthritis. (2012) *PLoS ONE*, 7 (3), art. no. e33534, . Q1.
17. Keszei, M., et al.,(MZ, 14/19) A novel isoform of the Ly108 gene ameliorates murine lupus. (2011) *Journal of Experimental Medicine*, 208 (4), 811-822. Q1.
18. Zumaquero, et al., (last author: MZ). Exosomes from human lymphoblastoid B cells express enzymatically active CD38 that is associated with signaling complexes containing CD81, Hsc-70 and Lyn. (2010) *Experimental Cell Research*, 316 (16),2692-2706. Q1.
19. Muñoz, P., et al., (MZ, 8/10). Antigen-induced clustering of surface CD38 and recruitment of intracellular CD38 to the immunologic synapse. (2008) *Blood*, 111 (7), 3653-3664. Q1.
20. Dominguez-Soto, A.,et al., (MZ, 9/12).The DC-SIGN-related lectin LSECtin mediates antigen capture and pathogen binding by human myeloid cells. (2007) *Blood*, 109 (12), 5337-5345. Q1.
21. Malavasi, F., et al.,(MZ, 9/16). CD38 and CD157 as receptors of the immune system: A bridge between innate and adaptive immunity. (2006) *Molecular Medicine*, 12 (11-12), 334-341. Q1.
22. Caparrós, E., et al., (MZ, 9/10). DC-SIGN ligation on dendritic cells results in ERK and PI3K activation and modulates cytokine production. (2006) *Blood*, 107 (10), 3950-3958. Q1.
23. Pavón, E.J., et a.,(MZ, 14/15). Proteomic analysis of plasma from patients with systemic lupus erythematosus: increased presence of haptoglobin alpha2 polypeptide chains over the alpha1 isoforms.(2006) *Proteomics*, 6 Suppl 1, S282-292. Q1.
24. Pavón, E.J., et al., (last author: MZ). Increased association of CD38 with lipid rafts in T cells from patients with systemic lupus erythematosus and in activated normal T cells (2006) *Molecular Immunology*, 43 (7), 1029-1039. Q2.
25. Muñoz, P., et al., (last author: MZ). CD38 Signaling in T Cells Is Initiated within a Subset of Membrane Rafts Containing Lck and the CD3- ζ Subunit of the T Cell Antigen Receptor. (2003) *Journal of Biological Chemistry*, 278 (50), 50791-50802. Q1.

PROYECTOS Y AYUDAS DE INVESTIGACIÓN

ACTIVOS

1.-Título: Biomarcadores proteómicos en células peritoneales y vesículas extracelulares circulantes en lupus: Alteraciones del acetiloma y del fosfoproteoma en ausencia de CD38. Ref: SAF2017-89801-R. AGENCY: M. de Economía, Industria y Competitividad; FINANCIACIÓN: 96.800 euros. // 3 years; until: 31.12.2020. PIs: PI1: Dr. Jaime Sancho; PI2: Dra. Mercedes Zubiaur. Institution: IPBLN-CSIC.

2.- Title: Plataforma de Proteómica, Genotipado y Líneas Celulares (PRB3). ProteoRed-ISCI. (PT17/0019/0010). AGENCY: M. de Economía y Competitividad. FINANCIACIÓN: 12.000,00 euros. From: 1.01.2018--31.12.2020. PI: Dr. Ignacio Casal (CIB-CSIC). PI of Associated team at IPBLN-CSIC: Dr. Jaime Sancho; and Role: Co-Investigador (CI): Mercedes Zubiaur.

FINALIZADOS

1.-Title: Plataforma de Recursos Biomoleculares y Bioinformaticos PRB2. REF: Exp. PT13/0001/0011, Instituto de Salud Carlos III (ISC III). M. de Sanidad. Dr. Jaime Sancho, IPBLN (PI) . Time: 01/01/14-01/01/16.. Role: Co-Investigador.

2.-Title: Analisis de la expresion diferencial y del fosfoproteoma en un modelo experimental de artritis reumatoide: Funcion de las proteinas CD38 y Art2. REF: SAF2011-27261, M. de Economia, Industria y Competitividad. Dr. Jaime Sancho, IPBLN, CSIC (PI). TIME: 01/01/12-12/31/14. Role: Co-Investigador.

3.-Title: Desarrollo de nuevos marcadores biologicos y de modelos animales de riesgo vascular en enfermedades autoinmunes e inflamatorias. REF: PC08-CTS-04046, Consejeria de Innovacion, Ciencia y Empresa. Junta de Andalucia. Dr. Jaime Sancho, IPBLN, CSIC (PI). TIME: 01/01/09-12/31/13. Role: Co-Investigador.

4.-Title: Estudio de las Alteraciones en la Senalizacion Intracelular y Busqueda de Biomarcadores. REF: SAF.2008-03685, M. Ciencia e Innovacion. Dr. Jaime Sancho, IPBLN, CSIC (PI). TIME: 01/01/08-12/01/10. Role: Co-Investigador.

5.-Title: Estudio de los mecanismos moleculares de las alteraciones en la senalizacion intracelular en procesos inflamatorios crónicos. REF: PI061502, ISCI- ISCI / Fondo Investigacion Sanitaria/ M. Sanidad y Consumo. Role: PI Zubiaur, Mercedes. TIME: 01/01/06-01/01/09.

6.-Title: Estudio de los mecanismos moleculares de las alteraciones en la señalización intracelular en enfermedades autoinmunes. REF: 200820I216, Proyecto Intramural. CSIC. M. de Ciencia e Innovacion. Role: PI Zubiaur, Mercedes. TIME: 10/01/08-12/31/09.

7.-Title: El Proteoma Redox Comparado. REF: P06-CVI-01611, Consejeria de Innovacion, Ciencia y Empresa. Junta de Andalucia. Dr. JA Barcenaa, UCO, Cordoba (PI) . TIME: 01/01/07-01/01/09. Role: Co-Investigador.

8.-Title: Papel de CD38 en la regulación de los procesos inflamatorios en enfermedades autoinmunes. REF: PI030389, M. de Sanidad y Consumo, Fondo de Investigacion Sanitaria. Role: PI Zubiaur, Mercedes. TIME: 01/01/04-01/01/06.

9.-Title: Papel de CD38 en la función de los linfocitos T que regulan procesos inflamatorios inducidos por infecciones y procesos tumorales. REF: 01/1073, ISCIII / Fondo Investigación Sanitaria/ M. Sanidad y Consumo. Role: PI Zubiaur, Mercedes. TIME: 01/01/01-01/01/03.

10.-Title: Estudio de la Inmunorregulación de los Linfocitos T de Pacientes con Lupus Eritematoso Sistémico. REF: 209/02, Consejería de Salud, Junta de Andalucía. PI: Dr. JL Callejas, HUSC, Granada. Role: Co-Investigador: Dr. Zubiaur, Mercedes. TIME: 01/01/02-01/01/03.

TESIS DIRIGIDAS RECIENTEMENTE

Supervisor of UGR Degree Thesis and Practical training; Biology,

2015, Ms. Veronica Prados Maniviesa;

2016, Ms. Kistiñe Astigarraga

2017, Ms. Carolina Franco Herrera;

2019, D^a Maria Torres Saez

TRABAJOS FIN DE MÁSTER DIRIGIDOS

2006 Dña. Esther C. Zumaquero

2010, D. Rubén Perandrés

2013, D. Carlos Alberto Casañas

2014, D. Carlos Bringas Roldan

2015, D. Jose Diaz Cuellar

2016, D^a Veronica Preados Maniviesa

2017, D. Jose Angel Robles Guirado

2018, D. Miguel Angel Palacios Pedrero

2019 Dña. Africa Martinez Blanco