MINISTERIO DE CIENCIA, INNOVACIÓN Y UNIVERSIDADES

CURRICULUM VITAE (maximum 4 pages)

CV date	04/09/2018

Part A. PERSONAL INFORMATION

First and family name	José R. Regueiro		
ID number	50417137X	Age	60
Researcher numbers	Researcher ID	B-5499-2014	
	Orcid code	0000-0001-8442-7762	

A.1. Current position

Name of University	Universidad Complutense de Madrid (UCM)		
Department	Immunology, Ophthalmology and ENT / School of Medicine		
Address and Country	c/ Dr. Severo Ochoa 9, 28040 Madrid, Spain		
Phone number	+34913941631	E-mail	regueiro@med.ucm.es
Current position	Research and PhD Vice Dean / Full Professor of Immunology	From	June 13, 2018 / Nov 2, 2009
UNESCO codes	2412, 3207.10, 2415		
Keywords	T lymphocyte, congenital immunodeficiencies, TCR		

A.2. Education

PhD	University	Year
Biology	Complutense University	1985
Immunology	Complutense University	2004

A.3. Scientific research performance

Number of sexenios* / last granted on	6 / June 2017
Total number of citations Web of Science	1,537
Average number of citations during the last five years	60
Total number of publications in Q1 / D1 (%)	44 / 37 (84)
h-index Web of Science / Google Scholar	22 / 25
Theses supervised (total / last 10 years)	19 / 7

***** Government-approved six-year research periods

Part B. CV SUMMARY *(max. 3500 characters, including spaces)*

Scientific trajectory /technical achievements

More than 30 years of research on both sides of the immune synapse (HLA first, TCR later). More than 20 research projects funded by national and international agencies, most as PI. Nearly 100 scientific articles published in international journals, including N Eng J Med, Lancet and Nat Immunol. 19 PhD theses supervised, all with the highest rating, 7 with UCM and / or Doctor europeus awards. More than 25 trained students and postdocs who hold positions in the scientific, academic, health or technology fields. Recruited researchers: 10 Ramón y Cajal and 3 Juan de la Cierva postdocs since 2006.

In 1986 we described the first selective primary immunodeficiency (PID) of T lymphocytes, which we later proved to be due to mutations in CD3 gamma, a chain of the T lymphocyte receptor for antigen (TCR). This allowed us to analyze its role in T selection and in TCR structure, dynamics and signaling, and to develop diagnostic algorithms (Garcillán 2015) and gene therapy (Pacheco-Castro 2003) for similar pathologies. We have demonstrated unexpected properties for CD3 chains, such as their differential role in humans versus mice (Recio 2007), including its differential stoichiometry in alpha/beta vs gamma/delta TCR isotypes (Siegers 2007). We have generated in vitro PID cell models (Martín-Fernández 2005) and characterized in them the first complete Bcl-10 (Torres 2014) or IRF4 PID (Bravo 2018), partial CD3 delta PID (Gil 2011, Garcillán 2014), as well as a new CD247 PID (Marín 2017) and cellular aspects of complement PID (Jiménez-Reinoso 2018).

Interests and medium / long-term aims of research line

T lymphocyte and TCR physiopathology, especially of their congenital PID, a field we have pioneered. We study in vitro (human cell lines) and in vivo (mice) PID models using cellular biology techniques (flow cytometry, cultures), molecular biology and biochemistry to

understand the pathophysiology of alpha/beta vs gamma/delta T lymphocytes. We have observed that double haploinsufficiency of CD3 gamma and delta in mice selectively eliminates IFN-gamma-producing gamma/delta T lymphocytes (Muñoz-Ruiz 2016) by an undefined mechanism, which is relevant to malaria susceptibility.
We have also studied the role of accessory signals in lymphocyte biology, such as those relayed by GITR, which selectively amplifies Treg (Liao 2010) or SLAM / CD150, which besides being a bacterial sensor (Berger 2010), can enrich TCR signals and regulate T lymphocyte differentiation and function. We are currently studying how complement proteins (C3, CD46, CFI) impact T cell function using primary and immortalized patient-derived T- and B- cell lines.

Part C. RELEVANT MERITS (last 10 years)

C.1. Publications

Journal articles / reviews (10 most relevant, *last, **co-last, authors/position when >10)

1. **Rowe JH, et al 19/18. *Patients with* CD3G *mutations reveal a role for human CD3γ in Treg diversity and suppressive function*. **Blood**. 131(21):2335-2344 (2018). IF15 D1. *Human CD3γ deficiency impairs surface TCR expression and signaling and thus T-cell development, selection, and fate, leading to high self-reactive CD4+ T cells and low and impaired Tregs, which may cause the autoimmunity features of this condition.*
2. *Marin AV, Cárdenas PP, Jiménez-Reinoso A, Muñoz-Ruiz M, **Regueiro JR**. *Lymphocyte integration of complement cues*. **Semin Cell Dev Biol.** pii: S1084-9521(17)30135-0 (2018) IF6 D1. *Reviews current data, views and puzzles on the emerging topic of regulation of lymphocytes by complement proteins or fragments in humans and mice.*
3. Bravo García-Morato M, et al 29/27. *New human combined immunodeficiency caused by interferon regulatory factor 4 (IRF4) deficiency inherited by uniparental isodisomy*. **J Allergy Clin Immunol.** 141(5):1924-1927.e18 (2018) IF13 D1. *Human IRF4 deficiency caused lethal severe dermatitis, agammaglobulinemia, and eosinophilia with normal lymphocyte counts, despite a reduction in memory T- and B-cells, and severely reduced Treg, Th17, and Tfh cells.*
4. *Jiménez-Reinoso A, et al 16/16. *Human plasma C3 is essential for the development of memory B, but not T, lymphocytes*. **J Allergy Clin Immunol.** 141(3):1151-1154.e14 (2018). IF13 D1. *Side-by-side study of B- and T-cell features in the very rare conditions C3 and factor I deficiencies. Plasma C3 is shown to be essential for the development of memory B, but not T, lymphocytes in a plasma C3 level–dependent fashion. Very low plasma C3 levels do not preclude the expression of intracellular C3 fragments in lymphocytes.*
5. Blázquez-Moreno A, Pérez-Portilla A, Agúndez-Llaca M, Dukovska D, Valés-Gómez M, Aydogmus C, Ikinciogullari A, **Regueiro JR**, Reyburn HT. *Analysis of the recovery of CD247 expression in a PID patient: insights into the spontaneous repair of defective genes*. **Blood**.130 (10):1205-1208 (2017). IF15 D1. *Detailed analysis of spontaneously arising somatic mutations that recover CD247, and thus TCR expression, in a CD247-deficient patient. Genetic variation in CD247 is frequent and shared with other PID genes in which reversion occurs. We suggest that the intrinsic mutability of a gene determines the likelihood of the emergence of somatic revertants on which selection subsequently acts.*
6. **Marin AV et al 23/24. *Primary T-cell immunodeficiency with functional revertant somatic mosaicism in CD247*. **J Allergy Clin Immunol.** 139:347-349 (2017). IF13 D1. *Mild lymphopenia and functional revertant somatic mosaicism should not confound the fact that CD247 deficiency is a very severe condition that requires urgent transplantation, but is easy to diagnose by intracellular flow cytometry or the surface TCR phenotype of obligate carriers.*
7. Muñoz-Ruiz M, Ribot JC, Grosso AR, Gonçalves-Sousa N, Pamplona A, Pennington DJ, **Regueiro JR**, Fernández-Malavé E/Silva-Santos B. *TCR signal strength controls thymic differentiation of discrete proinflammatory γδ T cell subsets*. **Nat Immunol**. 17: 721–727 (2016). IF 22 D1. *TCR signal strength within specific thymic developmental windows is a major determinant of the generation of proinflammatory gd T cell subsets and their impact on pathophysiology.*
8. *Garcillán B, et al 11/11. *γδ T lymphocytes in the diagnosis of human TCR immuno-deficiencies*. **Front Immunol** 6: 20 (2015). IF6 Q1. *Pooling our unpublished work and previous studies, we proposed some technical tricks to identify γδ T cells in TCR PID patients and made the point that their careful analysis can help to inform a rapid differential diagnosis, with clinical benefit. In turn, the results shed light on γδ T cell biology and TCR structure.*

9. Torres JM, et al 22/19. *Inherited BCL10 deficiency impairs hematopoietic and non-hematopoietic immunity*. **J Clin Invest** 124:5239–48 (2014). IF13 D1. *We characterized a first case of autosomal-recessive, complete BCL10 (B cell CLL/lymphoma 10) deficiency in a child with broad PID, including defects of both hematopoietic and nonhematopoietic immunity, indicating that inherited BCL10 deficiency should be considered in patients with combined immunodeficiency with B cell, T cell, and fibroblast defects.*
10. *Garcillán B, Mazariegos MS, Fisch P, Res PC, Muñoz-Ruiz M, Gil J, López-Granados E, Fernández-Malavé E and **Regueiro JR**. *Enrichment of the rare CD4+ γδ T cell subset in patients with atypical CD3δ deficiency.* **J Allerg Clin Immunol.** 133: 1205-8 (2014). IF12 D1. *Atypical CD3delta deficiency leads to reduced surface TCR expression and preserved gd, but not ab, T-cell numbers with high CD4+ gd T cells, supporting low TCR-dependence for positive selection of CD4⁻ gd T cells and disrupted negative selection of CD4+ gd T cells.*

Selected books and chapters

1. **Regueiro** JR, Alsina L. *Inmunodeficiencias primarias y secundarias*. In: *Farreras Rozman, Medicina Interna*. 18ª Edition. Elsevier Spain. Barcelona pp2587-95 (2016). ISBN: 9788490229965.
2. **Regueiro** JR, Recio MJ. 11. T-Cell–Receptor Complex Deficiency. In: Primary immunodeficiency diseases, a molecular and genetic approach, 3rd edition. HD Ochs, CIE Smith, JM Puck eds. Oxford University Press pp 156-162 (2013). ISBN 9780195389838
3. **Regueiro** JR, López-Larrea C, González S, Martínez-Naves E*. Inmunología: biología y patología del sistema inmunitario. Editorial Médica Panamericana*, Madrid. 4ª ed. (2010, 2014) ISBN 9788498350036. Translated into Italian (2011) and Portuguese (2014). 5th edition in preparation (2019).

C.2. Research projects and grants (last 7)

1. The Complement system in health and disease (Complemento II-CM), CAM, CIB CSIC, FJD, UCM, HULP, HU12O, 2018-21, 828.092 €, Rodriguez de Córdoba S (Regueiro JR), Ref. B2017/BMD3673.
2. Excellence network for complement in health and disease, MINECO, Univ. Complutense, 2/2017-2/2019, 20.000 €, Rodríguez de Córdoba S (Regueiro JR), Ref. SAF2016-81876-REDT
3. Surface and intracellular T lymphocyte activation physiopathology, MINECO 2014, Regueiro JR & Fdez.-Malavé E, Univ. Complutense, 01/2015-12/2018, 275.000€, Ref. SAF2014-54708-R
4. Excellence network for cancer immunotherapy (REINCA), MINECO, Univ. Complutense, 10/2014-10/2016, 32.000 €, Lasarte JJ (Regueiro JR), Ref. SAF2014-53563-REDT
5. Fisiopatología de la activación del linfocito T, MICINN 2011, Regueiro JR, Univ. Complutense, 2012-2015, 193.600 € + 1 FPI student, Ref. SAF2011-24235
6. Fisiopatología del TCR/CD3, ISCIII 2008, Regueiro JR, Univ. Complutense, 2009-2011, 164.000 €, Ref. PI080921
7. Fisiopatología del complejo TCR/CD3, MEC 2006, Regueiro JR, Univ. Complutense, 2007-2009, 110.000 €, Ref. BFU2005-01738/BMC

C.3. Contracts

Study to assess the pharmacokinetics, safety and immunogenicity of single doses of Belatacept (BMS-224818) administered subcutaneously to healthy subjects. Bristol-Myers Squibb. 2006-7. Regueiro JR. 46.000€

C.4. Patents

C.5. Positions, institutional responsibilities

2018. Research and PhD Vice Dean, School of Medicine, Universidad Complutense.
2012. Head, Dept. of Microbiology, School of Medicine, Universidad Complutense, Madrid.
2012. President, Spanish Society for Immunology.
Coordinator for the three main public Universities in Madrid of the following programs:
2009. Joint Master in Immunology
2007. Joint Immunology PhD
1995. Head, Center of Immunological Techniques. Universidad Complutense. Madrid.

1993. Associate Professor of Immunology, School of Medicine, Universidad Complutense
1989. Associate Professor of Immunology, School of Medicine, University of Valladolid. Board: Martínez-A C, López de Castro JA, Poljack R, Stutman O, Coutinho A, Rubinstein P, Palacios R, Parkhaus M.
1986. Head, Cellular and Humoral Immunology Laboratory. Dept. of Immunology (Head A. Arnaiz-Villena), Hospital 12 de Octubre, Madrid.

C.6. Participation in international committees and representations

IER (Invited External Review) of scientific proposals for the ERC (European Research Council), proposed by the LS6 (Life Sciences 6) panel of experts of the Consolidator Grant 2018 Call, chaired by Dr. Caetano Reis e Sousa.
Editorial Board. Primary Immunodeficiencies, a specialty of Frontiers in Immunology. ISSN 1664-3224, IF6, Frontiers, from 2015, Review Editor
Editorial Board. Journal of Clinical Immunology ISSN 0271-9142 IF3,2, Springer (Clinical Immunology Society), Jul 2015-2017.
Associate Editor LymphoSign Journal, The Journal of Inherited Immune Disorders. Canadian Science Publishing, from 2013.
Scientific Expert Committee for topic 8 (health) for ERANET LAC joint calls, Network of the European Union and the Community of Latin American and Caribbean States on Joint Innovation and Research Activities funded by the European Commission (2013-2017), Translational research and innovation projects on infectious diseases, 2016
Scientific advisory board for the Centre of Chronic Immunodeficiency (Freiburg). Freiburg University. Maria Blettner, Mainz; Andrew Cant, Newcastle; Stephan Meuer, Heidelberg; David Nadal, Zurich; Martina Prelog, Würzburg; José Regueiro, Madrid; Antonius Rolink, Basel; Adrian Thrasher, London. Second funding period 2013-18.
Project evaluator for the German Federal Ministry of Education and Research. DFG (Deutschen Forschungsgemeinschaft). From 2013.
Review board for Integrated research and treatment centres. German Federal Ministry of Education and Research. Klaus Berger, Münster; Andrew Cant, Newcastle; Alain Fischer, Paris; Hans-Jürgen Laws, Düsseldorf; Hans Messner, Toronto; Susan Pierce, USA; Martina Prelog, Würzburg; José Regueiro, Madrid; Miriam Wittmann, Leeds; Thomas Voit, Paris.
Evaluator. European commision-funded proyects *for* 5th-7th Framework Programmes. Mid-term review (2003). FP7 Health Innovation (2012). Since 2000.
Evaluator of *Programa Nacional de Ciencias Básicas*. Colciencias (Colombia). Immunology proyects. 2004 and 2011.
Reviewer of Clin Exp Immunol, ISSN 1365-2249, IF3. Wiley, Bristish Society for Immunology. From 2008.

C.7. Memberships of scientific societies

1994-present: European Society for Immunodeficiencies (ESID).
1986-present: Sociedad Española de Inmunología (SEI).

C.8. Three selected PhD thesis

1. **Miguel Muñoz-Ruiz.** Role of the TCR in effector γδ T cell development and function, Complutense Univ. School of Medicine, 2009-2016. Nat Immunol 17:721-7 (2016). **European mention** (stayed with Bruno Silva-Santos, Lisboa and Adrian C Hayday, London) and **UCM PhD award.** Dra. Menéndez-Fundación LAIR best thesis award. Currently postdoc in London (The Francis Crick Institute, c/o Adrian C Hayday)
2. **Beatriz Garcillán.** Role of CD3γ and CD3δ chains in human TCR expression and function, Complutense Univ. School of Medicine, 2008-2014. J Allergy Clin Immunol 133: 1205-8 (2014). **European mention** (stayed with Pieter C. Res, Amsterdan and W Schamel, Freiburg) and **UCM PhD award**. Currently postdoc in Melbourne (The Peter Doherty Institute for Infection and Immunity, c/o Fabienne Mackay).
3. **José Carlos Rodríguez-Gallego**, Primary immunodeficiencies of IRAK-4 (IL-1 Receptor-Associated Kinase-4) and MyD88 (Myeloid Differentiation primary response gene 88), Complutense Univ. School of Medicine, 2004-2010. Science 321:691-696 (2008). **UCM PhD award.** Currently head of the Cellular Immunology lab at Hospital Univ. de Gran Canaria Doctor Negrín, Spain.