

## Part A. PERSONAL INFORMATION

<b>CV date</b>	Oct 27, 2021
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First and family name	José R. Regueiro		
ID number	50417137X	Age	63
Researcher numbers	Orcid code	<a href="https://orcid.org/0000-0001-8442-7762">0000-0001-8442-7762</a>	
	SCOPUS Author ID	7005510950	
	WoS Researcher ID	<a href="https://www.researcherid.com/rid/B-5499-2014">B-5499-2014</a>	

### 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	<a href="mailto:regueiro@med.ucm.es">regueiro@med.ucm.es</a>
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, immunodeficiencies, TCR, cancer immunotherapy		

### A.2. Education

PhD	University	Year
Biology	Complutense University	1985
Immunology*	Complutense University	2004

\*Ministry of Health-certified immunologist trained at Hospital 12 de Octubre, Madrid

### A.3. Scientific research/academic performance (Oct 2021)

Number of sexenios* / last granted on	6 / June 2017
Total number of citations <a href="#">Web of Science</a> / <a href="#">Google Scholar</a>	1.990 / 3.086
Average number of citations during the last full five years WoS	100
Total number of publications in Q1 / D1 (%)	40 / 38 (95)
h-index <a href="#">Web of Science</a> / <a href="#">Google Scholar</a> / <a href="#">Scopus</a>	24 / 28 / 23
Theses supervised (total / last 10 years)	21 / 6
Number of quinquenios** / last granted on	8 / June 2019

\* Government-approved six-year research periods

\*\* University-approved five-year academic 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. More than 100 scientific articles published in international journals, including N Eng J Med, Lancet and Nat Immunol. 21 PhD theses supervised, most 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: 11 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.

Last, our exposure to cancer immunotherapy (Regueiro, board member of <https://getica.org/> and invited speaker to several cancer immunotherapy courses for clinicians since 2016) has spurred our interest in designing specific immunotherapies for rare T cell lymphomas (Sézary syndrome), for which our long-term expertise in HLA and TCR biology may be useful.

## Part C. RELEVANT MERITS (last 10 years)

### C.1. Publications

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

1. \*Garcillán B, et al 13/13. *CD3G or CD3D knock-down in mature, but not immature, T lymphocytes similarly cripples the human TCR $\alpha\beta$  complex.* **Front Cell Dev Biol.** 2021 Jun 25; 9:608490. IF 6,7 Q1.
2. \*Marin AV, Cárdenas PP, Jiménez-Reinoso A, Muñoz-Ruiz M, **Regueiro JR.** *Lymphocyte integration of complement cues.* **Semin Cell Dev Biol.** 85:132-142 (2019) IF6 D1.
3. \*\*Rowe JH, et al 19/18. *Patients with CD3G mutations reveal a role for human CD3 $\gamma$  in Treg diversity and suppressive function.* **Blood.** 131(21):2335-2344 (2018). IF15 D1.
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.
5. Blázquez-Moreno A, Pérez-Portilla A, Agúndez-Llaca M, Dukovska D, Valés-Gómez M, Aydogmus C, Ikinogullari 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.
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.
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  $\gamma\delta$  T cell subsets.* **Nat Immunol.** 17: 721–727 (2016). IF22 D1.
8. \*Garcillán B, et al 11/11.  *$\gamma\delta$  T lymphocytes in the diagnosis of human TCR immuno-deficiencies.* **Front Immunol** 6: 20 (2015). IF6 Q1.
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.
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+  $\gamma\delta$  T cell subset in patients with atypical CD3 $\delta$  deficiency.* **J Allergy Clin Immunol.** 133: 1205-8 (2014). IF12 D1.

#### Selected books and chapters

1. **Regueiro JR**, Alsina L. *Inmunodeficiencias primarias y secundarias.* In: *Farreras Rozman, Medicina Interna.* 18<sup>a</sup> 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**, Martínez-Naves E, López-Larrea C, González S. *Inmunología: biología y patología del sistema inmunitario.* Editorial Médica Panamericana, Madrid. 5th ed. (2022) ISBN 9788491104209. Translated into Italian (2011) and Portuguese (2014).

### C.2. Research projects and grants (last 7, \*PI)

1. \*Novel comprehensive immunotherapy to specifically target the malignant clone in Sézary syndrome, an ultra-rare cancer of mature T lymphocytes, Proy estratégicos AECC 2020, i+12, 2021-3, 300.000€, Regueiro, 20, Ref. PROYE20084REGU / 4180112



2. \*Lymphocyte integration of TCR and complement cues, MICIU, Univ. Complutense, 01/2019-12/2021, 270.000€ al grupo + 56.700€ a la UCM + 1 FPI student, Regueiro JR & Fdez.-Malavé E, 6, Ref. RTI2018-095673-B-I00
3. The Complement system in health and disease (Complemento II-CM), CAM, CIB CSIC, FJD, UCM, HULP, HU12O, 2018-21, 828.092 €, Rodríguez de Córdoba S (Regueiro JR PI UCM), Ref. B2017/BMD3673.
4. Excellence network for complement in health and disease, MINECO, Univ. Complutense, 2/2017-2/2019, 20.000 €, Rodríguez de Córdoba S (Regueiro JR PI UCM), Ref. SAF2016-81876-REDT
5. \*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
6. \*T lymphocyte activation physiopathology, MICINN 2011, Regueiro JR, Univ. Complutense, 2012-2015, 193.600 € + 1 FPI student, Ref. SAF2011-24235
7. \*TCR physiopathology, ISCIII 2008, Regueiro JR, Univ. Complutense, 2009-11, 164.000 €, Ref. PI080921

### **C.3. Contracts, technology transfer (\*PI)**

1. \*Desarrollo de una nueva terapia para el tratamiento de enfermedades del sistema inmune, Agencia de Certificación en Innovación Española, Regueiro JR, Univ. Complutense, 2018-9, 1.150 €, Artículo 83, certificación de tipo Contenido y 1ª Ejecución según el RD 1432/2003,
2. \*Diseño y desarrollo de anticuerpos con capacidad inmunoadyuvante para el tratamiento del cáncer, DNV GL Business Assurance España, Regueiro JR, Univ. Complutense, 2018, 97 €, Artículo 83, revisión técnica como experto 4D (comité externo).

### **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.  
1995. Head, Central Facility 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 committees and representations (selection last 5 years)**

#### **International**

1. 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.
2. Editorial Board. Primary Immunodeficiencies, a specialty of Frontiers in Immunology. ISSN 1664-3224, IF 2020 6,4, Jul 2015-, Review Editor
3. Editorial Board. J Clin Immunol ISSN 0271-9142, IF 2020 6,8, Springer (Clin Immunol Society), Jul 2015-
4. Project evaluator for the Fondation pour la Recherche Médicale (FRM, <https://www.frm.org/en>), a French private foundation that supports excellence in biomedical research. 2020-2021
5. Scientific advisory board for the Centre of Chronic Immunodeficiency (Freiburg). Freiburg University. Second funding period 2013-18.
6. Peer review activity (IF 2020, certified reviews): New Eng J Med (75, 1), J Clin Immunol (7, 5), Front immunol (6, 7), Rheumatology (6, 1), Oncotarget (5, 1), Eur J Immunol (4, 4), Mol immunol (4, 4), Biomed Pharmacother (4, 1), Clin Dev Immunol (4, 1), J Pediatrics (4, 1), Int Immunopharmacol (4, 1), J Neuroimmunol (3, 1), World J Stem Cells (3, 1).

#### **National**

1. Colaborador del área BME para el seguimiento de recursos humanos (Programas: ayudas predoctorales FPI, doctorados industriales, JdIC, RyC, PEJ, Inncorpora, Emplea, Técnicos de

apoyo, Torres Quevedo), División de coordinación, evaluación y seguimiento científico-técnico, Agencia Estatal de Investigación, MICIU (2019).

2. Comité de ciencias médicas y de la salud (vocal), Unibasq (agencia de calidad del sist. universitario vasco). Temas: acreditación de profesores permanente; ikertramos (sexenios de no permanentes), 1/2015- 12/2017

## C.7. Memberships of relevant scientific societies

2016-: Spanish Group for Cancer Immuno-Biotherapy (GETICA). Board 2016-9

1994-: European Society for Immunodeficiencies (ESID).

1986-: Sociedad Española de Inmunología (SEI). President 2012-16

## C.8. Three selected PhD thesis (out of 21 since 1999, 6 in the last 10 years, +2 in progress)

1. [Miguel Muñoz-Ruiz](#). Role of the TCR in effector  $\gamma\delta$  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 immunology thesis award (2017). Currently postdoc in London (The Francis Crick Institute, c/o Adrian C Hayday).
2. [Beatriz Garcillán](#). Role of CD3 $\gamma$  and CD3 $\delta$  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, Amsterdam and W Schamel, Freiburg) and **UCM PhD award**. After a postdoc in Melbourne (The Peter Doherty Institute for Infection and Immunity, c/o Fabienne Mackay), she is currently Medical Scientific Liaison in Janssen.
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.

## C.9. Scholarships for students (last 5 years)

### a) *Programas nacionales*

FPU MICIU; FPU19/03136; Área Biomedicina; Fernández Megino, Rebeca; 01/11/20-31/10/24. PDIBM FPI MICIU; PRE2019-088150; Carlos Daniel Chacón Arguedas; 12/2020 - 24 PDBioqBioMolecBiomed FPI MINECO; BES-2012-055054; Jiménez Reinoso, Anaïs; Dic 2012-Nov 2016 PDBBMB FPU MICINN; AP2008-00324; Garcillán Goyoaga, Beatriz; 10/8/2009 - 10/8/2013 PDInmunología

### b) *Programas CCAA*

CAM contrato; S2017/BMD-3673; Lucientes Continente, Laura; 2018-22

CAM contrato; PEJD-2017-POST/BMD-4917; Jiménez-Reinoso Anaïs; Mar 2017-2018

CAM contrato; PEJ-2017-AI/BMD-6205; Fernández Megino, Rebeca; Mar 2018-20, 45.000€ (contrato de ayudante de investigación financiado por el Fondo Social Europeo a través del Programa Operativo de Empleo Juvenil y la Iniciativa de Empleo Juvenil (YEI) de la CAM)

### c) *Programas locales*

FPU UCM; Medrano Garcia, Sandra; May 2019-23 PDIBM. Tesis defendida en Oct 2021, director E Fdez.

Ayuda post-MIR imas12; Guillen Vera, Daiana; Feb 2018-19

FPU UCM; Briones Contreras, Alejandro; Feb 2017-20 PDIBM (programa de doctorado de Inv. Biomédica)

FPI UCM-Harvard; CT46/15; Marín Marín, Ana V; May 2016-20 PDBBMB