

**Part A. PERSONAL INFORMATION**

		<b>CV date</b>	2-02-2020
First and Family name	Maria Esther Lafuente Duarte		
Researcher numbers	Researcher ID	K-5684-2014	
	Orcid code	0000-0001-8466-1022	

**A.1. Current position**

Name of University/Institution	Universidad Complutense de Madrid		
Department	Inmunología, Oftalmología y Otorrinolaringología		
Address and Country	Pza Ramón y Cajal, s/n, Madrid, Spain		
Phone number	E-mail	<a href="mailto:melafuente@med.ucm.es">melafuente@med.ucm.es</a>	
Current position	Associate Professor of Immunology	From	11/07/2011
Espec. cód. UNESCO	2412-Inmunología		
Palabras clave	Epitope, Antigen, MHC, T-cell, APC, Phagocytosis, Cell Adhesion		

**A.2. Education**

Year	University	Degree	Title
1990	U. Granada	First degree	Biology (Biochemistry)
1996	U. Granada	PhD	Biology (Bioche &. Mol. Biol)

**A.3. JCR articles, h Index, thesis supervised**

- Six year research stretches: 3: Last 2009-2014.
- 5 year teaching track 2 Last 2011-2016
- Thesis supervised 2: 2012 and 2017
- Thesis ongoing 2:
- Publications (PubMed): 32 (25 art., 5 rev.)
- Total citations (G. Scholars) 2015
- Total CITATION Scopus 1517
- First quartile (Q1): 16
- First decile (D1): 7
- h-index (G. Scholars) 19
- H index (Scopus) 17

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

PhD in Biology by the University of Granada, Spain, I carried out my doctoral thesis characterizing the ItrgpE protein and its function in multidrug resistance in *Leishmania tropica* (09 / 1991-06 / 1996), at the Parasitology Institute López Neyra, CSIC, Granada.

My research training was completed with different pre-doctoral and postdoctoral stays at internationally renowned centers such as the Hebrew University (Israel), University of Cambridge (UK), Imperial College of London (UK), CBMSO (Madrid), Dana Farber Cancer institute-Harvard (MA, USA) or Cancer Center at MGH-Harvard (MA, USA). My postdoctoral training was multidisciplinary studying internal translation of proteins (IRES) in *S. pombe*, in the Departments of Biochemistry of the University of Cambridge-and the University of Kent England, UK (09 / 1996-05 / 1998 and the IRES structure of HCV virus at CBMSO Madrid (01 / 1999-12 / 2000).

At Dana-Farber Cancer Institute (Boston, MA, USA) (2001-2005) I characterized a new protein that we called RIAM involved in cell adhesion, from this moment I started my career as an independent researcher studying the function of the protein RIAM in leukocytes during phagocytosis and antigenic presentation In June 2006 I returned to Spain with a Ramón y Cajal contract, joining the Department of Microbiology I- Immunology of the School Medicine of the U. Complutense of Madrid where I have established a research group studying leukocyte adhesion, phagocytosis and collaborating with other groups such as those of Dr. Pedro. A. Reche (UCM) interested in the

antigenic presentation and with Dr. Carlos Cabañas (CSIC) interested in the study of adhesion molecules modulating proteins. Since July -2011 I am Associated Professor of the University (PTU), Immunology area in the Department of Immunology, Ophthalmology and ORL, School Medicine of the U. Complutense of Madrid.

### Main scientific achievements

I have a continuous scientific production that stands out for its impact. In total I have published 31 original articles / reviews that exceed 1667 citations (source SCOPUS, WOS) (index H = 16 Scopus). The production is multidisciplinary highlighting the performed in Immunology and Molecular Biology. Among the most important scientific achievements of my career is the discovery and characterization of a new protein called RIAM regulating the function of integrins that plays an important role in adhesion and leukocyte function (Lafuente EM, Dev Cell 2004, Medrano I et al, 2013) with a relevant role in cancer and involved in inflammatory diseases.

### Scientific interests

My short and long-term scientific interests are focused in A) discovery of immunotherapeutic molecules B) The regulatory mechanisms of oral mucosal epithelia, as innate immunity condition the response of adaptive immunity. C) Molecular mechanism that regulate cell adhesion and its implication in Immunological responses

## Part C. RELEVANT MERITS

### C.1. Publications (including books)

1. Quinzo, M.J., **Lafuente, E.M.**, Zuluaga, P., Flower, D.R., Reche, P.A. Computational assembly of a human Cytomegalovirus vaccine upon experimental epitope legacy. **2019** BMC Bioinformatics 20,476
2. Molero-Abraham M, Sanchez-Trincado JL, Gomez-Perosanz M, Torres-Gomez A, Subiza JL, **Lafuente EM**, Reche PA. Human Oral Epithelial Cells Impair Bacteria-Mediated Maturation of Dendritic Cells and Render T Cells Unresponsive to Stimulation. Front Immunol. **2019** Jun 28;10:1434. doi: 10.3389/fimmu.2019.01434. eCollection 2019.
3. J Alonso-Padilla, **EM Lafuente**, PA Reche . Computer-aided design of an epitope-based vaccine against epstein-barr virus. Journal of immunology research 2017 Volume 2017, 2017, Article number 9363750. Citations 7
4. Patsoukis N, Bardhan K, Weaver JD, Sari D, Torres-Gomez A, Li L, Strauss L, **Lafuente EM**, Boussiotis VA. (2017). The adaptor molecule RIAM integrates signaling events critical for integrin-mediated control of immune function and cancer progression. Sci Signal. Aug 22;10(493). pii: eaam8298. **Q1 (37/292)** BIOCHEMISTRY & MOLECULAR BIOLOGY Citations 1.

**Brief resume:** RIAM is a protein discovered by our group in 2004. Since its implication on cell adhesion was describe by us this protein has receive great attention by the scientific community. Here we review its role in innate and adaptive immunity and the implication in cancer .

5. Molero-Abraham M, Glutting JP, Flower DR, **Lafuente EM**, Reche PA. (2015) EPIPOX: Immunoinformatic Characterization of the Shared T-Cell Epitome between Variola Virus and Related Pathogenic Orthopoxviruses. J Immunol Res.;2015:738020. **Q2 63/151** Immunology. Citations 3

**Brief resume:** Here we used Variola virus genomes available on data base to characterize the entire T-cell epitome. We identified 124 proteins shared between various species of pathogenic orthopoxviruses and targeted them for T-cell epitope prediction obtaining We recognized 8,106, and 8,483 unique class I and class II MHC-restricted T-cell epitopes shared by all orthopoxviruses. We developed EPIPOX an immunological resource designed to facilitate reverse vaccinology.

6. Raquel Reyes, Alicia Monjas, María Yáñez-Mó, Giulia Morlino, Alvaro Gilsanz, Yesenia Machado, **Esther Lafuente**, Peter Monk, Francisco Sánchez-Madrid and Carlos Cabañas. (2015). Different states of integrin LFA-1 aggregation are controlled through its association with tetraspanin CD9. *Biochimica et Biophysica Acta (BBA)*. 1853 (10), pp. 2464-2480 **Q1 (50/290)** BIOCHEMISTRY & MOLECULAR BIOLOGY. Citations 10

**Brief resume:** here we demonstrate that the tetraspanin CD9 regulates the activity of LFA-1 a beta 2 integrin involved in leukocyte adhesion by regulating its clustering in the cell surface but not its affinity for the ligand ICAM-1 .

7. Molero-Abraham M, Lafuente EM, Flower DR & **Reche P** . (2013) Selection of conserved epitopes from hepatitis C virus for pan-population stimulation of T-cell responses. *Clin Dev Immunol.*, 2013,601943. (IF: 2.94; **Q2**: Immunology, 67/144)

**Brief resume:** In this article, we designed an optimal epitope-based vaccine against HCV consisting of conserved and experimentally defined CD8 T cell epitopes that would induce protective response in any individual regardless of their genetic background. In addition, we implemented a web server at <http://imed.med.ucm.es/epimhc>, to identify optimal epitope-vaccine ensembles.

8. Medraño-Fernandez I, Reyes R, Olazabal I, Rodriguez E, Sánchez-Madrid F, Boussiotis VA, Reche PA, Cabañas C, **Lafuente EM** (2013). RIAM (Rap1-interacting adaptor molecule) regulates complement-dependent phagocytosis. *Cell Mol Life Sci*. 2013 Jul;70(13):2395-410. **Q1 (34/292)** BIOCHEMISTRY & MOLECULAR BIOLOGY Citations 11

**Brief resume:** RIAM is a protein discovered by our group in 2004 as a protein involved in cell adhesion. In this article we clearly demonstrate that RIAM regulates complement receptor CR3 an integrin involved in phagocytosis revealing the signaling pathway involved in Outside signaling to CR3

9. Gilsanz A, Sánchez-Martín L, Gutiérrez-López MD, Ovalle S, Machado-Pineda Y, Reyes R, Swart GW, Figdor CG, **Lafuente EM**, Cabañas C. (2013). ALCAM/CD166 adhesive function is regulated by the tetraspanin CD9. *Cell Mol Life Sci*. Feb;70(3):475-93. **Q1(34/292)** BIOCHEMISTRY & MOLECULAR BIOLOGY . Citations 26

**Brief resume:** The cell adhesion molecule ALCAM is involved in APC-T cell interaction however little is known about its regulation. Here we describe that the tetraspanin CD 9 regulates ALCAM function by regulating both molecule clustering and expression in the cell surface by a mechanism that abrogates its proteolytic processing

10. Martínez-Naves, E., **Lafuente, E.M.** and Reche P.A. (2011). Recognition of the ligand-type specificity of classical and non-classical MHC I molecules. *FEBS Lett.*, 585:3478-3484 **Q2 (141/ 292)** BIOCHEMISTRY & MOLECULAR BIOLOGY. Citations 5

11. Hernández-Varas P, Coló GP, Bartolomé RA, Paterson A, Medraño-Fernández I, Arellano-Sánchez N, Cabañas C, Sánchez-Mateos P, **Lafuente EM**, Boussiotis VA, Strömblad S, Teixidó J (2011). Rap1-GTP-interacting adaptor molecule (RIAM) protein controls invasion and growth of melanoma cells) *J Biol Chem*. May 27;286 (21):18492-504. **Q2 (75/ 292)** BIOCHEMISTRY & MOLECULAR BIOLOGY Citations 25.

**Brief resume:** RIAM is a protein discovered by our group in 2004 implicated in integrin regulation and cell adhesion .Here we demonstrate RIAM role in cancer since reducing with RIAM expression results in reduced tumor growth and metastasis formation. We determine that RIAM is implicated in beta-1 integrin activation, controlling cell migration, cell growth, and apoptosis

12. Díez-Rivero CM, **Lafuente EM** and Reche PA (2010) Computational analysis and modeling of cleavage by the immunoproteasome and the constitutive proteasome. *BMC Bioinformatics*, 11: 479.(IF: 3.028;**Q1 (46/160)**) BIOTECHNOLOGY & APPLIED MICROBIOLOGY Citations: 14

**Brief resume:** Protective CD8 T cell epitopes result from antigens cleaved by the proteasome and the

*immunoproteasome. Here, we trained n-grams on peptides eluted from MHC I molecules and CD8 T cell epitopes developing models to predict cleavage by the proteasome and the immunoproteasome, respectively. These models outperformed competing methods and are available for free public use at <http://imed.med.ucm.es/Tools/PCPS/>*

13. Patsoukis N, **Lafuente EM**, Meraner P, Kim Js, Dombkowski D, Li L, Boussiotis VA. (2009). RIAM regulates the cytoskeletal distribution and activation of PLC-gamma1 in T cells. *Sci Signal*. Dec 1;2(99):ra79. **Q1 (37 /292)** BIOCHEMISTRY & MOLECULAR BIOLOGY. Times Cited 13  
**Brief resume:** *RIAM is a protein discovered by our group in 2004 implicated in integrin regulation and cell adhesion .Here we demonstrate RIAM binds directly to PLC-gamma1 and promotes its recruitment to F-actin cytoskeleton and PLC-gamma1 binding to cytoskeleton is necessary for its activation. We demonstrate that RIAM regulates TCR signaling and T cell activation independently of its role in integrin activation*

### C.2. Research projects and grants

1. *Papel de la pequeña GTPase Rap1 y su efector RIAM in Tumorigenesis.* Ministerio de Innovación y Ciencia, España (SAF 2007-2011) : 140,000 € Duración 01/01/2007 a 31/05/2011. Principal Investigador **Esther Lafuente Duarte**
2. *Papel de fRIAM y Rap1 en la función leucocitaria y en tumorigenesis.* Comunidad de Madrid (CCG08-UCM/SAL-4259) 15.000 €. Duración 01/01/2008 a 31/12/2008. Principal Investigador **Esther Lafuente Duarte**
3. *Papel de RIAM en la función leucocitaria .* Comunidad Autónoma de Madrid, Spain (CCG09-UCM/BIO-3769) 15,000 € Duración 01/01/2009 to 31/12/2009. Principal Investigador: **Esther Lafuente Duarte**
4. *Papel de la pequeña GTPase Rap1 in Tumorigenesis.* Ministerio de Educación y Ciencia. Ramón y Cajal Project. 10,000 €. Duración 01/06/2006 a 31/05/2008. Principal Investigador **Esther Lafuente Duarte.**
5. *“REGULACION FUNCIONAL DE ALCAM/CD166, INTEGRINAS  $\beta$ 2 Y RECEPTORES DE LA QUIMIOCINA CXCL12: IMPLICACIONES EN ADHESION, MIGRACION, FAGOCITOSIS Y METASTASIS”* Ministerio de Economía y Competitividad SAF2012-34561. IP: **Carlos Cabañas Gutierrez**
6. *DESARROLLO ASISTIDO POR COMPUTADORA DE VACUNAS DE EPITOPOS: APLICACION AL RHINOVIRUS HUMANO.* Ministerio de Economía y Competitividad Ref: BIO2014-54164-R. Duración 01/01/2015 al 31/12/2017 Concedido: 108.900,00 €. Investigador Principal **PEDRO ANTONIO RECHE GALLARDO**

### C.5. Direction of PhD thesis

- 1.1. *Papel de la proteína adaptadora RIAM en la fagocitosis mediada por complemento 11 de Mayo de 2012. Doctorando: Iria Medraño Fernández.* Doctorado en Bioquímica. UCM: **Esther Lafuente Duarte** y Carlos Cabañas Gutiérrez.
  - 1.2. *Estudio de las respuesta de linfocitos T condicionados por células epiteliales de la mucosa oral. 15 Septiembre 2017. Doctorando: María Magdalena Molero Abraham .* Doctorado en Biomedicina. UCM. Directores: Pedro A. Reche y **Esther Lafuente Duarte**
  - 1.3. *Papel de RIAM, VASP y Vinculina en la fagocitosis mediada por complemento En curso. Doctorando: Alvaro Torres Gómez.* Becario FPU 2016. Doctorando en Biomedicina. UCM. Directores: **Esther Lafuente Duarte** y Carlos Cabañas Gutiérrez .
  - 1.4. *. Estudio de la función moduladora de la respuesta inmune mediada por células epiteliales de la mucosa oral. En curso. Doctorando: José Luis Sánchez Trincado* Doctorado en Biomedicina. UCM. Directores: **Esther Lafuente Duarte** y Pedro A. Reche -
2. TFM

- 2.1. Papel de RIAM en la activación del receptor del complemento CR3/ $\alpha$ M $\beta$ 2 (2013-14). Sara A. Robles Mateo. Master oficial en Investigación en Inmunología. Universidad Complutense de Madrid. Director: Esther Lafuente Duarte.
- 2.2. The VASP-RIAM axis in Complement-Mediated Phagocytosis (2014-15). Álvaro Torres Gómez. Master oficial en Investigación en Inmunología. Universidad Complutense de Madrid. Director: Esther Lafuente Duarte.
- 2.3. Papel de Vinculina en la activación del receptor del complemento CR3/ $\alpha$ M $\beta$ 2 (2016-17). Felix Pardo Bernad. Master oficial en Investigación en Inmunología. Universidad Complutense de Madrid. Director: Esther Lafuente Duarte.

### 3. TFG

- 3.1. Papel de VASP en la regulación de la fagocitosis dependiente de complemento (2013-14). Álvaro Torres Gómez. Trabajo Fin de grado de Bioquímica. Universidad Complutense de Madrid. Director: Esther Lafuente Duarte
- 3.2. VINCULINA COMO REGULADOR DEL PROCESO DE FAGOCITOSIS DEPENDIENTE DE RECEPTORES DEL COMPLEMENTO (2014-15). Aldara Martin. Trabajo fin de grado de Bioquímica. Universidad Complutense de Madrid. Director: Esther Lafuente Duarte.
- 3.3. RIAM, VASP Y VINCULINA COMO NUEVOS REGULADORES DE LA FAGOCITOSIS DEPENDIENTE DEL COMPLEMENTO (2015-16). Beatriz Herrero. Trabajo fin de grado de Bioquímica. Universidad Complutense de Madrid. Director: Esther Lafuente Duarte.
- 3.4. PAPEL DE VASP EN FAGOCITOSIS DEPENDIENTE DE RECEPTORES DEL COMPLEMENTO (2016-17). Daniel Gonzalez Cava . Trabajo fin de grado de Bioquímica. Universidad Complutense de Madrid. Director: Esther Lafuente Duarte.

### **C.5, Institutional responsibilities**

-2016-2017. **Academic Secretary of the Department of Immunology, Ophthalmology & ORL**, F. de Medicina, U. Complutense de Madrid

-2017-Present. Coordinator for the **Nutrition Practicum Program**. Grade of Nutrition at U. Complutense de Madrid