



AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2017

Turno de personas con discapacidad

Nombre: GONZALO ASENSIO, JESUS
Referencia: RYC-2017-23255
Área Científica: **Biología Fundamental y de Sistemas**
Correo Electrónico: jagonzal@unizar.es

Título:

Synthetic biology approaches to develop multivalent vaccines in Mycobacterium tuberculosis

Resumen de la Memoria:

During my PhD under direction of Prof. Carlos Martín, I paved the way for the construction of a tuberculosis vaccine. I discovered a virulence gene controlling many pathogenic phenotypes of *M. tuberculosis*. This finding was achieved during a stay in the lab of Prof. Brigitte Gicquel at Institut Pasteur Paris (2x J Bacteriol 2008, J Biol Chem 2008). During this stay, I had the opportunity to meet some relevant scientists including Prof. Stewart T. Cole and Prof. Roland Brosch with whom I continue a fruitful collaboration.

In this period, I also performed a stay in the lab of Prof. Marcel Behr at McGill University (Canada), a pioneer in the field of microarrays applied to *M. tuberculosis*. Results from this stay ended in the publication of the first virulence network in a *M. tuberculosis* strain isolated from a patient. (PLoS one 2008) This manuscript has reached >100 cites.

In parallel, I continued the construction of a tuberculosis vaccine according to European recommendations (Vaccine 2009 and Vaccine 2013). Notably, this vaccine named MTBVAC is currently in phase Ib clinical evaluation in newborns. I am inventor of the MTBVAC international patent that has extended to EU, USA, Canada, Japan, Russia, China, India, Brazil. The patent is licensed to the Spanish biopharmaceutical Biofabri. This achievement represents a hallmark in vaccinology, being the first-time after a century that a live vaccine against tuberculosis is tested in humans.

I also performed a stay in the laboratory of Prof. García del Portillo at CNB-CSIC training in RNA technology with the human pathogen *Salmonella* (RNA biology 2012, PLoS one 2013). Later, I applied this knowledge to study virulence networks in *M. tuberculosis* by whole-genome sequencing techniques (RNA-seq and ChIP-seq). This approach resulted on the identification, for the first time, of the biological role of a non-coding RNA in this pathogen and its implications on the enhanced immunogenicity of the MTBVAC vaccine (PLoS pathogens 2014).

I deciphered the secretion of the most important virulence factor in *M. tuberculosis* that also explains its absence in the vaccine. These results were published as senior corresponding author. (Infect and Immun 2014, mBio 2015). In another study I demonstrated how polymorphisms have modelled the evolution of the Mycobacterium genus and its adaptation to different hosts (PNAS 2014). This latter work received excellent criticisms and it is considered a milestone in the field.

I recently discovered the key role of immunodominant antigens on the protection of the MTBVAC vaccine and how this phenotype depends on the host genetic background (Nature Commun 2017, Frontiers Immunol 2017). In a related study as senior corresponding author, I explored the evolution of epitopes in the *M. tuberculosis* Complex and its implication on immunogenicity (Genome Biol & Evol 2016).

In 2016, I obtained funding as Principal Investigator of an Explora project (MINECO), in which I plan to implement synthetic biology techniques to the Mycobacterium genus. I have directed three Thesis and I am now supervising three PhD students who try to develop new multivalent vaccines based on MTBVAC.

Resumen del Currículum Vitae:

Education:

- 2002: Degree in Biochemistry
- 2003 Master in Molecular and Cellular Biology
- 2006 PhD in Biochemistry

Positions:

- 2003-2006: FPU grant from the Spanish MECD.
- 2006-2007: post-doctoral contract National project MECD
- 2007-2008: post-doctoral contract European project FP6
- 2009-2010: post-doctoral contract National project MCIINN
- 2009-2010: JAE-DOC grant
- 2010-2013: JUAN DE LA CIERVA grant
- 2013-2014: post-doctoral contract European project FP7
- 2014-present: Profesor Ayudante Doctor University of Zaragoza

Publications:

19 research articles, 4 reviews and 4 book chapters



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748 citations. Average 37.4 cites/article
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Research articles:

2017 Frontiers Immunology. IF=6.429, Q1, first author
2017 Nature Communications. IF=12.124, D1, second author
2017 Genome Biology and Evolution. IF=4,098, Q1, senior corresponding author*
2015 mBio. IF=6.786, D1, senior corresponding author*
2015 Journal Inorganic Biochemistry. IF=3.274, Q1, second author
2014 PNAS. IF=9.809, D1, first author
2014 Infection and Immunity. IF=4.156, Q1, senior corresponding author*
2014 PLoS pathogens. IF=8.136, D1, first author
2013 PLoS one. IF=3.534, Q1, first author
2013 Vaccine. IF=3.492, Q2, third author
2012 RNA Biology. IF=4.841, Q1, second author
2011 Microbiology. Q2, fourth author
2010 PLoS pathogens. IF=9.079, D1
2009 Vaccine. IF=3.616, Q2, second author
2008 PLoS one. IF=4.411, Q1, first author
2008 Journal Bacteriology. IF=3.940, Q1, first author
2008 Journal Bacteriology. IF=3.940, Q1, fourth author
2008 Journal Biological Chemistry. IF=5.808, Q1, first author

Participation I+D+I:

PI of Explora project (MINECO 2016) and young researcher project (University of Zaragoza 2015). Participation in 4 consecutive European Projects since 2002 Participation in 9 National projects from MINECO and ISCIII

Direction of graduate and undergraduate students:

2017 Thesis Esther Broset
2017 Thesis Carmen Arnal
2016 Master Juan Calvet
2015 Master Irene Pérez
2014 Thesis Luis Solans
2014 Master Alberto Cebollada
2007 Master Ainhoa Arbués

Patents:

International patent on Tuberculosis Vaccine extended to European countries, USA, Canada, Japan, China, Russia, India, Brazil. Licensed to the Spanish Biopharmaceutical Biofabri

Contributions to congresses:

15 talks in International Congresses and 18 talks in National congresses. Corresponding author in 21 oral presentations.
Opening lecture in a national congress, invited speaker in an international symposium. One oral presentation awarded with best communication diploma

Roles as Reviewer, Evaluator and Editor:

Reviewer

D1: mBio, Nucleic Acids Research
Q1: Journal of Infectious Diseases, Journal of Antimicrobial Chemotherapy, Scientific Reports, PLoS one, BMC microbiology, Molecular Microbiology
Q2: Vaccine, Tuberculosis, FEMS Microbiology letters, Biochimica et Biophysica Acta, Biochemistry, Bioorganic & Medicinal Chemistry Letters

Evaluator

2017 ANR (France)
2015 CONICET (Argentina)
2015 ColCiencias (Colombia)
2014 ANEP (Spain)

Editor

2017 Associate Editor Frontiers in Immunology



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Academic duties and sociocultural dissemination:

Accreditation for Profesor Titular by the ANECA

>1.000 teaching hours as non-permanent lecturer

Participation in Pint of Science

Article in Investigación y Ciencia

Direction of FECYT-funded research documentary (6000 views; <https://vimeo.com/96893588>)