OMB No. 0925-0001 and 0925-0002 (Rev. 09/17 Approved Through 03/31/2020)

BIOGRAPHICAL SKETCH

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| --- |
| NAME: Rodriguez, Gloria Marcela |
| eRA COMMONS USER NAME (credential, e.g., agency login): MRODRIGUEZ |
| POSITION TITLE: Associate Professor |

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

|  |  |  |  |
| --- | --- | --- | --- |
| INSTITUTION AND LOCATION | DEGREE(if applicable) | END DATEMM/YYYY | FIELD OF STUDY |
| Pontificia Universidad Javeriana, Bogota,Colombia. | BS | 10/1986 | Bacteriology |
| New York University, New York | Ph.D | 05/1999 | Microbiology |
| Public Health Research Institute, New York, NY | Postdoctoral Fellow | 02/2003 | Mycobacteriology |

### A. Personal Statement

The main focus of the studies in my laboratory is the role of metal homeostasis in host-pathogen interactions. I am particularly interested in the effects of metal ion restriction resulting from nutritional immunity on the pathogenesis of *M. tuberculosis (Mtb)*. My early training in bacteriology, cell biology and immunology, combined with over 25 years in the mycobacterial field, has given me the right foundation to study the biology of the tuberculous bacillus and the complex interplay between *Mtb* and its host.

My group has significantly contributed to the current understanding of the molecular machinery and mechanisms of metal acquisition and regulation in mycobacteria. We identified the main iron transporter in *Mtb* IrtAB, defined the iron limitation response of Mtb and characterized the essential master regulator of iron metabolism IdeR, the mechanism of its dual function as repressor and activator of iron related genes and its essential role in virulence. We also defined the role of the iron storage protein ferritin in *Mtb* physiology and persistence and its value as protective antigen. My group also discovered and characterized the main manganese (Mn) transporter MntABC and the Mn uptake regulator MntR.

Our recent studies have shown that the ultimate response of *Mtb* to Fe-deprivation is survival without replication, upregulation of host survival factors and antibiotic tolerance that may be critical for establishment of latent infection.

Overall the research program in my laboratory has been based on combining *in vitro*, *ex vivo* and *in vivo* approaches to address the molecular mechanisms involved in *Mtb* response to metal homeostasis challenges in the host. Gupta S, Rodriguez GM. Mycobacterial extracellular vesicles and host pathogen interactions. Pathog Dis. 2018 Jun 1;76(4)PubMed PMID: [29722822](http://www.ncbi.nlm.nih.gov/pubmed/29722822/); PubMed Central PMCID: [PMC5930244](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC5930244/).

1. Kurthkoti K, Amin H, Marakalala MJ, Ghanny S, Subbian S, Sakatos A, Livny J, Fortune SM, Berney M, Rodriguez GM. The Capacity of *Mycobacterium tuberculosis* to Survive Iron Starvation Might Enable It To Persist in Iron-Deprived Microenvironments of Human Granulomas. MBio. 2017 Aug 15;8(4)PubMed PMID: [28811344](http://www.ncbi.nlm.nih.gov/pubmed/28811344/); PubMed Central PMCID: [PMC5559634](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC5559634/).
2. Rodriguez GM, Neyrolles O. Metallobiology of Tuberculosis. Microbiol Spectr. 2014 Jun;2(3)PubMed PMID: [26103977](http://www.ncbi.nlm.nih.gov/pubmed/26103977/); PubMed Central PMCID: [PMC5180607](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC5180607/).
3. Rodriguez GM, Prados-Rosales R. Functions and importance of mycobacterial extracellular vesicles. Appl Microbiol Biotechnol. 2016 May;100(9):3887-92. PubMed PMID: [27020292](http://www.ncbi.nlm.nih.gov/pubmed/27020292/); PubMed Central PMCID: [PMC4879809](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4879809/).

**B. Positions and Honors**

Positions and Employment

|  |  |
| --- | --- |
| 1986 - 1990 | Research Assistant , Instituto de Immunologia, Bogota |
| 1990 - 1994 | Research Assistant, New York University, NewYork, NY |
| 1994 - 1999 | Graduate Student, New York University. , New York, NY |
| 1999 - 2003 | Post-doctoral Fellow , Public Health Research Institute, New York, NY |
| 2003 - 2006 | Assistant Professor, PHRI, University of Medicine and Dentistry of New Jersey, Newark, NJ |
| 2007 - 2017 | Assistant Professor, New Jersey Medical School, Rutgers University, Newark, NJ |
| 2017 -  | Associate Professor, New Jersey Medical School, Rutgers University, Newark, NJ |

Other Experience and Professional Memberships

|  |  |
| --- | --- |
| 2006 -  | Member, American Society of Microbiology |
| 2008 -  | Member, Latinoamerican Society of tuberculosis and other mycobacteriosis (SLAMTB) |
| 2010 -  | Member, American Association for Advancement of Science |

Honors

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| --- | --- |
| 1999 - 2001 | Postdoctoral Research Fellowship, UNCF-Park Davis Scientific initiatives Partnership |
| 2001 - 2003 | Fellowship in Pulmonary Research, Parker B. Francis Foundation  |
| 2011 | Faculty Award, Hispanic Center for Excellence. University of Medicine and Dentistry of New Jersey. |

### C. Contribution to Science

1. My first publications were in the field of immunology and cell biology of antigen processing and presentation in the context of MHC class II molecules. In those studies I characterized the activity of proteases involved in antigen processing and the nature of the cellular compartments where they function. Importantly, the result of that work was one of the first demonstrations that in contrast to MHC class I molecules, MHC class II molecules could bind and present long peptides. This discovery had broad implications for antigenic epitope analysis and design.
	1. Rodriguez GM, Diment S. Destructive proteolysis by cysteine proteases in antigen presentation of ovalbumin. Eur J Immunol. 1995 Jul;25(7):1823-7. PubMed PMID: [7621859](http://www.ncbi.nlm.nih.gov/pubmed/7621859/).
	2. Diment S, Eidelman M, Rodriguez GM, Orlow SJ. Lysosomal hydrolases are present in melanosomes and are elevated in melanizing cells. J Biol Chem. 1995 Mar 3;270(9):4213-5. PubMed PMID: [7876179](http://www.ncbi.nlm.nih.gov/pubmed/7876179/).
	3. Rodriguez GM, Diment S. Role of cathepsin D in antigen presentation of ovalbumin. J Immunol. 1992 Nov 1;149(9):2894-8. PubMed PMID: [1328388](http://www.ncbi.nlm.nih.gov/pubmed/1328388/).
2. In the field of tuberculosis pathogenesis I have made seminal contributions in the area of iron acquisition and regulation. Iron plays an essential role in host-pathogen interactions because it is essential, elusive, and potentially toxic. To proliferate, pathogens must compete for iron in the host and tightly regulate intracellular iron levels to avoid toxic effects of excess iron. As a graduate student working with Dr. Issar Smith I reported for the first time the gene expression response of *M. tuberculosis* to changes in iron availability and identified IdeR as the central regulator of iron uptake and storage. Later as independent investigator my laboratory demonstrated the essentiality of IdeR for *M. tuberculosis* survival in the host, and discovered IrtAB, the main iron transporter in *M. tuberculosis* essential for virulence. We also reported on the role of iron storage proteins in virulence, protection against iron deficiency, oxidative stress, and antibiotic resistance. We demonstrated that immunization with a ferritin (BfrB) mutant could confer protection against subsequent infection with virulent *M. tuberculosis* in a mouse model. The protection elicited by immunization with the *bfrB* mutant is comparable to BCG vaccination with respect to reduction of bacterial burden. However, significant distinctions in disease pathology and host genome-wide lung transcriptome suggest improved containment of Mtb infection in animals vaccinated with the *bfrB* mutant compared to BCG.
	1. Subbian S, Pandey R, Soteropoulos P, Rodriguez GM. Vaccination with an Attenuated Ferritin Mutant Protects Mice against Virulent *Mycobacterium tuberculosis*. J Immunol Res. 2015;2015:385402. PubMed PMID: [26339659](http://www.ncbi.nlm.nih.gov/pubmed/26339659/); PubMed Central PMCID: [PMC4539171](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4539171/).
	2. Pandey R, Rodriguez GM. IdeR is required for iron homeostasis and virulence in *Mycobacterium tuberculosis*. Mol Microbiol. 2014 Jan;91(1):98-109. PubMed PMID: [24205844](http://www.ncbi.nlm.nih.gov/pubmed/24205844/); PubMed Central PMCID: [PMC3902104](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3902104/).
	3. Pandey R, Rodriguez GM. A ferritin mutant of *Mycobacterium tuberculosis* is highly susceptible to killing by antibiotics and is unable to establish a chronic infection in mice. Infect Immun. 2012 Oct;80(10):3650-9. PubMed PMID: [22802345](http://www.ncbi.nlm.nih.gov/pubmed/22802345/); PubMed Central PMCID: [PMC3457556](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3457556/).
	4. Rodriguez GM, Smith I. Identification of an ABC transporter required for iron acquisition and virulence in *Mycobacterium tuberculosis*. J Bacteriol. 2006 Jan;188(2):424-30. PubMed PMID: [16385031](http://www.ncbi.nlm.nih.gov/pubmed/16385031/); PubMed Central PMCID: [PMC1347291](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1347291/).
3. Manganese (Mn) transport and regulation in *M. tuberculosis*. Although Fe-restriction is the most prominent and well-understood example of nutritional immunity, Mn sequestration has recently emerged as an important mechanism of host resistance to several bacterial and fungal infections. Our recent studies discovered key Mn homeostatic mechanisms in *Mtb*, which comprises a Mn dependent transcriptional regulator and two Mn transporters, MntH and MntABCD. We found that *Mtb* strains deficient for Mn import are highly sensitive to conditions of low Mn availability and fail to proliferate in THP-1 macrophages.
	1. Pandey R, Russo R, Ghanny S, Huang X, Helmann J, Rodriguez GM. MntR(Rv2788): a transcriptional regulator that controls manganese homeostasis in *Mycobacterium tuberculosis*. Mol Microbiol. 2015 Dec;98(6):1168-83. PubMed PMID: [26337157](http://www.ncbi.nlm.nih.gov/pubmed/26337157/); PubMed Central PMCID: [PMC5157835](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC5157835/).
4. Extracellular vesicle formation in *Mtb*. We discovered that increased production of membrane vesicles is part of the response of *Mtb* to iron limited conditions as encountered in the host. In addition we uncovered distinct composition of vesicles produced under iron limitation including the presence of a potent siderophore that can function in adaptation to iron limitation. This opened a new chapter in the study of mechanisms used by *Mtb* to interact with the host.
	1. Gupta S and Rodriguez GM. Mycobacterial extracellular vesicles and host pathogen interactions. Pathogens and Disease. 2018;76(4).
	2. Rodriguez GM, Prados-Rosales R. Functions and importance of mycobacterial extracellular vesicles. Appl Microbiol Biotechnol. 2016 May;100(9):3887-92. PubMed PMID: [27020292](http://www.ncbi.nlm.nih.gov/pubmed/27020292/); PubMed Central PMCID: [PMC4879809](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4879809/).
	3. Prados-Rosales R, Weinrick BC, Piqué DG, Jacobs WR Jr, Casadevall A, Rodriguez GM. Role for *Mycobacterium tuberculosis* membrane vesicles in iron acquisition. J Bacteriol. 2014 Mar;196(6):1250-6. PubMed PMID: [24415729](http://www.ncbi.nlm.nih.gov/pubmed/24415729/); PubMed Central PMCID: [PMC3957709](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3957709/).
5. Iron-restriction induced persistence of *M. tuberculosis*. Although *Mtb* needs iron for growth, recently, we uncovered the remarkable ability of *Mtb* to persist for long time in conditions of Fe-starvation, able to tolerate antibiotics and ready to reactivate replication when iron becomes available. In conjunction with analysis of the iron-environment of human granulomas that showed microenvironments in which *Mtb* likely experiences drastic Fe-deprivation, this discovery suggest that Fe-deprivation in the lung might trigger a state of persistence in *Mtb* and promote chronic latent TB infection. Because latent TB is a major problem for TB diagnostics, treatment and control, these findings aid understanding the physiology of persistent *Mtb* and provide new avenues for therapeutic research.
	1. Kurthkoti K, Amin H, Marakalala MJ, Ghanny S, Subbian S, Sakatos A, Livny J, Fortune SM, Berney M, Rodriguez GM. The Capacity of *Mycobacterium tuberculosis* To Survive Iron Starvation Might Enable It To Persist in Iron-Deprived Microenvironments of Human Granulomas. MBio. 2017 Aug 15;8(4)PubMed PMID: [28811344](http://www.ncbi.nlm.nih.gov/pubmed/28811344/); PubMed Central PMCID: [PMC5559634](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC5559634/).

Complete list of Publish work in MyBibliography<https://www.ncbi.nlm.nih.gov/sites/myncbi/14wUPqdykabQ5/bibliography/46010642/public/?sort=date&direction=ascending>

### D. Additional Information: Research Support and/or Scholastic Performance

R21 AI130628-01 04/1/2017-03/30/2019

Iron dependent Membrane Vesicle Production in *M. tuberculosis*.

The goal of this project was to conduct a screen for mutants with altered vesicle production and investigate the role of iron-regulators in controlling extracellular vesicle release in *M. tuberculosis.* (there is no overlap with this application)

Role: PI

R21 AI123970-01 03/01/16-02/28/2018

Manganese acquisition and *Mycobacterium tuberculosis* virulence.

This project seeks to determine the relevance of newly identified manganese transporters in counteracting host Mn restriction and *M. tuberculosis* virulence in the mice model of TB.

 Role: PI

RO3 AI12206 06/14/16-05/31/18

Defining the Iron environment of M. tuberculosis granulomas

The goal of this project was to employ rabbit lung tissue sections to determine iron-restriction related proteins present in TB granulomas at different stages of acute and chronic infection and get an insight into the iron environment in the granuloma.

Role:PI

RO1 AI 044856 7/1/2010-6/30/2015

Mechanisms and regulation of *Mycobacterium tuberculosis* iron acquisition.

The goal of this project was to characterize the molecular mechanisms involved in iron acquisition and regulation in *M. tuberculosis* and their potential as targets for vaccine development.

Role: PI