OMB No. 0925-0001 and 0925-0002 (Rev. 10/15 Approved Through 10/31/2018)

# BIOGRAPHICAL SKETCH

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NAME: Marcela I Henao-Tamayo

eRA COMMONS USER NAME (credential, e.g., agency login): mhenao7

POSITION TITLE: Assistant Professor, Department of Microbiology, Immunology & Pathology

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.)*

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| --- | --- | --- | --- |
| INSTITUTION AND LOCATION | DEGREE  *(if applicable)* | Completion Date MM/YYYY | FIELD OF STUDY |
| School of Medicine, Univ of Antioquia, Colombia | M.D. | 1999 | Medicine |
| University of Antioquia, Colombia | M.Sc. | 2004 | Medical Sciences and Immunology |
| Colorado State University | Ph.D. | 2009 | Microbiology and Immunology |
| Colorado State University | Post-Doc | 2009-2011 | Immunology |

# Personal Statement

I am an Assistant Professor at Colorado State University, member of the internationally recognized Mycobacterial Research Laboratories (MRL), and Co-Director of the CSU Flow Cytometry Core Facility. Over the past decade, I have devoted much of my time to studying the ability of BCG and other new candidate vaccines to generate memory T cell-mediated immunity, performing much of this work with the newly emerging clinical isolates of *Mycobacterium tuberculosis*. I started working in the tuberculosis field 19 years ago as a medical doctor in a developing country, where I realized the need for better vaccine and chemotherapy strategies to stop tuberculosis from killing four people every minute. While finishing my Master degree I met Dr. Patrick Brennan, a highly respected scientist in the TB field, who invited me to come to CSU as a Visiting Scientist. My subsequent experience there was so encouraging that I elected to stay and so I joined Ian Orme’s laboratory as a Ph.D. candidate. Since then, I have devoted my studies to investigating the pathogenesis and immune response to *M. tuberculosis,* with a central interest in the nature of the memory T cell response to vaccines (including BCG). Recently I had the honor to be appointed the Co-Director of the new CSU Flow Cytometry Core facility, where I have developed numerous protocols to perform studies on both mice and guineas pigs infected with virulent clinical strains of TB, something that I now have a decade of experience doing.

Members of my laboratory include, undergraduate and graduate students, postdoctoral fellows and research scientists. I believe that the diversity in gender, color and nationality in my laboratory is a result of me being a Latin American woman—students feel welcome as I am an underrepresented minority in our field. Thanks to my initial training as a medical doctor in South America, students and technical staff in the lab often include ambitious college graduates who continue on to graduate, veterinary, and medical schools. To adequately train all personnel to work inside the Biohazard Level 3 facility. To work efficiently and risk-free in the Biohazard Level 3 facility, protocols and techniques need to be adequately written and prepared. There is little room for mistakes, and all data collected is annotated in laboratory books and scanned out in order to keep appropriate records. All results are analyzed using commercial software and every experiment is repeated at least twice with multiple replicas in order to efficiently lead to a valid conclusion. The results prepared by the laboratory members are always reported to me and I verify that they are accurate. Animal gender, age and pathological conditions are kept strictly monitored. Additionally, we work with a biostatistician in order to ensure we are using adequate controls and numbers of animals and in each experiment.

Notably, the different actions of data recording, data pre-processing, and analysis are often presented as a single entity using spreadsheets or proprietary software, as mentioned in the grant proposal, which results in key failure points for reproducibility at the stages of data recording and pre-processing. I can recognize in my daily research work that there is a critical need for better data recording and pre-processing to enable reproducible and clear sharing across my research teams and ensure that the rigor and reproducibility we enforce experimentally in our research persists through data recording and pre-processing. The current proposal, which focuses in improving the reproducibility of experimental data recording, will elucidate how the use of improved data recording practices and pre-processing code scripts for these steps dramatically improves reproducibility.

I firmly believe I have the knowledge, enthusiasm, training and leadership necessary to successfully carry out the proposed project with my highly capable collaborators.

1. Ian Orme and Marcela Henao-Tamayo. Trying to see the forest through the trees: deciphering the nature of memory Immunity to Mycobacterium tuberculosis *Frontiers in Immunology* 2018; 9: 461. PMID: 29568298
2. Henao-Tamayo M, Obregón-Henao A, Creissen E, Orme I, Shanley C, and Ordway D. Differential expression of BCG vaccine derived efficacy in C3Heb/FeJ and C3H/HeOuJ mice exposed to a clinical strain of Mycobacterium tuberculosis, Clin Vaccine Immunol. 2015 Jan;22(1):91-8. PMID: 25392011
3. Henao-Tamayo M, Ordway DJ, Orme IM. Memory T cell subsets in tuberculosis: What should we be targeting? Tuberculosis (Edinb). 2014 Jun 17. PMID: 24993316
4. Henao-Tamayo, M, Ordway, D. J., Irwin, S. M. Shang, S., Shanley, C., Orme, I. M. Phenotypic definition of effector and memory T-lymphocyte subsets in mice chronically infected with Mycobacterium tuberculosis. Clin Vaccine Immunol 2010; 17, 618-625. PMCID 2849327
5. Henao-Tamayo M, Palaniswamy GS, Smith EE, Shanley CA, Wang B, Orme IM, Basaraba RJ, DuTeau NM, Ordway D. Post-exposure vaccination against Mycobacterium tuberculosis. Tuberculosis (Edinb). 2009; 89:142-8. PMID:19264552

# Positions and Honors Positions

2015 - Co-Director of CSU Flow Cytometry and Cell Sorting Facility, Colorado State University, Fort Collins, CO

2014 - Assistant Professor**,** Department of Microbiology, Immunology & Pathology, Colorado State University, Fort Collins, CO

2011 – 2014 Research Scientist, Department of Microbiology, Immunology & Pathology, Colorado State University, Fort Collins, CO

2009 – 2011 Post Doctoral Fellow, Department of Microbiology, Immunology & Pathology, Colorado State University, Fort Collins, CO

2004 – 2009 PhD Student, Department of Microbiology, Immunology & Pathology, Colorado State University, Fort Collins, CO

2003 – 2004 Visiting Scientist, Orme Laboratory, Department of Microbiology, Immunology & Pathology, Colorado State University, Fort Collins, CO

2001 – 2003 Research Fellow/MD, Group of Cellular Immunology and Immunogenetics, School of Medicine, University of Antioquia, Medellin, Colombia

2000 Research Scientist/MD, Group of Cellular Immunology and Immunogenetics, School of Medicine, University of Antioquia, Medellin, Colombia

1999 Young Investigator, Group of Cellular Immunology and Immunogenetics, School of Medicine, University of Antioquia, Medellin, Colombia

# Honors

* Honorary Member School of Medicine 2015, Universidad de Antioquia, Columbia
* AAUW American Association of University Women International Fellow 2010
* Special Mention for Young Investigators 2000. University of Antioquia. Medellin – Colombia

# Other Experience and Professional Memberships

2006- The American Association of Immunology 2008-American Society of Microbiology

2010- TBnet

2011- STOP TB Drugs Group, World Health Organization

2010- AAUW (American Association of University Women)

2004 DAKOCytomation MOFLO certified in 2004 to present operator course for cell sorting

2006 BD LSRII operator course certified in 2006 to present multi-parameter "12-color" LSR II Flow Cytometer operation and analysis.

2012 BD FACSAria III cell sorting operator course certified in 2012 to present multi-parameter cell sorting operation and analysis.

# Contribution to Science

*Mycobacterium tuberculosis* (*Mtb*) infects one third of the world’s population and is a leading cause of morbidity and mortality. Furthermore, TB is frequently associated with HIV infection in a significant number of cases and is a primary pathodiagnostic of progression to AIDS. Ominously, the global health consequences of TB are likely to increase in coming years with the emergence of drug-resistant TB strains and the lack of effective vaccines. Presently, the global tuberculosis (TB) epidemic affects over 8 million cases per year, and MDR-TB rates are estimated to be in excess of 650,000/year.

* 1. My studies in the area of tuberculosis have shown, amongst other things, that BCG vaccination induces effector memory T cells but very few central memory T cells (which are the ones that supposedly confer long lasting protection after vaccination), possibly explaining the variability and limited longevity of this vaccine. Furthermore, in order to evaluate the acquired immune response during the clinically relevant re- infection process occurring in developing countries, I pioneered the re-challenge model of tuberculosis infection. My results indicated that memory immunity is far from stable, and prone to attrition, perhaps by transitioning to short lived cells. Disappearance of CD4+ central and effector memory cells in the lungs of re-infected animals, correlated with the high expression of the exhaustion marker PD-1, which could explain why treated TB patients in Africa are more likely to get re-infected after treatment.
     1. Henao-Tamayo MI, Ordway DJ, Irwin SM, Shang S, Shanley C, Orme IM. Phenotypic definition of effector and memory T-lymphocyte subsets in mice chronically infected with Mycobacterium tuberculosis. Clin Vaccine Immunol. 2010 4:618-25. PMID:20107011
     2. Henao-Tamayo M, Irwin SM, Shang S, Ordway D, Orme IM. T lymphocyte surface expression of exhaustion markers as biomarkers of the efficacy of chemotherapy for tuberculosis. Tuberculosis (Edinb). 2011: July;91(4):308-13. PMID21530406
     3. Henao-Tamayo M, Obregón-Henao A, Ordway DJ, Shang S, Duncan CG, Orme IM. A mouse model of tuberculosis reinfection. Tuberculosis (Edinb). 2012;92:211-7. PMID: 21530406
  2. For many years the tuberculosis animal research field mainly used laboratory adapted strains, while the differences in immune response to infection with clinical strains were completely unknown. With a team of investigators I started comparing the basic biology of laboratory vs. newly emerging clinical strains of *M. tuberculosis*. These studies demonstrated that in contrast to the laboratory strain, clinical isolates initiate an early robust pro-inflammatory type 1 immune response, which is then replaced by the emergence of Foxp3+ regulatory T cells. These studies were corroborated both in the mouse, as well as, in the guinea pig model. Furthermore, based on my interest in vaccines, I evaluated the impact that highly virulent clinical strains of

1. *tuberculosis* have on the immune response generated after BCG vaccination. My studies showed that contrasting to laboratory adapted bacterial strains in which BCG induced protection is maintained during chronic stages of the disease, infection with highly virulent clinical strains wanes after an early protection (30 days). This loss in protection correlated with the arrival of increasing numbers of regulatory T cells in the lungs of infected mice
   1. Ordway DJ, Shang S, Henao-Tamayo M, Obregon-Henao A, Nold L, Caraway M, Shanley CA, Basaraba RJ, Duncan CG, Orme IM. Mycobacterium bovis BCG-Mediated Protection against W-Beijing Strains of Mycobacterium tuberculosis Is Diminished Concomitant with the Emergence of Regulatory T Cells. Clin Vaccine Immunol. 2011;18:1527-35. PMID: 21795460; PMCID:
   2. Shang S, Harton M, Tamayo MH, Shanley C, Palanisamy GS, Caraway M, Chan ED, Basaraba RJ, Orme IM, Ordway DJ. Increased Foxp3 expression in guinea pigs infected with W-Beijing strains of M. tuberculosis. Tuberculosis 2011 Sep;91(5):378-85 PMID: 21737349
   3. Ordway D, Henao-Tamayo M, Harton M, Palanisamy G, Troudt J, Shanley C, Basaraba RJ, Orme IM. [The hypervirulent Mycobacterium tuberculosis strain HN878 induces a potent TH1 response](http://www.ncbi.nlm.nih.gov/pubmed/17579073) [followed by rapid down-regulation.](http://www.ncbi.nlm.nih.gov/pubmed/17579073) J Immunol. 2007 Jul 1;179(1):522-31. PMID: 17579073.
   4. Recently, while studying a new strain of mice in order to develop a new vaccine screening model, I found a predominant cell type in the lungs of three different murine models that develop lung necrosis after *M. tuberculosis* infection. In contrast, these cells were barely present in control strains that did not undergo necrosis. MDSCs (Myeloid Derived Suppressor cells) have previously been described in cancer models and in models of chronic inflammation where, importantly, they have been shown to have a potent immunosuppressive effect that can adversely affect disease outcome.
      1. Henao-Tamayo M, Obregón-Henao A, Creissen E, Orme I, Shanley C, and Ordway D. Differential expression of BCG vaccine derived efficacy in C3Heb/FeJ and C3H/HeOuJ mice exposed to a clinical strain of Mycobacterium tuberculosis, Clin Vaccine Immunol. 2015 Jan;22(1):91-8. PubMed PMID: 25392011; PMCID: PMC4278923.
      2. Obregón-Henao A, Henao-Tamayo M, Orme I and Ordway DJ. Gr1intCD11b+ Myeloid-Derived Suppressor Cells in Mycobacterium tuberculosis Infection. Plos One. 2013 Nov 1;8(11). PMID: 24224058; PMCID: PMC3815237.

**Complete list of publications:** [http://www.ncbi.nlm.nih.gov/sites/myncbi/marcela.henao-](http://www.ncbi.nlm.nih.gov/sites/myncbi/marcela.henao-tamayo.2/bibliography/40832324/public/?sort=date&amp;direction=ascending) [tamayo.2/bibliography/40832324/public/?sort=date&direction=ascending](http://www.ncbi.nlm.nih.gov/sites/myncbi/marcela.henao-tamayo.2/bibliography/40832324/public/?sort=date&amp;direction=ascending).

# Research Support Ongoing Research

**1 R01 AI127475 - 01AI** (Henao-Tamayo,PI) 07/01/2017 – 06/30/2021 4.0 calendar

NIH/NIAID $1,520,000

“Vaccine induced memory immunity in tuberculosis”

The purpose of this R01 application is to investigate whether memory immunity induced in mice after vaccination with different types of candidates [rBCG, protein fusion in adjuvant, live attenuated mutant] induce similar or different subsets of CD4 memory T cells.

**CSU - Internal Facility** (Henao-Tamayo,PI) 07/01/2016 - 06/30/2019 1.77 calendar

Colorado State University $250,000

"Flow Cytometry Core Facility"

The purpose of this core is to manage multiple flow cytometers across the campus, provide support and continued training for current and potential users.

**1 R01AI105053-01** (Rodell, PI) 08/22/2013 – 07/31/2018 2.40 calendar

NIH/NIAID $1,487,000 (sub only)

“Recombinant yeast vaccines for sensitive and drug-resistant M. tuberculosis”

The purpose of this subcontract to GlobeImmune is to test the efficacy of TB vaccines made using their unique yeast based expression platform. We will immunize animals with these vaccines and test their capacity to protect against subsequent infection with TB using our standard animal challenge models at CSU