BIOGRAPHICAL SKETCH

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NAME: Aguayo-Hiraldo, Paibel

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

POSITION TITLE: Assistant Professor of Clinical Pediatrics

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 DATE MM/YYYY	FIELD OF STUDY
University of Puerto Rico, Humacao, PR	B.S.	12/2002	Applied Microbiology, Biology
San Juan Bautista School of Medicine, Caguas, PR	M.D.	05/2009	Medicine
University of South Florida, Tampa, FL	Residency	06/2013	Internal Medicine and Pediatrics
Baylor College of Medicine, Houston, TX	Fellowship	06/2016	Pediatric Hematology and Oncology

A. Personal Statement

I am the medical director of the outpatient transplantation and cellular therapy clinic at Children's Hospital Los Angeles. I am interested in direct patient care, which takes about 70% of my time with a dedicated 25% to clinical research. Within the transplant and cellular therapy realm, I have dedicated most of my time as a faculty working on improving patient outcomes before, during, and after their stem cell transplant or cellular therapy. One of the aspects that piqued my interest since med school is barriers to care and treatment-related complications. As a bone marrow transplant physician born and raised in Puerto Rico, I know the limitations of findings a well HLA-matched stem cell source for racial and ethnic minorities both in national and international stem cell donor banks. Because of this, one of my earlier projects worked on finding better stem cell sources and improving outcomes using umbilical cord blood for pediatric patients with malignant and non-malignant disorders utilizing cord blood transplant (UCBT). Although UCBT has been accepted as a great alternative donor source for both malignant and non-malignant diseases, this has been associated with delayed immune reconstitution, infections, and higher risk for relapse. We believe this to be related to the choice of conditioning regimen that includes ATG or Campath, which acts as an in-vivo T cell depletion. By removing these agents from the conditioning regimen preceding UCBT, we found earlier engraftment, -T and -B cell immune reconstitution and, less viral infections. Preliminary data analysis showed less GVHD without compromising graft vs. leukemia as the rates of relapse are similar or better when compared to matched unrelated donors. Most recently, I've joined a multi-institutional study interested in analyzing functional tests that can be used to screen and risk stratify patients at risk for Transplant-Associated Microangiopathy (TA-TMA). The main goal of this study, currently in the early phases of enrollment, is to improve survival with early intervention and treatment with Eculizumab. On the other hand, as part of the Mount Sinai Acute Graft Vs. Host Disease International Consortium we are embarking on a project to determine the effectiveness of itacitinib- a selective JAK1 inhibitor, as the primary treatment of newly diagnosed, low-risk acute GVHD defined by standard risk criteria and low-risk biomarkers. While successfully treating leukemias and other disorders, a transplant can be associated with severe infections, increasing treatment-related mortality. I worked in developing virus-specific immunotherapy to prevent and treat viral infections, specifically developing an immunotherapeutic target to treat respiratory viral infections.

Immunotherapy can be accessed through commercial means or clinical trials. In many cases, it has proven to be a life-saving therapy even for refractory leukemias, but the access to this therapy may be limited to many in our communities. For this reason, I joined the Patient Advocacy group of the Consortium for Pediatric Cellular Immunotherapy whose main goal is to "Accelerate cellular immunotherapy for the treatment of life-threatening

disorders." As part of this group, we are exploring barriers to access to immunotherapy in our respective catchment areas. Cancer treatment continues to improve the chances of survival, but a patient's location and socioeconomic status may be a factor limiting access to potentially life-saving immunotherapy. Identifying barriers to care can bridge the gap between potentially life-saving treatments and the patients who need them.

I see myself with a career as a clinician/clinical researcher working to improve patient outcomes through hematopoietic stem cell transplant and immunotherapy, as well as developing early diagnosis and effective treatment options for complications arising post-BMT. A few of my latest project publications are below.

1. Increased viral variants in children and young adults with impaired humoral immunity and persistent SARS CoV-2 infection: A Consecutive case series. TT Truong, A Tyutov, R Yee, L Goldberg, D Bhojwani, P Aguayo-Hiraldo et al. EBioMedicine. 2021 May;67:103355. PMID 33915337. PMCID: PMC8072072.
2. 2. SARS CoV-2 in Childhood Cancer in 2020: A Disease of Disparities. Johnston E, Martinez I, Davis E, Caudill C, Richman J, Brackett J, Dickens D, Kahn A, Schwalm C, Sharma A, Patel P on behalf of the POCC Consortium**, Bhatia S, *Levine J, *Wolfson J (*co-senior authors). SARS-CoV-2 in Childhood Cancer in 2020: A Disease of Disparities. (**P Aguayo-Hiraldo, Member of POCC Consortium). Journal of Clinical Oncology. *Journal of Clinical Oncology* 39, no. 34 (December 01, 2021) 3778-3788.
3. 3. Evaluation of Elafin as a Prognostic Biomarker in Acute graft-versus-Host Disease. M Gethachew Zewde, G Morales, I Gandhi, U Ozbek, P Aguayo-Hiraldo et al. Transplantation and Cellular Therapy. Vol 27, Issue 12, Dec 2021. 988e1-e7.
4. Towards Functional Immune monitoring in Allogeneic Stem cell transplant recipients. Naik S, Vasileiou S, Aguayo-Hiraldo P, Mukhi S, Martinez C, Krance RA, Gottschalk S, Leen A. Biol Blood Marrow Transplant, Jan 2020. (ahead of print) PMID 31927102
5. Aguayo-Hiraldo PI, Arasaratnam RJ, Tzannou I, Kuvalekar M, Lulla P, Naik S, Martinez CA, Piedra PA, Vera JF, Leen AM. Characterizing the Cellular Immune Response to Parainfluenza Virus 3. J Infect Dis. 2017 Jul 15;216(2):153-161. PubMed PMID: 28472480; PubMed Central PMCID: PMC5853958.
6. Tzannou I, Nicholas SK, Lulla P, Aguayo-Hiraldo PI, Misra A, Martinez CA, Machado AA, Orange JS, Piedra PA, Vera JF, Leen AM. Immunologic Profiling of Human Metapneumovirus for the Development of Targeted Immunotherapy. J Infect Dis. 2017 Sep 15;216(6):678-687. PubMed PMID: 28934427; PubMed Central PMCID: PMC5853664.

B. Positions and Honors

Positions and Employment

2009 - 2013	Resident Physician- Internal Medicine and Pediatrics, University of South Florida, Tampa, FL
2013 - 2016	Post-graduate Clinical Fellow- Pediatric Hematology and Oncology, Baylor College of Medicine, Houston, TX
2013 - 2017	Peer Review Analyst, MCMC, Bethesda, MD
2016 - 2017	Instructor- Clinical Pediatrics (BMT), Baylor College of Medicine, Houston, TX
2017 - 2018	Assistant Professor Clinical Pediatrics, Baylor College of Medicine, Houston, TX
2018 -	Assistant Professor Clinical Pediatrics, University of Southern California, Los Angeles, CA

Other Experience and Professional Memberships

2009 -	Member, American Academy of Pediatrics
2012 -	Member/Diplomate, American College of Physicians
2013 -	Member, American Society of Hematology
2014 –	Member, ASBMT
2014-2015	Member, International Society for Antiviral Research

Honors

2013 - 2013	Internal Medicine Jeopardy Delegate, Society of General Internal Medicine
2016	Travel Award- Abstract/Poster Presentation, American Society Blood and Marrow Transplant

C. Contribution to Science

1. Early on in my career, one of the diseases that picked my interest was Chronic Lymphocytic Leukemia (CLL), which is commonly seen in the elderly adult population and which can present in a myriad of ways from indolent disease associated with prolonged clinical course an eventual death not associated to CCL. This inspired a group of us, led by Dr. Pinilla at Moffitt Cancer Center, to look at several factors, including the Incidence of Secondary malignancies in this patient population as well as factors that may affect the outcomes in these patients. Before I left Moffitt (adult cancer center) to pursue a fellowship in Pediatric Hematology and Oncology we had submitted and published two abstracts in which we found (a) that mutations in IGVH appear to be associated with improved OS in patients with isolated 13q deletion when compared to patients with unmutated IGVH and isolated 13q deletion and (b) that second malignancies are frequent in CLL patients with several factors potentially contributing to this including Immunosuppression, increased UV light exposure and longer life expectancy in low-risk CLL. Resulted publications:

   a. Samir Dalia, Julio C. Chavez, Gelenis Domingo, Estrella M. Carballido, **Paibel I. Aguayo-Hiraldo**, Kendra Lynn Sweet, Robert M. Crescentini, Lubosh Sokol, Celeste M. Bello, Jennifer L. Cultrera, Bijal D. Shah, Jeffrey E. Lancet, Rami S. Komrokji, Eduardo M. Sotomayor, Javier Pinilla-Ibarz. Incidence of second and secondary malignancies in patients with CLL: A single-institution experience. J Clin Oncol 30, 2012 (poster, ASCO annual meeting 2012)(suppl; Abstr 6568). H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL

   b. Gelenis C. Domingo, Samir Dalia, Julio C. Chavez, Estrella M. Carballido, **Paibel I. Aguayo-Hiraldo**, Kendra Lynn Sweet, Robert M. Crescentini, Lubomir Sokol, Jennifer L. Cultrera, Bijal D. Shah, Jeffrey E. Lancet, Eduardo M. Sotomayor, Rami S. Komrokji, Javier Pinilla-Ibarz. Impact of immunoglobulin heavy chain variable region mutational status on the outcome of patients with chronic lymphocytic leukemia harboring isolated 13q deletion. J Clin Oncol 30, 2012 (ASCO annual meeting poster 2012) (suppl; abstr 6608). H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL

2. One of my interests is in immune reconstitution and control of infections in the post-allogeneic stem cell transplant recipients, specifically how the tempo and mode of reconstitution or lack of thereof, may affect the quantity and the response to infections by this exquisitely immunosuppressed population. Based on this, I have been participating in several studies. With Dr. Leen's guidance, I formulated a project investigating suitable antigens to develop an adoptive therapy approach for PIV-3. We demonstrated that specific CD4+ and CD8+ T cells exist in the peripheral blood of healthy subjects and established a hierarchy of immunogenicity of 7 PIV-3 antigens. We described the polyfunctionality of these cells, proving that they were able to produce effector cytokines with a Th1 profile upon exposure to immunogenic PIV-3 antigens including TNF-α, IFN-γ and GM-CSF as well as demonstrated production of Granzyme B. We proved that PIV-3 specific T cells reacted to, and killed autologous PIV-3 loaded cells, thus suggesting that the development of PIV-3 specific T cells had great promise in preventing and treating PIV-3 infections in post-transplant recipients.

   a. Aguayo-Hiraldo PI, Arasaratnam RJ, Tzannou I, Kuvalekar M, Lulla P, Naik S, Martinez CA, Piedra PA, Vera JF, Leen AM. Characterizing the Cellular Immune Response to Parainfluenza Virus 3. J Infect Dis. 2017 Jul 15;216(2):153-161. PubMed PMID: 28472480; PubMed Central PMCID: PMC5853958
   b. Arasaratnam RJ, Tzannou I, Gray T, Aguayo-Hiraldo PI, Kuvalekar M, Naik S, Gaikwad A, Liu H, Miloh T, Vera JF, Himes RW, Munoz FM, Leen AM. Dynamics of virus-specific T cell immunity in pediatric liver transplant recipients. Am J Transplant. 2018 Sep;18(9):2238-2249. PubMed PMID: 29900673; PubMed Central PMCID: PMC6117219.
   c. Tzannou I, Nicholas SK, Lulla P, Aguayo-Hiraldo PI, Misra A, Martinez CA, Machado AA, Orange JS, Piedra PA, Vera JF, Leen AM. Immunologic Profiling of Human Metapneumovirus for the Development of Targeted Immunotherapy. J Infect Dis. 2017 Sep 15;216(6):678-687. PubMed PMID: 28934427; PubMed Central PMCID: PMC5853664.

3. During the COVID pandemic starting in 2020, most scientific papers focused in the general population in terms of describing incidence, length of illness and proper isolation and deisolation guidelines. Clinically, in

the oncology and post-hematopoietic stem cell transplant world, our view was quite different. Therefore, we launched into properly investigating the diverse presentation and length of infectivity in our patients and how this could pose challenges for vaccination and isolation/de-isolation guidelines.

a. Increased viral variants in children and young adults with impaired humoral immunity and persistent SARS CoV-2 infection: A Consecutive case series. TT Truong, A Tyutov, R Yee, L Goldberg, D Bhojwani, P Aguayo-Hiraldo et al. EBioMedicine. 2021 May;67:103355. PMID 33915337. PMCID: PMC8072072.

b. SARS-CoV-2 in Childhood Cancer in 2020: A Disease of Disparities. Johnston E, Martinez I, Davis E, Caudill C, Richman J, Brackett J, Dickens D, Kahn A, Schwalm C, Sharma A, Patel P on behalf of the POCC Consortium**, Bhatia S, *Levine J, *Wolfson J (*co-senior authors). SARS-CoV-2 in Childhood Cancer in 2020: A Disease of Disparities. (**P Aguayo-Hiraldo, Member of POCC Consortium). Journal of Clinical Oncology. *Journal of Clinical Oncology* 39, no. 34 (December 01, 2021) 3778-3788.

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

Current Research Support

CLIN2-10392 (Pulsipher)
12/01/17-11/30/22
California Institute of Regenerative Medicine
Antiviral Cellular Therapy for Enhancing T-cell Reconstitution Before or After Hematopoietic Stem Cell Transplantation (ACES)
This project is a multicenter phase I/II study of partially HLA-matched Viral-Specific T-cell therapy testing feasibility, efficacy, safety, and immune reconstitution of banked trivirus cells to treat refractory CMV, adenovirus, and EBV infections in patients post-transplant or with primary immune deficiencies.
Role: Co-Investigator

Completed Research Support

T32 HL92332-12, NIH- T32 Heslop, Helen (PI)
07/01/15-06/30/16
Adoptive T cell therapy for the prevention and treatment of PIV-3 infections post-HSCT.
The goal of this project was to design a study that would allow us first to identify potentially immunogenic targets present on Parainfluenza virus 3. Then evaluate the T cell response towards this virus and developed an adoptive Immunotherapy approach for the prevention and treatment of PIV-3 infections in post-allogeneic stem cell transplant recipients.
Role: Co-Investigator