BIOGRAPHICAL SKETCH

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NAME: Perez, Daniel

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

POSITION TITLE: Georgia Research Alliance Distinguished Investigator

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)*	Completion Date MM/YYYY	FIELD OF STUDY
Universidad Nacional de Cordoba, Cordoba, Argentina	BS	10/1989	Biochemistry
University of Nebraska Medical Center, Lincoln, NE	PhD	12/1995	Molecular Virology
University of Nebraska, Lincoln, NE	Postdoctoral	02/2000	Molecular Virology

A. **Personal Statement.**

With over three decades of dedicated experience in influenza virus research, I have cultivated a comprehensive expertise encompassing molecular virology, reverse genetics, and host range studies. My research program, distinguished by its innovative combination of reverse genetics and diverse animal models, has yielded significant advancements in our understanding of influenza pathogenesis and transmission dynamics across avian and mammalian species. In response to the SARS-CoV-2 pandemic, my research group expanded its scope to encompass in vitro, and in vivo studies focused on unraveling the complexities of SARS-CoV-2 pathogenesis. This multifaceted approach has allowed for the exploration of intricate host-pathogen interactions, shedding light on the mechanisms underlying influenza virus infection and spread. My laboratory's pioneering work in developing attenuation strategies for influenza A and B viruses has led to the creation of live attenuated vaccines exhibiting exceptional safety and efficacy in pre-clinical trials. This breakthrough represents a significant step forward in the development of next-generation influenza vaccines that can effectively prevent disease transmission and reduce the severity of illness. One of these promising strategies is currently under a preliminary licensing agreement for potential application in swine and other animal species, underscoring the translational potential of our research findings. Beyond vaccine development, my team has also made substantial contributions to the field of diagnostics. Our successful development of a monoclonal antibody, now licensed to Zoetis and incorporated into the FluDetect rapid avian influenza diagnostic kit, exemplifies our commitment to developing innovative tools for the rapid and accurate detection of influenza viruses. This point-of-care strip test represents a significant advancement in field diagnostics, enabling timely interventions and control measures for avian influenza outbreaks.

My leadership experience in large-scale research initiatives, including my role as Program Director of the USDA-NIFA-funded "Prevention and Control of Avian Influenza in the US" project, demonstrates my ability to effectively manage complex multi-institutional projects and foster collaborations among diverse research teams. This experience has equipped me with the skills necessary to navigate the intricacies of large-scale research endeavors, ensuring efficient coordination, communication, and resource allocation. Furthermore, my laboratory's active participation in NIAID-NIH Centers of Excellence for Influenza Research, both past (CRIP-CEIRS) and present (CRIPT-CEIRR), highlights our ongoing commitment to collaborative research and knowledge exchange within the broader scientific community. These collaborations have fostered the development of novel research approaches and facilitated the sharing of valuable insights and resources, ultimately accelerating progress in the fight against influenza.

As the proposed PI for AVIC@UGA, I am confident that my comprehensive experience, spanning basic research, translational development, and large-scale project leadership, makes me uniquely qualified to guide the center's research agenda. I am committed to fostering a collaborative and innovative research environment that aligns with the FDA's AVIC goals, while promoting the highest standards of scientific rigor, ethical conduct, and public engagement.

Grants and Contracts: Active/Recently Completed

NATIONAL INSTITUTES OF HEALTH (NIH)

01 Sept 2024-31 Aug 2029 (Anticipated). Role: Co-Investigator. PI: Anice Lowen (Emory). $1,738,841 (UGA).

Title: Host dependence of influenza A virus spatio-temporal dynamics

National Institute of Food and Agriculture (NIFA) – U.S. Department of Agriculture (USDA), Grant 2024-67015-42736

01 July 2024-30 June 2027. Role: PI/Project Director. $650,000.

Title: Mass Vaccination Against H9N2 Avian Influenza with Novel Modified Live Virus Vaccines

National Science Foundation, Grant 2318557

01 Sep 2023–31 Aug 2026. Role: Co-investigator. PI: McCall, L-M (UC-San Diego). Amount: $484,100 (UGA).

Title OSIB: Metabolic cartography of influenza A virus infection and host-pathogen interaction in the natural and accidental host.

National Institute of Food and Agriculture (NIFA) – U.S. Department of Agriculture (USDA), Grant 2022-67015-37205

01 Jan 2022–30 Apr 2025. Role: Co-investigator. PI: De Souza Rajao, D (UGA). Amount: $610,000 (UGA).

Title: safe and broadly cross-protective live attenuated influenza virus vaccines for use in swine.

NATIONAL PORK BOARD, Grant 21085

01 Mar 2022–31 Aug 2024. Role: Co-investigator. PI: De Souza Rajao, D (UGA). Amount: $103,785.

Title: Risk factors associated with the adaptation of influenza viruses between humans and pigs.

NATIONAL INSTITUTES OF HEALTH (NIH), National Institute of Allergy and Infectious Diseases (NIAID), Grant R01AI154894

01 Jul 2020–31 Jul 2024. Role: PI – MPI: Lowen A, Koelle K (Emory University). Amount: $829,076.00 (UGA).

Title: Role of spatial structure in shaping viral population diversity and evolution.

NIH, NIAID Centers of Excellence for Influenza Research and Response (CEIRR), Center for Research on Influenza Pathogenesis and Transmission (CRIPT)

18 Sept 2023–17 Sept 2024. Role: Project Leader. PI: Garcia-Sastre, A (ISMMS). Amount: $338,000 (UGA).

Title: Option 17A - Insights for pandemic preparedness: H5N1 pathogenesis, within-host virus diversity, and virus-host gene expression in mammals. Subcontract 0258-A745-4609.

NIH, NIAID CEIRR, CRIPT – Option 15B, Cross-collaborative research project

1 May 2023–30 Apr 2024. Role: Project Leader. PI: Garcia-Sastre, A (ISMMS). Amount: $90,787 (UGA).

Title: Option 15B - Coordinated Evolution and Assessment of H5Nx viruses in Central and South America. Subcontract #: 0258-B723-4609,

NIH, NIAID CEIRR, CRIPT – Option 15A, Cross-collaborative research project, 18 Sept 2023–17 Sept 2024 Subcontract: 0258-A714-4609,

Title: Mechanisms of sex differences in influenza B virus pathogenesis.

Role: Project Leader. Principal Investigator: Garcia-Sastre, A (ISMMS). Amount: $338,000 (UGA).

NIH, NIAID CEIRR, CRIPT – Contract 75N93021C00014, Severable Options, Subcontract #: 0258-C504-4609, 1 April 2021–31 Mar 2027

Title: Antigenic analyses of H9 subtype influenza viruses. Animal model of influenza B virus sex differences.

Role: Project Leader. Principal Investigator: Garcia-Sastre, A (ISMMS). Amount: Base and Options 1 and 2 $853,469, Options 3-6, pending (UGA).

NIFA – USDA Grant 2021-67015-34032, 01 Aug 2020 –28 Feb 2026.

Title: US-UK-China Collab: Predictive phylogenetics for evolutionary and transmission dynamics of newly emerging avian influenza viruses.

Role: Project Leader. Principal Investigator: Kapczynski, D (USDA), Digard, P (UK). Amount: $382,852 (UGA)

NIFA – USDA Grant# 2021-67015-33406

01 Jan 2021–31 Dec 2025

Title: US-UK Collab: The evolutionary ecology of pathogen emergence via cross-species transmission in the avian-equine influenza system,

Role: Collaborator. Principal Investigator: Andrew Park. Amount: $1,064,846 (UGA)

NIFA – USDA Grant# 2020-67015-31539

01 Apr 2020–30 Jun 2024

Title: Broadly protective modified live attenuated influenza vaccines for poultry.

Role: Principal investigator. Amount: $500,000 (UGA).

Peer-review publications relevant to this proposal, highlight our ability to work with multiple groups

1. Curran SJ, Griffin EF, Ferreri LM, Kyriakis CS, Howerth EW, Perez DR, Tompkins SM. Swine influenza A virus isolates containing the pandemic H1N1 origin matrix gene elicit greater disease in the murine model. Microbiol Spectr. 2024 Mar 5;12(3):e0338623. doi: 10.1128/spectrum.03386-23. Epub 2024 Feb 1. PubMed PMID: 38299860; PubMed Central PMCID: PMC10913740.
2. Kanekiyo M, Gillespie RA, Midgett M, O'Malley KJ, Williams C, Moin SM, Wallace M, Treaster L, Cooper K, Syeda H, Kettenburg G, Rannulu H, Schmer T, Ortiz L, Da Silva Castanha P, Corry J, Xia M, Olsen E, Perez D, Yun G, Graham BS, Barratt-Boyes SM, Reed DS. Refined semi-lethal aerosol H5N1 influenza model in cynomolgus macaques for evaluation of medical countermeasures. iScience. 2023 Oct 20;26(10):107830. doi: 10.1016/j.isci.2023.107830. eCollection 2023 Oct 20. PubMed PMID: 37766976; PubMed Central PMCID: PMC10520834.
3. Lee CY, Raghunathan V, Caceres CJ, Geiger G, Seibert B, Cargnin Faccin F, Gay LC, Ferreri LM, Kaul D, Wrammert J, Tan GS, Perez DR, Lowen AC. Epistasis reduces fitness costs of influenza A virus escape from stem-binding antibodies. Proc Natl Acad Sci U S A. 2023 Apr 25;120(17):e2208718120. doi: 10.1073/pnas.2208718120. Epub 2023 Apr 17. PMID: 37068231
4. Hufnagel DE, Young KM, Arendsee ZW, Gay LC, Caceres CJ, Rajão DS, Perez DR, Vincent Baker AL, Anderson TK. Characterizing a century of genetic diversity and contemporary antigenic diversity of N1 neuraminidase in influenza A virus from North American swine. Virus Evol. 2023;9(1):vead015. doi: 10.1093/ve/vead015. eCollection 2023. PubMed PMID: 36993794; PubMed Central PMCID: PMC10041950.

B. Positions, Scientific Appointments, and Honors

Positions and Employment

2015-	Georgia Research Alliance Distinguished Investigator, University of Georgia, Athens, GA
2015-	Caswell S. Eidson Chair in Poultry Medicine, University of Georgia, Athens, GA
2013-2015	Professor of Virology, University of Maryland, College Park, MD
2007-2013	Associate Professor, University of Maryland, College Park, MD
2003-2007	Assistant Professor, University of Maryland, College Park, MD
2000-2003	Junior Faculty, St. Jude Children's Research Hospital, Memphis, TN

Other Experience and Professional Memberships

	Member, American Association for the Advancement of Science
2014-	Member, Scientists for Science
2003-	Lifetime Member, American Society for Virology
2000-	Member, American Society for Microbiology

Honors

2020	Zoetis Animal Health Award, College of Veterinary Medicine, University of Georgia

2018 Microbiome Partnership Development Award, UNITED KINGDOM Travel Sponsorship, Foreign & Commonwealth Office / Department of Business, Energy, and Industrial Strategy, United Kingdom

2010 Research Excellence Award, University of Maryland

2008 Pfizer Animal Health Award, Virginia-Maryland Regional College of Veterinary Medicine

2005 Junior Faculty Award, University of Maryland

2005 Research Excellence Award, University of Maryland

1993 Widaman Distinguished Graduate Assistant Award, University of Nebraska-Lincoln

1991 Student Research Forum Award, University of Nebraska Medical Center

C. Contributions to Science

1. I identified the amino acids in the PB1 polymerase subunit that interact with the PA polymerase subunit. These amino acids are located in the polymerase core, which is a region of the polymerase that is essential for enzyme activity. Disrupting the interaction between the PB1 and PA polymerase subunits by mutating these amino acids results in a decrease in polymerase activity and a reduction in viral replication.
   a. My research has identified a novel antiviral target for influenza viruses. By disrupting the interaction between the PB1 and PA polymerase subunits, we can inhibit viral replication and potentially prevent or treat influenza infection.
   b. Pérez DR, Donis RO. A 48-amino-acid region of influenza A virus PB1 protein is sufficient for complex formation with PA. J Virol. 1995 Nov;69(11):6932-9. PMCID: PMC189611.
   c. Perez DR, Donis RO. Functional analysis of PA binding by influenza a virus PB1: effects on polymerase activity and viral infectivity. J Virol. 2001 Sep;75(17):8127-36. PMCID: PMC115057.
2. I played a pivotal role in the development of plasmid-based influenza virus reverse genetics systems, revolutionizing the study and comprehension of influenza viruses. My primary contribution involved designing and producing expression vectors for the polymerase complex, which were instrumental in virus rescue. Additionally, I spearheaded the development of alternative influenza reverse genetics systems, paving the way for in vivo reverse genetics with far-reaching implications for vaccine development and gene therapy strategies utilizing the influenza virus replication machinery. My research on plasmid-based and in vivo reverse genetics systems has had a significant impact on our understanding of influenza viruses. This technology has been used to develop new vaccines, antivirals, and gene therapies for influenza. It has also been used to study the molecular mechanisms of influenza virus replication, transcription, and pathogenesis.
   a. Neumann G, Watanabe T, Ito H, Watanabe S, Goto H, Gao P, Hughes M, Perez DR, Donis R, Hoffmann E, Hobom G, Kawaoka Y. Generation of influenza A viruses entirely from cloned cDNAs. Proc Natl Acad Sci U S A. 1999 Aug 3;96(16):9345-50. PMCID: PMC17785.
   b. Hoffmann E, Stech J, Guan Y, Webster RG, Perez DR. Universal primer set for the full-length amplification of all influenza A viruses. Arch Virol. 2001 Dec;146(12):2275-89.
   c. Jackson D, Hossain MJ, Hickman D, Perez DR, Lamb RA. A new influenza virus virulence determinant: the NS1 protein four C-terminal residues modulate pathogenicity. Proc Natl Acad Sci U S A. 2008 Mar 18;105(11):4381-6. PMCID: PMC2393797.
   d. Chen H, Angel M, Li W, Finch C, Gonzalez AS, Sutton T, Santos J, Perez DR. All-in-one bacmids: an efficient reverse genetics strategy for influenza A virus vaccines. J Virol. 2014 Sep 1;88(17):10013-25. PMCID: PMC4136356.
3. My research provided compelling evidence of Japanese quail's significant role in the emergence of avian influenza viruses with an expanded host range. The recognition of Japanese quail and other minor poultry as biologically significant hosts in the emergence and spread of influenza viruses with expanded host range prompted the banning of quail in live bird markets in Hong Kong. My laboratory made the groundbreaking discovery of the airborne transmission potential of avian influenza viruses using the ferret model. This groundbreaking research shed light on the molecular changes that facilitate the airborne transmission of influenza viruses that typically circulate in avian species. My laboratory's pioneering work on the airborne transmission of avian influenza viruses has significantly impacted our understanding of the virus's potential for human-to-human transmission. This knowledge has guided public health measures and vaccine development strategies to combat the threat of influenza pandemics.

a. Sorrell EM, Wan H, Araya Y, Song H, Perez DR. Minimal molecular constraints for respiratory droplet transmission of an avian-human H9N2 influenza A virus. Proc Natl Acad Sci U S A. 2009 May 5;106(18):7565-70. PMCID: PMC2670882.

b. Kimble JB, Sorrell E, Shao H, Martin PL, Perez DR. Compatibility of H9N2 avian influenza surface genes and 2009 pandemic H1N1 internal genes for transmission in the ferret model. Proc Natl Acad Sci U S A. 2011 Jul 19;108(29):12084-8. PMCID: PMC3141953.

c. Sutton TC, Finch C, Shao H, Angel M, Chen H, Capua I, Cattoli G, Monne I, Perez DR. Airborne transmission of highly pathogenic H7N1 influenza virus in ferrets. J Virol. 2014 Jun;88(12):6623-35. PMCID: PMC4054360.

d. Carnaccini S, Cáceres CJ, Gay LC, Ferreri LM, Skepner E, Burke DF, Brown IH, Geiger G, Obadan A, Rajao DS, Lewis NS, Perez DR. Antigenic mapping of the hemagglutinin of the H9 subtype influenza A viruses using sera from Japanese quail (Coturnix c. japonica). J Virol. 2023 Oct 6;97(10):e0074323. doi: 10.1128/jvi.00743-23. Online ahead of print. PMID: 37800947

4. In response to the COVID-19 pandemic, we initiated studies to evaluate various antiviral strategies against SARS-CoV-2 and to develop animal models that would facilitate a deeper understanding of the role of microbiome alterations in disease outcomes. GC-376, a representative Mpro inhibitor, has demonstrated antiviral efficacy against Feline Infectious Peritonitis (FIP) CoV in experimentally infected cats. Employing the transgenic K18-hACE2 mouse model, we observed that GC-376-treated mice challenged with SARS-CoV-2 exhibited reduced viral loads, milder tissue lesions, and diminished inflammation compared to vehicle-treated SARS-CoV-2-challenged controls. These initial findings also revealed a correlation between infection dosage and decreased microbial diversity and taxonomic abundances of the Firmicutes phylum, particularly Lachnospiraceae, in the cecum of mice. Additionally, virus dose-dependent alterations were observed in the lungs, with decreased Bacteroidetes and increased Firmicutes and Proteobacteria. Furthermore, our development of a "geriatric" hamster model revealed that SARS-CoV-2 infection resulted in high vRNA loads in the nasal turbinates (NT), lungs, and trachea, along with elevated pulmonary lesion scores later in infection. Throughout SARS-CoV-2 disease progression, dysbiosis was evident in the pulmonary microbial dynamics, with the enrichment of opportunistic pathogens mirroring similar outcomes observed in humans with severe COVID-19. These findings underscore the intricate relationship between the gut microbiome and SARS-CoV-2 infection, highlighting the potential for microbiome-targeted interventions to modulate disease severity and outcomes. Further research is warranted to fully elucidate the underlying mechanisms and therapeutic implications of this interplay.

a. Seibert B, Cáceres CJ, Carnaccini S, Cardenas-Garcia S, Gay LC, Ortiz L, Geiger G, Rajao DS, Ottesen E, Perez DR. Pathobiology and dysbiosis of the respiratory and intestinal microbiota in 14 months old Golden Syrian hamsters infected with SARS-CoV-2. PLoS Pathog. 2022 Oct 24;18(10):e1010734. doi: 10.1371/journal.ppat.1010734. eCollection 2022 Oct. PMID: 36279276

b. Olivero NB, Gonzalez-Reiche AS, Re VE, Castro GM, Pisano MB, Sicilia P, Barbas MG, Khan Z, van de Guchte A, Dutta J, Cortes PR, Hernandez-Morfa M, Zappia VE, Ortiz L, Geiger G, Rajao D, Perez DR, van Bakel H, Echenique J. Phylogenetic analysis and comparative genomics of SARS-CoV-2 from survivor and non-survivor COVID-19 patients in Cordoba, Argentina. BMC Genomics. 2022 Jul 14;23(1):510. doi: 10.1186/s12864-022-08756-6. PMID: 35836127

c. Seibert B, Cáceres CJ, Cardenas-Garcia S, Carnaccini S, Geiger G, Rajao DS, Ottesen E, Perez DR. Mild and Severe SARS-CoV-2 Infection Induces Respiratory and Intestinal Microbiome Changes in the K18-hACE2 Transgenic Mouse Model. Microbiol Spectr. 2021 Sep 3;9(1):e0053621. doi: 10.1128/Spectrum.00536-21. Epub 2021 Aug 11. PMID: 34378965

d. Cáceres CJ, Cardenas-Garcia S, Carnaccini S, Seibert B, Rajao DS, Wang J, Perez DR. Efficacy of GC-376 against SARS-CoV-2 virus infection in the K18 hACE2 transgenic mouse model. Sci Rep. 2021 May 5;11(1):9609. doi: 10.1038/s41598-021-89013-w. PMID: 33953295.

https://www.ncbi.nlm.nih.gov/myncbi/18mhR0TuVno/bibliography/public/