

**BIOGRAPHICAL SKETCH**

Provide the following information for the Senior/key personnel and other significant contributors.  
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Jonathan R. Lai

eRA COMMONS USER NAME: JONATHANLAI

POSITION TITLE: Professor of Biochemistry

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       | Completion Date<br>MM/YYYY | FIELD OF STUDY           |
|------------------------------------------|--------------|----------------------------|--------------------------|
| Queen's University, Kingston, ON, Canada | B. Sc. Hons. | 06/1999                    | Biochemistry             |
| University of Wisconsin, Madison, WI     | Ph. D.       | 08/2004                    | Biophysics and Chemistry |
| Harvard Medical School, Boston, MA       | Post-Doc.    | 08/2004-11/2007            | Biological Chemistry     |

**A. Personal Statement**

A major focus of our group has been the use of antibody isolation, and protein engineering methods to develop novel immunotherapeutics and immunogens. We have been engaged in this area for over 18 years and spanned multiple viral pathogens including the filoviruses, flaviviruses, and alphaviruses. Specifically, with NYSBC, we seek to determine the structure of therapeutic antibodies in complex with their antigens. Additionally, we have developed new immunogens with improved properties and seek to determine the structures of antibodies in complex with those immunogens.

- 1) Quiroz, J. A., Malonis, R. J., Thackray, L. B., Cohen, C. A., Pallesen, J., Jangra, R. K., Brown, R. S., Hofmann, D., Holtsberg, F. W., Shulenin, S., Nyakatura, E. K., Durnell, L. A., Rayannavar, V., Daily, J. P., Ward, A. B., Aman, M. J., Dye, J. M., Chandran, K., **Diamond, M. S.**, Kielian, M., **Lai, J. R.\*** Human Monoclonal Antibodies against Chikungunya virus Target Multiple Distinct Epitopes in the E1 and E2 Glycoproteins. *PLoS Pathog.*, **2019**, *15*, e1008061. (PMCID: PMC6837291).
- 2) Malonis, R. J., Earnest, J. T., Kim, A. S., Angeliadis, M., Holtsberg, F. W., Aman, M. J., Jangra, R. K., Chandran, K., Daily, J. P., **Diamond, M. S.**, Kielian, M., **Lai, J. R.\*** Near-germline human monoclonal antibodies neutralize and protect against multiple arthritogenic alphaviruses. *Proc. Natl. Acad. Sci. USA*, **2021**, *118*, e2100104118. (PMCID: PMC8449321)
- 3) Kim, A. S.; Kafai, N. M.; Winkler, E. S.; Gilliland, T. C. Jr; Cottle, E. L.; Earnest, J. T.; Jethva, P. N.; Kaplonek, P.; Shah, A. P.; Fong, R. H.; Davidson, E.; Malonis, R. J.; Quiroz, J. A.; Williamson, L. E.; Vang, L.; Mack, M.; Crowe, J. E. Jr; Doranz, B. J.; **Lai, J. R.**; Alter, G.; Gross, M. L.; Klimstra, W. B.; Fremont, D. H., **Diamond, M. S.\*** Pan-protective Anti-alphavirus Human Antibodies Target a Conserved E1 Protein Epitope. *Cell*, **2021**, *184*, 4414-4429. (PMCID: PMC8382027)
- 4) Georgiev, G. I.; Malonis, R. J.; Wirchnianski, A. S.; Wessel, A. W.; Jung, H. S.; Cahill, S. M.; Nyakatura, E. K.; Vergnolle, O.; Cowburn, D.; **Diamond, M. S.**; **Lai, J. R.\*** Resurfaced Zika Virus EDIII Nanoparticle Immunogens Elicit Neutralizing and Protective Responses In Vivo. *Cell Chem. Biol.* **2022**, *29*, 811-823. (PMCID: PMC9133142)

Highlighted on-going projects:

NIH/NIAID R01-AI158194 (PI: Lai, J. R.)

01/01/2021 – 12/31/2025

*Structure-Based Design of Broad Flavivirus Immunogens.* Goals: To evaluate engineered “resurfaced” proteins based on Dengue virus and Zika virus E as new vaccine candidates.

Role: PI

NIH/NIAID U19-AI181960 (MPIs: Diamond, M.S; Kuhn, R.J.) 06/01/2024-05/30/2029

*Flavivirus and Alphavirus ReVAMPP (FLARE)*. Goals: Develop antigen designs, vaccine platforms, and monoclonal antibodies (mAbs) against prototype Flaviviruses and Alphaviruses and establish their efficacy in animal models of disease. With our industry partners, we will optimize protein nanoparticle, virion/VLP-based, and mRNA vaccine platforms, and extended half-life mAb-based treatments to rapidly respond to emerging flaviviruses and alphaviruses with pandemic potential using a pathogen prototype approach. A key goal is to optimally pair specific antigen designs and vaccine platforms or mAb combinations so that successful paradigms can be adapted in a “plug and play” manner to viruses within the same family to rapidly combat future outbreaks, epidemics, and pandemics.

Role: Project 3 Lead

## **B. Positions and Honors**

### **Employment**

1999 – 2004 Graduate Research, University of Wisconsin (Advisor: Samuel H. Gellman), Madison, WI  
2004 – 2007 Postdoctoral Fellow, Harvard Medical School (Advisor: Christopher T. Walsh), Boston, MA  
2007 Postdoctoral Fellow, Harvard Medical School (Advisor: Stephen C. Harrison), Boston, MA  
2007 – 2013 Assistant Professor of Biochemistry, Albert Einstein College of Medicine, Bronx, NY  
2013 – 2018 Associate Professor of Biochemistry, Albert Einstein College of Medicine, Bronx, NY  
2018 – Professor of Biochemistry, Albert Einstein College of Medicine, Bronx, NY  
2022 – Dan Danciger Professor of Biochemistry, Albert Einstein College of Medicine, Bronx, NY

### **Honors**

1999 – 2001 Queen’s University Honor Matriculation Scholarship  
2002 – 2004 Natural Sciences and Engineering Research Council of Canada Post-Graduate B Scholarship  
2004 – 2007 Helen Hay Whitney Post-Doctoral Fellowship  
2009 – 2012 Arnold and Mabel Beckman Young Investigator Award  
2015 – 2020 Irma T. Hirschl/Monique Weill-Caulier Career Scientist Award  
2021 XSeed Award by Deerfield

### **Professional Memberships and Other Service**

Current Memberships: American Chemical Society (since 2002), American Association for the Advancement of Science (2006), American Peptide Society (2010), New York Academy of Sciences (2010), The Antibody Society (2013), The Protein Society (2014), American Society for Virology (2014)

2010 – New York Academy of Sciences Chemical Biology Interest Group Steering Committee  
2010 – 2014 NCI Study Section for Innovative Molecular Analysis Technologies (ZCA1 SRLB-Q)  
2011 Ad Hoc Reviewer for NSF Chemistry of Life Sciences Program  
2013, 2014 Ad Hoc Reviewer for DFG Germany (Deutsch Forschungsgemeinschaft)  
2013 Chair, Scientific Committee of the 23<sup>rd</sup> American Peptide Symposium  
2014 NIAID Special Emphasis Panels for HIV-1 Vaccine Innovation (ZA1 BLF-A (J2), ZA1 KP-A (J1))  
2015 Ad Hoc Reviewer for NIH Synthetic and Biological Chemistry B Study Section  
2015 NIH Topics in Virology Study Section (ZRG1 IDM-W)  
2015 – 2023 Reviewer, Arnold and Mabel Beckman Foundation  
2015 – 2017 Organizing Co-chair, 25th American Peptide Symposium (Whistler, BC, Canada, 2017)  
2016 NIAID Special Emphasis Panel ZAI1-UKS-A-M2  
2016 Ad Hoc Reviewer for NIH IMM-S10B Study Section  
2016 Ad Hoc Reviewer for NIH IMM-S02M Study Section  
2018 – 2023 Chartered Member of Vaccines for Microbial Diseases Study Section  
2019 – 2023 Elected Vice-Speaker of Einstein Faculty Senate  
2021 – 2023 Executive Committee, Arnold and Mabel Beckman Foundation

### C. Contributions to Science (from 81 total publications; \* indicates corresponding author(s))

**1. Engineering resurfaced EDIII immunogens for DENV and ZIKV.** We performed phage display-based combinatorial scanning mutagenesis to map functional epitopes on DENV E glycoprotein DIII for recognition by two related broadly neutralizing antibodies and then used this information to develop resurfaced EDIII immunogens.

- a. Georgiev, G. I.; Malonis, R. J.; Wirchnianski, A. S.; Wessel, A. W.; Jung, H. S.; Cahill, S. M.; Nyakatura, E. K.; Vergnolle, O.; Dowd, K. A.; Cowburn, D.; Pierson, T. C.; Diamond, M. S.; **Lai, J. R.\*** Resurfaced ZIKV EDIII nanoparticle immunogens elicit neutralizing and protective responses in vivo. *Cell Chem. Biol. Cell Chem. Biol.* **2022**, 29, 811-823. (PMCID: PMC9133142)
- b. Frei, J. C.; Wirchnianski, A. S.; Govero, J.; Vergnolle, O.; Dowd, K. A.; Pierson, T. C.; Kielian, M.; Girvin M. E.; Diamond, M. S.; **Lai, J. R.\*** Engineered Dengue Virus Domain III Proteins Elicit Cross-Neutralizing Antibody Response in Mice. *J. Virol.* **2018**, 92, pii: e01023-18. (PMCID: PMC6146717)
- c. Frei, J. C.; Kielian, M.; **Lai, J. R.\*** Comprehensive mapping of functional epitopes on dengue virus glycoprotein E DIII for binding to broadly neutralizing antibodies 4E11 and 4E5A by phage display. *Virology*, **2015**, 485, 371-382. (PMCID: PMC4619145)

**2. Isolation and characterization of human antibodies targeting CHIKV and other alphaviruses.** We have recently developed a large panel of human mAbs from CHIKV convalescent donors using single B cell sorting.

- a. Malonis, R. J.; Earnest, J. T.; Kim, A. S.; Angeliadis, M.; Holtsberg, F. W.; Aman, M. J.; Jangra, R. K.; Chandran, K.; Daily, J. P.; Diamond, M. S.; Kielian, M.; **Lai, J. R.\*** Near-germline human monoclonal antibodies neutralize and protect against multiple arthritogenic alphaviruses. *Proc. Natl. Acad. Sci. USA*, **2021**, 118, e2100104118. (PMCID: PMC8449321)
- b. Kim, A. S.; Kafai, N. M.; Winkler, E. S.; Gilliland, T. C. Jr; Cottle, E. L.; Earnest, J. T.; Jethva, P. N.; Kaplonek, P.; Shah, A. P.; Fong, R. H.; Davidson, E.; Malonis, R. J.; Quiroz, J. A.; Williamson, L. E.; Vang, L.; Mack, M.; Crowe, J. E. Jr; Doranz, B. J.; **Lai, J. R.**; Alter, G.; Gross, M. L.; Klimstra, W. B.; Fremont, D. H.; **Diamond, M. S.\*** Pan-protective Anti-alphavirus Human Antibodies Target a Conserved E1 Protein Epitope. *Cell*, **2021**, 184, 4414-4429. (PMCID: PMC8382027)
- c. Quiroz, J. A.; Malonis, R. J.; Thackray, L. B.; Cohen, C. A.; Pallesen, J.; Jangra, R. K.; Brown, R. S.; Hofmann, D.; Holtsberg, F. W.; Shulenin, S.; Nyakatura, E. K.; Durnell, L. A.; Rayannavar, V.; Daily, J. P.; Ward, A. B.; Aman, M. J.; Dye, J. M.; Chandran, K.; Diamond, M. S.; Kielian, M.; **Lai, J. R.\*** Human Monoclonal Antibodies against Chikungunya virus Target Multiple Distinct Epitopes in the E1 and E2 Glycoproteins. *PLoS Pathog.*, **2019**, 15, e1008061. (PMCID: PMC6837291).
- d. Tong, K.; Hernandez, E. M.; Basore, K.; Fremont, D. H.; **Lai, J. R.\*** Chikungunya virus E2 B Domain Nanoparticle Elicits Homotypic Neutralizing Antibody in Mice. *Vaccine*, **2024**, 42, 126405. (PMCID: PMC11645211)

**3. Development of filovirus immunotherapies by bispecific antibody engineering.** We developed the first bsAbs antibodies capable of providing post-exposure protection of mice from multiple ebolavirus species. Recently, we developed the first broadly protective ebolavirus bsAbs.

- a. Wirchnianski, A. S.; Nyakatura, E. K.; Herbert, A. S.\*; Kuehne, A. I.; Abbasi, A. I.; Florez, C.; Storm, N.; McKay, L. G. A.; Dailey, L.; Kuang, E.; Abelson, D. M.; Wec, A. Z.; Chakraborti, S.; Holtsberg, F. W.; Shulenin, S.; Bornholdt, Z. A.; Aman, M. J.; Honko, A. N.; Griffiths, A.; Dye, J. M.; Chandran, K.\*; **Lai, J. R.\*** Design and Characterization of Protective Pan-Ebolavirus and Pan-Filovirus Bispecific Antibodies. *PLoS Path.* **2024**, 11, e1012134. (PMCID: PMC11037526)
- b. Nyakatura, E. K.; Zak, S. E.; Wec, A. Z.; Hofmann D.; Shulenin, S.; Bakken, R. R.; Aman, M. J.; Chandran, K.; Dye, J. M.; **Lai, J. R.\*** "Design and Evaluation of Bi-and Trispecific Antibodies Targeting Multiple Filovirus Glycoproteins" *J Biol Chem.*, **2018**, 293, 6201-6211. (PMCID: PMC5912469).
- c. Wec, A. Z.\*; Nyakatura, E. K.\*; Herbert, A. S.\*; Howell, K. A.; Holtsberg, F. W.; Bakken, R. R.; Mittler, E.; Christin, J. R.; Shulenin, S.; Jangra, R. K.; Bharrhan, S.; Kuehne, A. I.; Bornholdt, Z. A.; Flyak, A. I.; Saphire, E. O.; Crowe, J. E. Jr.\*; Aman, M. J.\*; Dye, J. M.\*; **Lai, J. R.\***; Chandran, K.\* "A 'Trojan Horse' Bispecific Antibody Strategy for Broad Protection against Ebolaviruses" *Science*, **2016**, 354, 350-354. (PMCID: PMC5647781) \* Co-equal first authors; \* Corresponding authors.
- d. Frei, J. C.; Nyakatura, E. K.; Zak, S. E.; Bakken, R. R.; Chandran, K.; Dye, J. M.\*; **Lai, J. R.\*** Bispecific Antibody Affords Complete Post-Exposure Protection of Mice from Both Ebola (Zaire) and Sudan viruses. *Sci. Rep.*, **2016**, 6, 19193. (PMCID: PMC4725817)

**4. Use of phage display to decipher structure, function, and recognition.** For many years, I have used phage display and other protein library techniques to understand aspects of protein structure, function and recognition in various systems.

- a. Lin, T. Y.; **Lai, J. R.\*** Interrogation of Side Chain Biases for Oligomannose Recognition by Antibody 2G12 via Structure-Guided Phage Display Libraries. *Bioorg. Med. Chem.*, **2017**, [Epub Sept. 15, doi: 10/1016]
- b. Uchime, O.; Dai, Z.; Biris, N.; Lee, D.; Sidhu, S. S.; Li, S.; **Lai, J. R.\***; Gavathiotis, E. Synthetic Antibodies Inhibit Bcl-2 Associated X-Protein (BAX) through Blockade of the N-Terminal Activation Site. *J. Biol. Chem.*, **2016**, 291, 89-102. (PMCID: PMC4697190)
- c. Liu, Y.; Higgins, C. D.; Overstreet, C. M.; Rai, K. R.; Chiorazzi, N.\*; **Lai, J. R.\*** Peptides that Bind Specifically to an Antibody from a Chronic Lymphocytic Leukemia Clone Expressing Unmutated Immunoglobulin Variable Region Genes. *Mol. Med.*, **2013**, 19, 245-252. (PMCID: PMC376952)
- d. Da Silva, G. F.; Harrison, J. S.; **Lai, J. R.** Contribution of Light Chain Residues to High Affinity Binding in an HIV-1 Antibody Explored by Combinatorial Scanning Mutagenesis. *Biochemistry*, **2010**, 49, 5464-5472. (PMCID: PMC2911358)

**5. Structural and mechanistic dissection of viral fusion proteins.** We have described several novel aspects of viral fusion, including the first X-ray structures of the post-fusion ectodomain conformations of the fusion subunits from MARV and the CAS Virus, an arena-like species in collaboration with Dr. Almo. In addition, we were the first to demonstrate a direct conformational effect of endosomal pH on filovirus GP2, and on-going work includes collaboration with Dr. Girvin. Finally, our studies of fusion subunits in membrane environments have yielded new and surprising information about mechanistic aspects of viral membrane fusion.

- a. Dai, Z.; Tao, Y.; Liu, N.; Brenowitz, M. D.; Girvin, M. E.; Lai, J. R.\* Conditional Trimerization and Lytic Activity of HIV-1 gp41 Variants Containing the Membrane-Associated Segments. *Biochemistry*, **2015**, 54, 1589-1599. (PMCID: PMC4348151)
- b. Koellhoffer, J. F.; Dai, Z.; Malashkevich, V. N.; Stenglein, M. D.; Liu, Y.; Toro, R.; Harrison, J. S.; Chandran, K.; DeRisi, J. L.; Almo, S. C.; **Lai, J. R.\*** Structural Characterization of the GP2 Core Domain from the CAS Virus, a Novel Arenavirus-like Species. *J. Mol. Biol.*, **2014**, 426, 1452-1468. (PMCID: PMC3951589).
- c. Koellhoffer, J. F.; Malashkevich, V. N.; Harrison, J. S.; Toro, R.; Bhosle, R. C.; Chandran, K.; Almo, S. C.; **Lai, J. R.\*** Crystal Structure of the Marburg Virus GP2 Core Domain in Its Post-Fusion Conformation. *Biochemistry*, **2012**, 51, 7665-7675. (PMCID: PMC3464016)
- d. Harrison, J. S.; Koellhoffer, J. K.; Chandran, K.; **Lai, J. R.\*** Marburg Virus Glycoprotein GP2: pH-Dependent Stability of the Ectodomain  $\alpha$ -Helical Bundle. *Biochemistry*, **2012**, 51, 2515-2525. (PMCID: PMC3314129)

Full publication list available at:

<https://www.ncbi.nlm.nih.gov/myncbi/jonathan.lai.1/bibliography/public/>

**BIOGRAPHICAL SKETCH**

Provide the following information for the Senior/key personnel and other significant contributors.  
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: ANA SOFIA FERREIRA RAMOS

eRA COMMONS USER NAME: FERREIRA-RAMOS\_AS

ORCID: <https://orcid.org/0000-0001-9937-3074>

POSITION TITLE: INSTRUCTOR

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       | Completion Date<br>MM/YYYY | FIELD OF STUDY          |
|----------------------------------------------------------------------------------------|--------------|----------------------------|-------------------------|
| University of Aveiro, Aveiro, Portugal                                                 | Bachelor     | 06/2010                    | Biology                 |
| University of Porto, Porto, Portugal                                                   | Master       | 10/2013                    | Biochemistry            |
| Aix Marseille University, Marseille, France                                            | PhD          | 07/2019                    | Structural Biochemistry |
| University of Lübeck, Lübeck, Germany                                                  | Postdoctoral | 10/2021                    | Structural Biochemistry |
| Institute of Functional Genomics (IGF), University of Montpellier, Montpellier, France | Postdoctoral | 04/2022                    | Structural Biochemistry |
| Icahn School of Medicine at Mount Sinai, New York, United States                       | Postdoctoral | 10/2023                    | Structural Biochemistry |

**A. Personal Statement**

I am an Instructor at the department of Biochemistry of Albert Einstein College of Medicine (New York, US), in the laboratory of Professor Jonathan Lai (Ph.D). I am currently conducting research focus on structural characterization of viral targets from alphaviruses and flaviviruses and aiming to contribute for the development of vaccines and immunotherapeutics. I have a broad background in structural biology with specific training and expertise in X-ray crystallography and cryo-EM. In collaboration with NYSBC we aim to determine the structure of therapeutic antibodies in complex with their antigens, and with immunogens that were previously developed by the Lai lab.

- 1) Maurer DP, Vu M, **Ramos ASF**, Dugan HL, Khalife P, Geoghegan JC, Walker LM, Bajic G, Schmidt AG. Conserved sites on the influenza H1 and H3 hemagglutinin recognized by human antibodies. *Sci Immunol. (in press)*  
(PDBs: **9BDF** and **9BDG**)
- 2) Feldman J, **Ferreira Ramos AS**, Vu M, Maurer D, Rosado V, Lingwood D, Bajic G, Schmidt A. Human naive B cells recognized pre-pandemic influenza virus hemagglutinins. *Sci Immunol.* 2025 Jan 24;10(103):eado9572. doi: 10.1126/sciimmunol.ado9572. Epub 2025 Jan 24. PubMed PMID: 39854479.  
(PDB: **8UME**)
- 3) **Ferreira-Ramos AS**, Sulzenbacher G, Canard B, Coutard B. Snapshots of ADP-ribose bound to Getah virus macro domain reveal an intriguing choreography. *Sci Rep.* 2020 Sep 2;10(1):14422. doi: 10.1038/s41598-020-70870-w. PubMed PMID: 32879358; PubMed Central PMCID: PMC7468284.  
(PDBs: **6QZU**, **6R0F**, **6R0G**, **6R0P**, **6R0R**, **6R0T**)

## B. Positions, Scientific Appointments, and Honors

- 11/2024 – present** **Instructor**, Department of Biochemistry, Albert Einstein College of Medicine (Jonathan Lai team), New York (UNITED STATES).  
Area of research: Antibody engineering and vaccine design.
- 05/2022 – 11/2024** **Postdoctoral fellow**, Department of Microbiology, Icahn School of Medicine at Mount Sinai (Bajic team), New York (UNITED STATES).  
Project: Understanding how the interplay of a rapidly evolving virus and the host humoral immune system can lead to better vaccines.
- 11/2021 - 04/2022** **Postdoctoral researcher**, Institute of Functional Genomics (Granier – Mouillac team), Montpellier (FRANCE).  
Project: Elucidating the molecular and structural bases of enzymatic processes and their regulation by the membrane proteins involved in ceramides *de novo biosynthesis*.
- 04/2019 – 11/2020** **Postdoctoral researcher**, Biochemistry Institute at the University of Lübeck (Redecke team), Lübeck (GERMANY).  
Project: Expanding the domain of serial crystallography: membrane proteins & “*in cellulose*” crystallization.
- 10/2015 – 07/2019** **Ph.D. student**, University of Aix-Marseille (AFMB laboratory – Canard team), Marseille (FRANCE).  
Thesis project: Inhibitors of the mRNA capping and structural studies on Macro domains from alphaviruses.
- 02/2014 – 09/2015** **Research assistant**, Instituto de Tecnologia Química e Biológica, Universidade Nova de Lisboa, Lisbon (PORTUGAL).  
Projects: Pathogenesis of Kaposi's sarcoma herpesvirus. Structural-function studies of MHV-68 M2 modulation of the antiviral immune response. Structural studies on LANA interactions and its impact on tumor viral latent infection.

## C. Contributions to Science

**1. Study of correlates of protection of influenza virus antibody mediated immune response.** During my postdoc at Icahn School of Medicine at Mount Sinai, and in collaboration with Aaron Schmidt at Harvard Medical School, we have discovered that naïve antibodies from human naïve B cells recognize hemagglutinins (HAs) from pre-pandemic influenza viruses. Overall, our study highlighted that humoral responses within the naïve repertoire that do not require, or require minimal, somatic hypermutation can both bind and neutralize pre-pandemic highly pathogenic influenza H5Nx viruses. I contributed to the study by determining the structure of the influenza hemagglutinin (HA) complex with the Fab HD16 D04 (PDB 8UME) by cryoEM. My results contributed to the validation of the epitope mapping experiments and helped understanding how naïve neutralizing monoclonal antibodies (mAb) binds to H5 HA. In addition, my work allowed to define the epitope, which overlaps with the vestigial esterase, and its contact residues, included residues that are broadly conserved among historical and contemporary H5 HA strains. In another study I have determined the cryo-EM structure of influenza H3 HA in complex with broad neutralizing antibodies (PDBs 9BDF and 9BDG) that were optimized through direct evolution from broad, subtype-neutralizing mAbs from human B cells targeting the H3 HA head as well as a unique mAb targeting the stem.

- a. Feldman J, **Ferreira Ramos AS**, Vu M, Maurer D, Rosado V, Lingwood D, Bajic G, Schmidt A. Human naïve B cells recognized pre-pandemic influenza virus hemagglutinins. *Sci Immunol.* 2025 Jan 24;10(103):eado9572. doi: 10.1126/sciimmunol.ado9572. Epub 2025 Jan 24. PubMed PMID: 39854479. (PDB: 8UME)
- b. Maurer DP, Vu M, **Ramos ASF**, Dugan HL, Khalife P, Geoghegan JC, Walker LM, Bajic G, Schmidt AG. Conserved sites on the influenza H1 and H3 hemagglutinin recognized by human antibodies. *Sci Immunol.* (in press)

Maurer DP, Vu M, **Ramos ASF**, Dugan HL, Khalife P, Geoghegan JC, Walker LM, Bajic G, Schmidt AG. Conserved sites on the influenza H1 and H3 hemagglutinin recognized by human antibodies. bioRxiv. 2024 Nov 2;. doi: 10.1101/2024.10.22.619298. PubMed PMID: 39484545; PubMed Central PMCID: PMC11526932.  
(PDBs: 9BDF and 9BDG)

**2. Structure-based studies on Getah virus Macro-domain.** During my PhD at Aix-Marseille University I studied alphavirus and I acquired competence in X-ray crystallography. To understand the implications on alphavirus replication caused by ADP-ribose binding and de-ribosylation of cellular proteins, part of my work was focused on understanding this mechanism. Therefore, I performed structure-based studies on Getah virus Macro-domain, which is a domain of the non-structural protein 3 (nsP3), which contains a peculiar substitution in the catalytic loop. Our crystallographic studies characterized several ADP-ribose poses in the binding site (PDBs: 6QZU, 6R0F, 6R0G, 6R0P, 6R0R, 6R0T) that may represent snapshots of the ADP-ribosylhydrolase mechanism, highlighting new residues to be further characterized.

a. **Ferreira-Ramos AS**, Sulzenbacher G, Canard B, Coutard B. Snapshots of ADP-ribose bound to Getah virus macro domain reveal an intriguing choreography. Sci Rep. 2020 Sep 2;10(1):14422. doi: 10.1038/s41598-020-70870-w. PubMed PMID: 32879358; PubMed Central PMCID: PMC7468284.  
(PDBs: 6QZU, 6R0F, 6R0G, 6R0P, 6R0R, 6R0T)

**3. Development of a high-throughput screening to select inhibitors targeting the nsP1 capping enzyme of Venezuelan equine encephalitis virus.** Using an immune-based assay, during my PhD., I contributed to the development of a high-throughput screening to select drugs against nsP1 capping enzyme of Venezuelan equine encephalitis virus. Our results showed that this high-throughput enzyme-based assay is a convenient way to select potent and specific hit compounds targeting the viral mRNA capping of Alphaviruses. We screened a library of 1220 approved compounds and identified 18 compounds inhibiting the nsP1 guanylation. Their IC<sub>50</sub> was determined and compounds from two series were further characterized and shown to inhibit the nsP1 MTase activity. These compounds barely inhibited a cellular MTase demonstrating their specificity towards nsP1. We also initiated analogues search and study activity relationship (SAR) to identify the active pharmacophore features.

a. **Ferreira-Ramos AS**, Li C, Eydoux C, Contreras JM, Morice C, Quérat G, Gigante A, Pérez Pérez MJ, Jung ML, Canard B, Guillemot JC, Decroly E, Coutard B. Approved drugs screening against the nsP1 capping enzyme of Venezuelan equine encephalitis virus using an immuno-based assay. Antiviral Res. 2019 Mar;163:59-69. doi: 10.1016/j.antiviral.2019.01.003. Epub 2019 Jan 11. PubMed PMID: 30639438.

**Complete List of Published Work in MyBibliography:**

<https://www.ncbi.nlm.nih.gov/myncbi/ana%20sofia.ferreira%20ramos.1/bibliography/public/>