

BIOMEDICAL & VETERINARY SCIENCES

GRADUATE PROGRAM



ANNOUNCES

The Doctor of Philosophy Seminar and Examination of

Christina Chuong

**"Effective Strategies for Preventing and Mitigating Emerging
Viruses"**

Monday, April 17th, 2023

11:00AM

Fralin Biotechnology Center

Auditorium



Bio

Christina attended the University of North Carolina at Chapel Hill where she obtained her B.S. in Chemistry (Biochemistry focus). She participated in undergraduate research in a protein chemistry lab lead by Dr. David Williams Jr. and worked on macromolecular structures involved with epigenetic regulation of gene expression. After graduation, she pursued experiences to further diversify her skill set and directly apply her scientific training to treat human disease. She joined Dr. Lawrence G. Lum's lab at the University of Virginia to study cancer immunotherapy techniques and its application in clinical trials. With his guidance, she studied the interaction between drug development and efficacy in phase I and II cancer trials as well as participated in delivering these treatments directly to patients. This job inspired her to work towards a career where she could develop innovative solutions and make significant contributions toward improving the lives of others. She applied to work as a lab technician at Virginia Tech for Dr. James-Weger Lucarelli, to transition into the Virology field. With his mentorship and encouragement, she then proceeded to pursue her PhD where she focused on projects related to preventing and treating viral disease. In her free time, Christina enjoys spending time with her husband (Cailean) and her two puppies (Hiro and Fenny) and entertaining friends with warm meals, board games, and disc-golfing.

Funded by

Center for Emerging, Zoonotic, and Arthropod-borne Pathogens
VMCVM Office of Research and Graduate Studies

Lay Language Abstract

The global response to the COVID-19 pandemic, and its far-reaching impact, revealed significant shortcomings in public health preparedness for emerging viruses. Despite efforts to develop vaccines and antivirals to prevent and treat disease, current mitigation strategies have proven insufficient to eradicate the pathogen. The emergence of viral outbreaks caused by viruses such as chikungunya (CHIKV) and SARS-CoV-2 underscores the ongoing threat posed by emerging infectious diseases. It is clear that improved countermeasures are urgently needed to address gaps in vaccine and antiviral development. CHIKV is a mosquito-borne virus that has caused millions of infections across hundreds of countries with emergent potential to become endemic in the US. Currently there are no vaccines available to the public, therefore, it is important to generate and administer an effective vaccine before further spread of the virus. To this end, we developed innovative live-attenuated vaccines (LAVs) against CHIKV using a weakened chimeric backbone of CHIKV and its close relative, Semliki Forest virus (SFV), along with vaccine-driven expression of antiviral cytokines to control viral replication. Vaccination of highly susceptible mice with these cytokine-expressing vaccines produced significantly decreased side-effects compared to the parental virus not expressing the cytokines. Additionally, these viruses had significantly restricted viral replication capabilities while robustly protected mice from a semi-lethal CHIKV infection. Our interferon-gamma (IFN γ) expressing vaccine had the greatest impact on viral replication, and we investigated the mechanism leading to this attenuation. To assess the clinical relevance of our vaccine platform, we redesigned the virus to express human IFN γ and identified a specific pattern of IFN γ -stimulated genes are potentially responsible for limiting CHIKV replication. Furthermore, we demonstrated the broad therapeutic use of IFN γ against other medically relevant alphaviruses. Overall, these studies establish an improved mechanism to create safer vaccines without compromising efficacy, and highlight the therapeutic potential of IFN γ against alphaviruses. Lastly, in a collaborative effort to respond to the COVID-19 pandemic, we also explored and characterized the use of a new class of antiviral drugs. With the advent of increasing drug resistance, it is essential to develop novel and resilient therapeutics. We demonstrated the first antiviral potential of rhodium organometallics, which were previously shown to be effective against multiple antibiotic-resistant bacteria. Two complexes demonstrated high virucidal activity against SARS-CoV-2 and low toxicity in mammalian cell lines. Moreover, these complexes can be further derivatized to improved efficacy, making them a promising new antiviral strategy.

Publications

Roesch, F.Ī, Cereghino C. Ī, Carrau, L., Hardy, A., Helder, R.F., Lacritick, A.H, Koh, C., Marano J.M., Bates T.A., Rai, P., **Chuong, C.**, Akter, S., Valet, T., Blanc, H., Brown, A., Michalak, P., LeRoith, T., Bloom, J., Marques, R.E., Saleh, C., Vignuzzi, M., & Weger-Lucarelli, J. Identification of a key residue for alphavirus adaptation to the urban vector *Aedes aegypti* through experimental evolution approaches. (2023) PLOS Pathogens [accepted].

Gannett C., Banks P., **Chuong, C.**, Weger-Lucarelli J., Meyers, E., & Lowell, A. (2023). Semisynthetic blasticidin S ester derivatives show enhanced antibiotic activity. RSC Medicinal Chemistry. <https://doi.org/10.1039/D2MD00412G>

Chuong, C., Cereghino, C., Rai, P., Bates, T.A., Oberer, M., & Weger-Lucarelli J. (2023). Enhanced safety of cytokine-expressing vaccines against chikungunya virus. <https://doi.org/10.21203/rs.3.rs-2439770/v1> [pre-print and in review]

Rai, P, **Chuong, C**, LeRoith, T, Smyth, JW, Julia Panov, Moshe Levi, Kylene Kehn-Hall, Nisha K. Duggal, James-Weger Lucarelli, Adenovirus transduction to express human ACE2 causes obesity-specific morbidity in mice, impeding studies on the effect of host nutritional status on SARS-CoV-2 pathogenesis, *Virology*, Volume 563, 2021, Pages 98-106, ISSN 0042-6822, <https://doi.org/10.1016/j.virol.2021.08.014>.

Chuong, C., DuChane, C. M., Webb, E. M., Rai, P., Marano, J. M., Bernier, C. M., Merola, J. S., & Weger-Lucarelli, J. (2021). Noble Metal Organometallic Complexes Display Antiviral Activity against SARS-CoV-2. *Viruses*, 13(6), 980. <https://doi.org/10.3390/v13060980>

Bates T.A., **Chuong, C.**, Rai, P., Marano, J.M., Waldman, A., Klinger, A, Reinhold, J.M., Lahondère, C, & Weger-Lucarelli, J. American *Aedes japonicus*, *Culex pipiens*, and *Culex restuans* mosquitoes have limited transmission capacity for a recent isolate of Usutu virus. *Virology*. 2021 Mar; 555:64-70. <https://doi.org/10.1016/j.virol.2020.12.023>

Marano, J. M., **Chuong, C.**, & Weger-Lucarelli, J. (2020). Rolling circle amplification: A high fidelity and efficient alternative to plasmid preparation for the rescue of infectious clones. *Virology*, 551, 58–63. <https://doi.org/10.1016/j.virol.2020.08.016>

Chuong, C.; Bates, T. A.; Akter, S.; Werre, S. R.; LeRoith, T.; Weger-Lucarelli, J., Nutritional status impacts dengue virus infection in mice. *BMC Biol* 18, 106 (2020). <https://doi.org/10.1186/s12915-020-00828-x>

Chuong, C., Bates, T. A., & Weger-Lucarelli, J. (2019). Infectious cDNA clones of two strains of Mayaro virus for studies on viral pathogenesis and vaccine development. *Virology*, 535, 227–231. <https://doi.org/10.1016/j.virol.2019.07.013>

Presentations

Chuong, C., Rai, P., Cereghino, C, & Weger-Lucarelli J. Interferon-gamma mediated alphavirus vaccine attenuation and therapeutic efficacy [oral presentation], 2023, March, BMVS Research in Progress Seminar Series, Blacksburg, Virginia

Chuong, C., Rai, P., Cereghino, C, & Weger-Lucarelli J. Interferon-gamma mediated alphavirus vaccine attenuation and therapeutic efficacy [poster presentation] 2023, March, Biomedical and Veterinary Sciences 32nd Annual Research Symposium, Blacksburg, Virginia

Chuong, C., Weger-Lucarelli J. Attenuation Mechanism of Interferon Gamma on Chikungunya Virus [oral presentation] 2022 CeZAP Infectious Diseases Symposium, Blacksburg, Virginia

Chuong, C.; Cereghino, C; Rai, P; Bates, TA; Oberer, M; Foley, A; Flinchum, B; Weger-Lucarelli J. Enhanced safety of cytokine-expressing vaccines against chikungunya virus [oral presentation] 2022 American Society for Virology 41st Annual Meeting, Madison, Wisconsin

Chuong, C.; Bates, TA; Rai, P; Weger-Lucarelli J. Protection against chikungunya virus via cytokine-expressing vaccines [poster presentation] 2021, March, Biomedical and Veterinary Sciences 31st Annual Research Symposium, Virtual, Blacksburg, Virginia

Chuong, C.; DuChane, CM; Webb, EM; Rai, P; Marano, JM; Bernier, CM; Merola, JS; Weger-Lucarelli J. Noble Metal Organometallic Complexes Display Antiviral Activity against SARS-CoV-2 [poster presentation] 2021 May VirginiaDrugDiscoveryRx, Virtual, Virginia

Chuong, C.; Bates, TA; Rai, P; Weger-Lucarelli J. Protection against chikungunya virus via cytokine-expressing vaccines [5 min flashtalk] 2021, March, Graduate Student Annual Research Symposium 37th Annual Research Symposium, Virtual, Blacksburg, Virginia

Chuong, C.; Weger-Lucarelli J. Protection against chikungunya virus via cytokine-expressing vaccines [oral presentation], 2020, September, BMVS Research in Progress Seminar Series, Blacksburg, Virginia

Awards and Academic Achievements

- Outstanding Poster Presentation Award, BMVS Annual Research Symposium, Virginia Tech, March 2023
- American Society for Virology Student Travel Award, University of Wisconsin-Madison, July 2022
- Graduate Research Development Program (GRDP) award, Virginia Tech, May 2022
- Infectious Disease (ID) Interdisciplinary Graduate Education Program (IGEP) Grant Award, Virginia Tech, March 2022
- Graduate Research Development Program (GRDP) award, Virginia Tech, Dec. 2019

Examination Graduate Committee

Major Advisor/Chair:

James Weger-Lucarelli, PhD
Assistant Professor
Department of Biomedical and Pathobiology

Graduate Advising Committee Members:

Xiang-jin Meng, MD, PhD
University Distinguished Professor
Department of Biomedical and Pathobiology

Nisha Duggal, PhD
Assistant Professor
Department of Biomedical and Pathobiology

Irving Coy Allen, PhD, MBA, MS
Associate Professor
Department of Biomedical and Pathobiology



VIRGINIA TECH™