BIOMEDICAL & VETERINARY SCIENCES GRADUATE PROGRAM

ANNOUNCES

The Doctor of Philosophy Seminar and Examination of

Rusha Pal

“Investigating novel treatment approaches to combat Clostridioides difficile”

Wednesday, December 7th, 2022
9:30AM
VMCVM Classroom 100
https://virginiatech.zoom.us/j/82291907217?pwd=akJONitzZmZHQSt1SktGZkdTdlJndz09
Passcode: Rusha

Bio

Rusha did her BS and MS in Microbiology from Kolkata, India. Her journey in the US began in January 2015 when she relocated to New Jersey with a dream of pursuing an advanced degree in the field of sustainability management. Later in 2017, Rusha joined the lab of Dr. Mohamed Seleem in Purdue University to pursue a PhD in the field of molecular bacteriology. Her research in the Seleem lab focused on utilizing a combination of both traditional and non-traditional approaches to identify a novel anticlostridial that can efficiently inhibit the growth of *Clostridioides difficile* which is responsible for causing debilitating diarrhea mostly in hospitalized patients.

Awards and Academic Achievements

Award of excellence in poster presentation. 2022 CeZAP Infectious Diseases Symposium, October 7th, 2022, Blacksburg, VA.

Best Student Poster Presentation (Second position) Inflammation, Immunology, and Infectious diseases Category at the Health and Disease: Science, Technology, Culture, and Policy by Purdue University held on February 28, 2019 for “Phenylthiazoles: Systemically active antibacterial agents effective against Methicillin resistant Staphylococcus aureus (MRSA)”.

Funded by

National Institute of Allery and Infectious Disease, National Institute of Health
VMCVM Office of Research and Graduate Studies

Lay Language Abstract

Clostridioides difficile is a prominent human pathogen that can colonize the gut and cause fatal infections. C. difficile is the most common cause of microbial healthcare-associated infection and results in substantial morbidity and mortality. The "most urgent worldwide public health threat" label has been assigned to C. difficile by the United States Centers for Disease Control and Prevention (CDC). There is a pressing need to develop new classes of antibiotics with improved efficacy to treat C. difficile infections (CDI).

To address the need for novel strategies to combat the growing problem of CDI, we screened FDA-approved drugs and natural products library in search of novel drugs that possess potent and specific anti-clostridial activity. Several promising hits were identified and evaluated successfully both in vitro and in vivo. The most potent and novel hits that displayed exceptional activity were mitomycin C, mithramycin A, aureomycin, NP-003875, NAT13-338148, NAT18-355531, and NAT18-355768. Furthermore, a murine model of C. difficile infection revealed that compound NP-003875 conferred 100% protection to the infected mice from clinical manifestations of the disease. Interestingly, these compounds were non-toxic to the gut microflora and human cells.

Our final approach has been to develop non-traditional therapeutics to target specific genes in C. difficile. These novel therapeutics are called peptide nucleic acids (PNA). Herein, we designed a PNA targeting RNA polymerase α subunit gene (rpoA) of C. difficile. The designed PNA could successfully inhibit the growth of the pathogen and expression of its virulence factors.

In conclusion, our research opened exciting possibilities that can be further evaluated to uncover new treatments for CDI.

Publications

Pal, R., & Seleem, M. N. (2022). Discovery of a novel natural product inhibitor of Clostridioides difficile with potent activity in vitro and in vivo. *PloS one*, *17*(8), e0267859.

Pal, R., Athamneh, A. I., Deshpande, R., Ramirez, J. A., Adu, K. T., Muthuirulan, P., ... & Seleem, M. N. (2022). Probiotics: insights and new opportunities for Clostridioides difficile intervention. *Critical Reviews in Microbiology*, 1-21.

Pal, R., Dai, M., & Seleem, M. N. (2021). High-throughput screening identifies a novel natural product-inspired scaffold capable of inhibiting Clostridioides difficile in vitro. *Scientific reports*, *11*(1), 1-7.

Hamann, H. J., Abutaleb, N. S., Pal, R., Seleem, M. N., & Ramachandran, P. V. (2020). β, γ-Diaryl α-methylene-γ-butyrolactones as potent antibacterials against methicillin-resistant Staphylococcus aureus. *Bioorganic Chemistry*, *104*, 104183.

Pal, R., & Seleem, M. N. (2020). Screening of natural products and approved oncology drug libraries for activity against Clostridioides difficile. *Scientific reports*, *10*(1), 1-8.

Vadlamani, R. A., Dhanabal, A., Detwiler, D. A., Pal, R., McCarthy, J., Seleem, M. N., & Garner, A. L. (2020). Nanosecond electric pulses rapidly enhance the inactivation of Gram-negative bacteria using Gram-positive antibiotics. *Applied microbiology and biotechnology*, *104*(5), 2217-2227.

Presentations

R. Pal & M. N. Seleem. (2022). Antisense inhibition of RNA polymerase α subunit of Clostridioides difficile. 2022 CeZAP Infectious Diseases Symposium, October 7th, 2022, Blacksburg, VA (Poster).

R. Pal and M.N. Seleem. High-throughput screening identifies a novel natural product-inspired molecule inhibiting Clostridioides difficile in vitro and in vivo. 31st Annual Research Symposium, March 25 & 26, 2021, Virginia-Maryland College of Veterinary Medicine, Blacksburg, VA (Poster).

R. Pal, H. Mohammad, N.S. Abutaleb, M. Elsebaei, M. Abouf, A. Ghiaty, A. S. Mahyoub, and M. N. Seleem. Phenylthiazoles: Systemically active antibacterial agents effective against methicillin resistant Staphylococcus aureus (MRSA). Sigma Xi Graduate Student Research Poster Award Competition, February 21, 2018, Purdue University, West Lafayette, IN. (Poster).

R. Pal & M. N. Seleem. (2022). Antisense inhibition of RNA polymerase α subunit of Clostridioides difficile. 2022 CeZAP Infectious Diseases Symposium, October 7th, 2022, Blacksburg, VA (Poster).

R. Pal and M.N. Seleem. High-throughput screening identifies a novel natural product-inspired molecule inhibiting Clostridioides difficile in vitro and in vivo. 31st Annual Research Symposium, March 25 & 26, 2021, Virginia-Maryland College of Veterinary Medicine, Blacksburg, VA (Poster).

R. Pal, H. Mohammad, N.S. Abutaleb, M. Elsebaei, M. Abouf, A. Ghiaty, A. S. Mahyoub, and M. N. Seleem. Phenylthiazoles: Systemically active antibacterial agents effective against methicillin resistant Staphylococcus aureus (MRSA). Sigma Xi Graduate Student Research Poster Award Competition, February 21, 2018, Purdue University, West Lafayette, IN. (Poster).

R. Pal, H. Mohammad, N.S. Abutaleb, M. Elsebaei, M. Abouf, A. Ghiaty, A. S. Mahyoub, and M. N. Seleem. Phenylthiazoles: Systemically active antibacterial agents effective against methicillin resistant Staphylococcus aureus (MRSA). Health and Disease: Science, Technology, Culture, and Policy, March 1, 2018, Purdue University, West Lafayette, IN. (Poster).

R. Pal, H. Mohammad, N.S. Abutaleb, M. Elsebaei, M. Abouf, A. Ghiaty, A. S. Mahyoub, and M. N. Seleem. Phenylthiazoles: Systemically active antibacterial agents effective against methicillin resistant Staphylococcus aureus (MRSA). Indiana Branch of the American Society of Microbiology (IBASM), April 7th, 2018, Indianapolis, IN. (Poster).

R. Pal, H. Mohammad, N.S. Abutaleb, M. Elsebaei, M. Abouf, A. Ghiaty, A. S. Mahyoub, and M. N. Seleem. Phenylthiazole compounds as antibacterial agents against methicillin-resistant Staphylococcus aureus (MRSA). Omicron Chapter of Phi Zeta, April 9, 2018, Purdue University, West Lafayette, IN. (Poster).

R. Pal, H. Mohammad, N.S. Abutaleb, M. Elsebaei, M. Abouf, A. Ghiaty, A. S. Mahyoub, and M. N. Seleem. Phenylthiazole compounds as antibacterial agents against methicillin-resistant Staphylococcus aureus (MRSA). Biomolecular Galaxy Symposium, May 9, 2018. Purdue University, West Lafayette, IN. (Poster).

R. Pal, H. Mohammad, N.S. Abutaleb, M. Elsebaei, M. Abouf, A. Ghiaty, A. S. Mahyoub, and M. N. Seleem. Identification of novel scaffolds to combat methicillin resistant Staphylococcus aureus (MRSA). Sigma Xi Graduate Student Research Poster Award Competition, February 20, 2019, Purdue University, West Lafayette, IN. (Poster).

R. Pal, H. Mohammad, N.S. Abutaleb, M. Elsebaei, M. Abouf, A. Ghiaty, A. S. Mahyoub, and M. N. Seleem. Phenylthiazoles: Systemically active antibacterial agents effective against methicillin resistant Staphylococcus aureus (MRSA). Health and Disease: Science, Technology, Culture, and Policy, February 28, 2019, Purdue University, West Lafayette, IN. (Poster)

R. Pal, H. Mohammad, N.S. Abutaleb, M. Elsebaei, M. Abouf, A. Ghiaty, A. S. Mahyoub, and M. N. Seleem. Identification of novel scaffolds to combat methicillin resistant Staphylococcus aureus (MRSA). Omicron Chapter of Phi Zeta, April 8, 2019, Purdue University, West Lafayette, IN. (Poster)

Examination Graduate Committee

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Mohamed Seleem, DVM, PhD
Professor
Department: Biomedical Sciences and Pathobiology

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