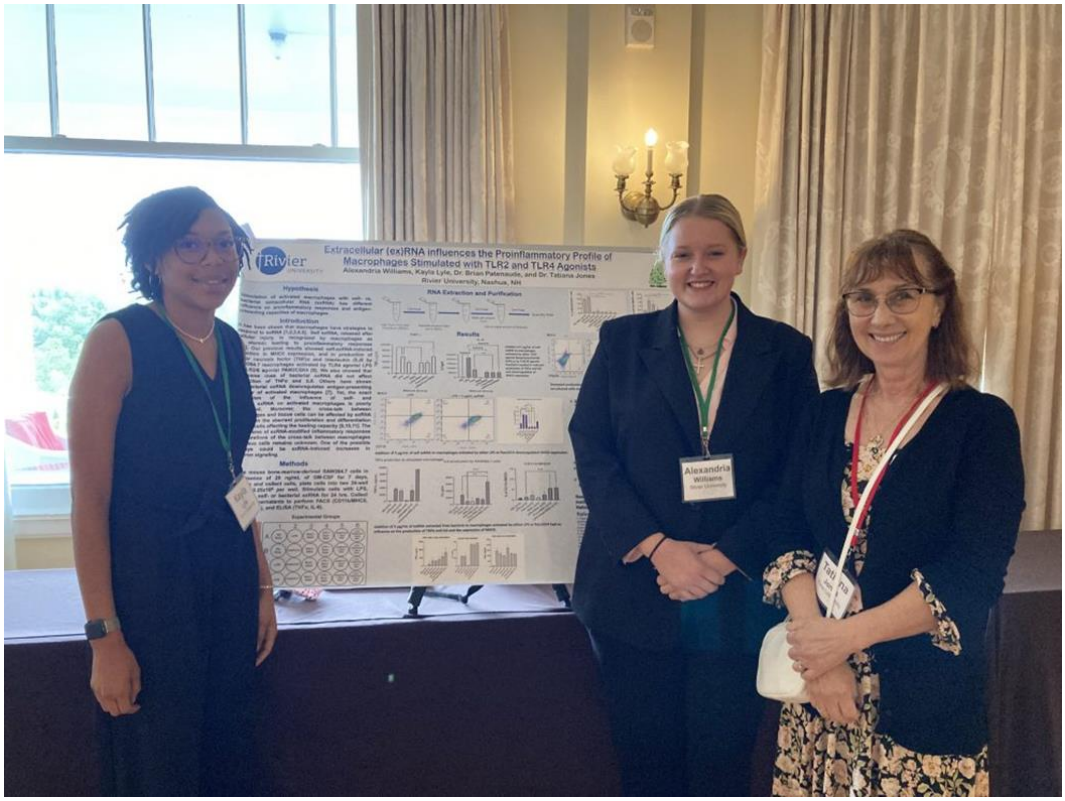
NH-INBRE BIOMEDICAL RESEARCH PROJECTS

(From *Rivier's News*, Spring 2024)

NH-INBRE biomedical research projects offer students the opportunity for faculty mentorship, advanced laboratory skills, and professional network development.



From left to right: Kayla Lyle '24, Alexandria Williams '24, and Dr. Tatiana Jones

Rivier University is a partner institution of the New Hampshire IDeA Network of Biomedical Research Excellence (NH-INBRE), a state-wide research consortium led by the Geisel School of Medicine at Dartmouth College and the University of New Hampshire. Funded by the National Institutes of Health, NH-INBRE biomedical research projects support outstanding biomedical faculty researchers and promising undergraduate students to lead and advance top-level biomedical research.

NH-INBRE Biomedical Research Projects

Rivier faculty members **Dr. Tatiana Jones**, **Dr. Hye Young Shin**, and **Dr. Brian Patenaude** were each awarded New Hampshire INBRE grants for summer 2023 research projects. In addition to supporting biomedical research, these grants include a stipend for Rivier student-researchers to develop their laboratory skills in the Science and Innovation Center on campus.

Self-extracellular (ex)RNA downregulates the proinflammatory profile of activated macrophages

Researchers: Alexandria Williams '24; Kayla Lyle '24; Brian Patenaude, Ph.D.; Tatiana Jones, M.D., Ph.D.

ISSN 1559-9388 (online version), ISSN 1559-9396 (CD-ROM version).

Investigation: The researchers confirmed their previous findings suggesting that RNA extracted from macrophages (self-exRNA) downregulates inflammatory responses of macrophages activated by the presence of photogenic molecules. Summer 2023 research's aim was to show that macrophage-derived RNA, not associated with proteins or contaminating DNA, influences the inflammatory responses of macrophages. This knowledge allowed the identification of intracellular mechanisms that engaged in the downregulation of inflammatory characteristics of activated macrophages. Understanding the mechanisms of exRNA-induced influences on the phenotype of innate immune cells, such as macrophages, will enable a deeper understanding of the mechanisms involved in healing, chronic inflammations, and autoimmunity.

In response to the query, *"Is it really RNA extracted from macrophages that downregulates macrophages' response to known pathogenic molecule?"* researchers compared the responses of macrophages activated by lipopolysaccharide to intact macrophages-derived (self-)exRNA and to self-exRNA that were digested with RNases, enzymes that destroy RNA prior to adding to the macrophages. Researchers hypothesized that stimulation of activated macrophages with self-exRNA added after digestion with RNases would restore the ability of activated macrophages to promote inflammation by increased production of inflammatory cytokines.

Outcomes: The initial hypothesis was confirmed. Stimulation of macrophages with intact self-exRNA in the experiments resulted in the downregulation of proinflammatory cytokines, whereas treatment of extracted RNA with RNases prior to adding to the cells restores the ability of macrophages to produce proinflammatory cytokines suggesting that RNA is responsible for downregulating inflammatory responses of macrophages.

Work on this project continues. Currently, researchers are trying to identify intracellular mechanisms triggered by self-exRNA that lead to the downregulation of inflammatory responses. Later this work will make a basis for the laboratory component of Rivier's Fall 2024 Immunology course. Student-researchers Alexandria Williams and Kayla Lyle developed exceptional laboratory technical and analytical skills, which continue to improve and expand upon through their ongoing participation in this research.

Incorporation of Zinc-Porphyrin into Poly(ethylene terephthalate) and Poly(methyl methacrylate) Plastics for the Photodynamic Inactivation of Staphylococcus aureus

Researchers: Irelynn Mullen '25; Tatiana Jones, M.D., Ph.D.; Brian Patenaude, Ph.D.

Investigation: This project aims to determine the antibacterial properties of the consumer plastics, poly(ethylene terephthalate) (PET) and poly(methyl methacrylate) (PMMA) against Staphylococcus aureus (*S.aureus*), when a photodynamic therapy agent, such as porphyrin, is covalently incorporated into their polymer structures. Porphyrin complexes are known to act as photosensitizers allowing for the generation of singlet oxygen when exposed to radiation in the white light spectrum. The resulting singlet oxygen, a reactive oxygen species, can induce bacterial cell death. To achieve the goal of generating antimicrobial plastics, researchers sought to develop and characterize a series of poly[ethylene-co-terephthalate-co-Zinc-meso-Tetraphenylporphine-4,4′,4″,4‴-tetracarboxylate] (PETZnP) and a series of poly[methylmethacrylate-co-Zinc-5,10,15,20-tetrakis(phenyl prop-2-enoate)porphine] (PMMAZnP) polymers. The synthesized polymers were to then be evaluated via qualitative and quantitative testing of the polymers' effectiveness in inhibiting the growth of *S.aureus* when irradiated with white light.

Outcomes: Student-researcher Irelynn Mullen was successfully able to synthesize the PETZnP polymer series and start the synthesis of the PMMAZnP polymer series. Preliminary quantitative testing of the polymers' effectiveness in inhibiting the growth of *S.aureus* when irradiated with white light resulted in polymer samples reducing bacterial counts to varying degrees. However, the results are not consistent due to the current polymer sampling methods. Further work into generating consistent polymer samples is required before future evaluation of their antibacterial properties can take place. Throughout this process, Irelynn has shown great problem-solving skills, expanded her organic synthesis knowledge, learned air-free techniques, and enhanced her microbiology laboratory techniques.

Targeting Overexpressed Cytokines as Potential Therapeutics to Target Glioma and Glioblastoma Patients

Researchers: Dyasia Casado ’24, Leah Nelson ’26, Hye Young Shin, Ph.D.

Investigation: This pilot grant research was the continuation of the team’s seed grant research in 2022 on rat GBM cells. Summer 2023 research aimed to define the major cytokine signaling of a unique subpopulation of CSCs in human Glioblastoma (GBM). GBM is the most fatal and highly aggressive brain cancer due to rapid cell growth, high invasion, resistance to advanced medical interventions, and its recurrence. A unique population of cancer stem cells (CSCs) in GBM has been identified as the major cause of its malignancy and resistance, and hence the identification of key regulators of CSCs in GBM will contribute to the finding of therapeutics for GBM patients. While tumorigenesis of normal cells undergoes several genetic and methylational alterations, the tumor expansion and progression are orchestrated physiologically by growth factors and cytokines. Particularly, cytokines either enhance tumor progression or have direct effects on cancer cell growth, and CSCs of GBM modulate its microenvironment with cytokines for cancer progression and metastasis. Researchers successfully identified several enhanced cytokines in CSCs of human GBM as compared to the regular GBM cancer cells. Considering basal up-regulation of key cytokines in regular GBM cancer cell populations, even more notably enhanced levels of key cytokines indicate that those are very significant targets for GBM therapeutics.

Outcomes: Researchers identified several key cytokines of human GBM-CSCs and will target those key cytokines to find potential therapeutic targets of GBM patients. In the future study, small compound and antibody screening of cytokine inhibitors targeting GBM-CSCs will be conducted, and it will potentially identify a potential therapeutic molecule for the treatment of GBM patients. Furthermore, the project has strengthened the research environment at Rivier University. A student of the seed grant research has been accepted to a Biotechnology master’s degree program at Northeastern University and has been working as a co-op researcher in a biotechnology company in Lexington, Massachusetts. Continuation of this pilot research will prepare additional students as competitive candidates for graduate schools and pharmaceutical companies in the New England area.

Research projects and findings were presented at the 2023 New Hampshire INBRE annual meeting (August 7-8, 2023). Alexandria Williams ’24 placed first in poster presentations, and Dr. Shin and Dr. Jones represented the University as selected speakers.

WEB: https://www.rivier.edu/academics/department/science/nh-inbre-at-rivier-university/. ■