Subject: Dissertation Defense - Kushal Baraily, PhD Bioscience
Date: Tuesday, March 24, 2026 at 4:27:06 PM Eastern Daylight Time
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Dissertation Defense Announcement
To: The George Mason University Community

Candidate: Kushal Baraily

Program: PhD in Bioscience

Date: April 7, 2026

Time: 1:00 PM Eastern Time (US and Canada)

Location: Via Zoom

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Committee Co-Chairs: Dr. Monique Van Hoek and Dr. Jeffrey Moran
Committee Members: Dr. Remi Veneziano, Dr. Farhang Alem

Title: Dual Strategies to Target Antibiotic Resistance: D-GATR-3 Antimicrobial Peptide and DNA Nanoswimmers

Abstract: Antimicrobial resistance (AMR) poses a major global health challenge and demands therapeutic strategies that extend beyond conventional antibiotic treatments. Bacteria develop AMR through several mechanisms, including genotypic resistance such as mutation and horizontal gene transfer, and by forming biofilms. In this thesis, we address these two mechanisms using two complementary approaches: antimicrobial peptide self-assembly and active nanoparticles based on programmable DNA nanotechnology. Addressing the first mechanism, we demonstrate the ability of the D-enantiomeric antimicrobial peptide D-GATR-3 to exert bactericidal activity against multidrug-resistant *Acinetobacter baumannii* via surface-triggered self-assembly. We show that interaction with bacterial surface components induces the formation of higher-order β-sheet-rich structures that drive bacterial agglutination and promote membrane disruption. This self-assembly behavior enables multivalent interactions with bacterial cells and enhances bactericidal activity in dense populations, providing insight into how peptide organization functions as a nanonet or nanotrap. Second, we evaluate active nanomaterials to address biofilm-mediated resistance. As a potential strategy to navigate the protective barrier posed by biofilms, we characterize the behavior of enzyme-powered DNA origami nanoswimmers as active nanotherapeutic platforms. Many enzymes, such as urease, generate a propulsive force in the presence of their substrates (urea in the case of urease). We demonstrate that urease-functionalized DNA nanoparticles exhibit negative chemotaxis in urea gradients, establishing a foundation for targeted delivery in complex environments, including biofilms. Finally, we evaluate exopolysaccharide-specific glycoside hydrolase enzymes (PslGh and PelAh) for the disruption of *Pseudomonas aeruginosa* biofilms, demonstrating that matrix specificity enhances dispersal efficiency and supports their future integration as a cargo for nanoswimmer-based delivery platforms.

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