Subject: Dissertation Defense - Huiyi Miao, PhD in Biosciences
Date: Tuesday, June 30, 2026 at 11:52:21 AM Eastern Daylight Time
From: SSB Faculty List on behalf of Diane St. Germain
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Dissertation Defense Announcement
To: The George Mason University Community

Candidate: Huiyi Miao

Program: PhD in Biosciences

Date: July 15, 2026

Time: 2:00 PM Eastern Time (US and Canada)

Location: via Zoom

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Committee Chair: Dr. Yuntao Wu

Committee members: Dr. Ramin Hakami, Dr. Mikell Paige, Dr. Paolo Lusso

Title: Engineering mRNA for Timed and Dosed Expression of a Retroviral Protease to Complement Virus-like Particles (VLP)-forming mRNA Vaccines Against Different Viral Pathogens

Abstract:

The COVID-19 pandemic underscored the central role of vaccines in global public health and established messenger RNA (mRNA) vaccines as a transformative immunization platform. The success of COVID-19 mRNA vaccines is attributable to nucleoside-modified mRNA, which enables efficient and sustained antigen expression in vivo, combined with lipid nanoparticle (LNP) delivery systems that protect mRNA from degradation, promote cellular uptake, and provide intrinsic adjuvant activity. These advances have positioned mRNA vaccines as a versatile and rapidly adaptable approach for combating infectious diseases.

Building on this platform, mRNA vaccines encoding HIV-1 env and gag were evaluated for their ability to drive in situ assembly of virus-like particles (VLPs) and to induce antiviral immune responses. VLPs present viral antigens in a highly ordered, repetitive, and membrane-associated configuration that closely mimics native virions, enhancing immune recognition. Because VLP maturation critically influences immunogenicity, a full-length gag–pol mRNA was incorporated to enable temporally regulated expression of the viral protease (Pro), thereby recapitulating key features of the HIV-1 replication cycle and promoting efficient Gag processing and particle maturation.

Inclusion of gag–pol mRNA resulted in the formation of mature VLPs that closely resemble native HIV-1 virions with respect to Env spike conformation, density, and antigenic integrity. Vaccination with this mature VLP–forming HIV-1 env-gag mRNA formulation led to increased titers of trimer-binding and neutralizing antibodies in a mouse model compared with immature VLP–forming constructs. Taken together, these findings demonstrate that controlled VLP maturation substantially improves the immunogenicity of mRNA vaccines and support mature VLP–based mRNA vaccination as a promising next-generation strategy for HIV-1. More broadly, this work establishes a conceptual and technological framework for extending maturation-optimized VLP mRNA vaccines to other emerging and re-emerging viral pathogens.