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University of Washington 6th Annual Center for Translational Muscle Research (CTMR) Symposium, Featured CTMR Investigator Talk – Friday, November 21, 2025

Title: Systems Bioengineering for Vascular Signaling and Women's Health: Mechanisms, Models, and Diagnostics

Abstract: This presentation explores how systems approaches quantitatively reveal hidden signaling mechanisms in vascular biology and women's health. In vascular biology, we challenge traditional views of growth factor signaling by uncovering cross-family binding and signaling between the PDGF and VEGF families. Using endothelial cells lacking PDGFRs, we show that PDGF-AA, -AB, and -BB activate VEGFR phosphorylation and downstream adaptors (PLCγ1, Akt, FAK), confirmed by ELISA and immunoblotting. Low PDGF doses (20 pM–1 nM) significantly increased VEGFR1 phosphorylation and adaptor activation more effectively than higher doses and enhance endothelial proliferation and migration. Our mass-action kinetics model, parameterized from experimental data, predicts that canonical PDGF:PDGFRα binding is modulated by VEGFR2 density, enabling PDGF–VEGFR2 binding. We also discover high-affinity ligand–ligand interactions between VEGF-A and PDGF-AA, -BB, -AB, and -DD (0.77–4.01 nM), revealing new layers of vascular signaling complexity.

In women's health, we address the challenge of variable oxytocin responsiveness during labor by characterizing oxytocin receptor variants and modeling binding dynamics to guide precision dosing. We identify pharmacological chaperones that rescue defective OXTR trafficking and enhance oxytocin responsiveness in cellular models and primary tissue from pregnant women. Finally, we have developed a diagnostic that predicts preeclampsia before symptoms appear by targeting vascularization markers on circulating cells. This test distinguishes severe preeclampsia from uncomplicated pregnancies (sensitivity: 89%, specificity: 75%, AUC = 0.85), outperforming current diagnostics that detect disease only after 23 weeks and opening the door for preventative interventions that save lives. Together, these findings show how quantitative and computational bioengineering approaches deepen our understanding of complex biological systems and enable earlier, more effective interventions.

This research is supported by the National Science Foundation (NSF PFI-TT: 2414865) and the National Institutes of Health (R01HL159946, R01HD096737, and R56HD096737).