Summer 8-29-2022

Circulating Notch1 in response to altered vascular wall shear stress in adults

Anthony Bain
University of Windsor, anthony.bain@uwindsor.ca

Matthew Badour
University of Windsor, badour5@uwindsor.ca

Rachel Stone
University of Windsor, stone11c@uwindsor.ca

Khushali Parikh
University of Windsor, parik111@uwindsor.ca

Olivia Meloche
University of Windsor, meloc11z@uwindsor.ca

See next page for additional authors

Consistent with the TCPS 2 (4.7) this is a research summary provided to participants and should not be considered a formal publication of results.

Principle and Co-Investigators
Anthony Bain, Matthew Badour, Rachel Stone, Khushali Parikh, Olivia Meloche, Nicholas Lester, and Renee Wulterkens

Notch1 has been proposed as a novel endothelial mechanosensor that is central for signalling adjustments in response to changes in vascular wall shear stress. However, there remains no controlled *in vivo* study in humans. Accordingly, we sought to address the question of whether plasma concentrations of Notch1 extracellular domain (ECD) is altered in response to transient changes in vascular wall shear stress. In 10 young healthy adults (6M/4F), alterations in shear were induced by supra-systolic cuff inflation around the forearm. Cuffs were also placed below the axilla and inflated to 40mmHg to trap the released Notch1 ECD. The opposite arm was treated as a time control with no distal cuff inflation. Plasma was collected from an antecubital vein of both arms at baseline, 20-min of wrist cuff inflation (low shear), as well as 1-min (high shear) and 15-min following wrist cuff release (recovery). The Notch1 ECD was quantified using a commercially available ELISA. Duplex ultrasound was used to confirm alterations in shear stress. In the experimental arm, concentrations of Notch1 ECD remained statistically similar to baseline at all time points except for immediately following cuff release where it was elevated by ~50% ($P=0.033$), coinciding with the condition of high antegrade shear. Concentrations of Notch1 ECD remained unchanged in the control arm through all time points. These data indicate that Notch1 is a viable biomarker for quantifying mechanotransduction in response to increased shear in humans, and it may underlie the vascular adaptations or mal-adaptations associated with conditions that impact antegrade shear.