1163-34-710 **Stéphanie Abo*** (sabo@uwaterloo.ca) and **Anita Layton** (anita.layton@uwaterloo.ca).
Sex-Specific Effects of Shiftwork-Mediated Disruptions of Circadian Rhythms on the Inflammatory Response.

Shift workers often experience circadian misalignment as their irregular work schedules disrupt the natural sleep-wake cycle, which in turn causes serious health problems associated with alterations in genetic expressions of clock genes. These alterations are sex-specific; however, the underlying mechanisms that govern the immune response to these effects remain unclear. To address this question, we have constructed a mathematical model of the mammalian pulmonary circadian clock coupled to an acute inflammation model. Shiftwork was simulated by an 8h-phase advance of the circadian system with sex-specific modulation of clock genes. The model reproduces the clock gene expression in the lung and the immune response to various doses of lipopolysaccharide (LPS). Our model predicts a reversal of the times of lowest and highest sensitivity to LPS, with males and females exhibiting an exaggerated response to LPS at circadian time (CT) 0, which is countered by a blunted immune response at CT12. Overall, females produce fewer pro-inflammatory cytokines than males and suffer more severe sequelea from shiftwork. Our model also predicts interesting IL-10 dynamics closer to CT0 at baseline. (Received September 11, 2020)