MSc DEFENCE Tuesday, July 26th, 2016
Student: Nicholas Swyngedouw
Title: THE INFLUENCE OF INTERLEUKIN-13 ON FORCE GENERATION IN AIRWAY SMOOTH MUSCLE TISSUE
Time and location: 2:00 pm PDT; Gourlay Conference Room, UBC Centre for Heart Lung Innovation, St. Paul's Hospital, 1081 Burrard St. Vancouver, BC
Supervisors: Chun Seow and Peter Paré

ABSTRACT

Rationale: Airway smooth muscle (ASM) has been implicated in the pathophysiology of asthma by contributing to excessive airway narrowing and Airway Hyperresponsiveness (AHR). Furthermore, inflammation has also been suggested as a mechanism contributing to AHR in asthmatics. Levels of Interleukin-13 (IL-13), an inflammatory mediator, are increased in asthmatic sera and can alter the expression of specific contractile genes and proteins in cultured ASM cells. In cultured cells, IL-13 can cause increased ASM contractility and force generation in response to different contractile agonists such as acetylcholine (ACh), KCl, or histamine. However, there remains a lack of consensus regarding whether IL-13 can induce changes in mechanical properties of ASM tissue in response to all, or only some, contractile agonists. Our objective was to investigate the influence of IL-13 on the force generation of isolated ASM tissue in response to a variety of agonists.

Methods: Ovine tracheal smooth muscle was isolated, bathed in Krebs saline solution, and then equilibrated using electrical field stimulation. In order to obtain baseline mechanical measurements, tissues were either contracted with a range of ACh concentrations, pre-stimulated with ACh then relaxed with progressively increasing doses of isoproterenol (ISO), or contracted with single a single concentration of KCl or histamine (n=5 per condition). Paired samples from each tissue were then pinned at constant (in situ) length and incubated for 24h or 72h with or without IL-13 (50 ng/mL) in serum-free DMEM. Tissue responses were compared to their baseline (t=0) measurements after incubation to determine the influence of IL-13.

Results/Conclusions: Compared to non-exposed tissues, IL-13 did not increase maximal force or sensitivity to a range of ACh concentrations after either 24 or 72h (n=5 each), nor did it impede the relaxation of ASM induced by ISO after 24h (n=5). Likewise, response to KCl was not changed by IL-13 after 72h (n=5). Response to histamine was ~120% higher compared to control (t=72h) after treatment (% of baseline maximal force, n=5, p=0.03). These findings contrast with previous work done in ASM cell culture experiments. In tissue strips, IL-13 did not induce significant changes to ASM mechanics in response to ACh, ISO, or KCl treatment. However, IL-13 did influence histamine-induced contractile response suggesting a potential avenue by which airway inflammation influences ASM contraction.