**Specific Aims**

The immune system is a necessary and complex aspect of the human body, but when it fails to function properly the results affect the patient’s quality of life. Allergic rhinitis is one of the most common afflictions in the United States, with symptoms that include sinus swelling, pressure, and sneezing.Allergic rhinitis is an antibody (IgE) mediated hypersensitivity reaction of the nasal mucosa, which upon interaction with an allergen recruit phagocytic and cytotoxic cells.1 These cells release cytokines, to stimulate t-cells, such as transforming growth factor beta isoform 1 (TGFB1). TGFB1 stimulates T-regulatory cells, which in turn attempt to suppress the immune response.However, TGFB1 has also been shown to stimulate T17 cells, which work to increase inflammation.2 Interestingly, patients with allergic rhinitis have an increased expression of TGFB1.1 The paradox here is essentially ‘how much is too much’. TGFB1 can indirectly both stimulate and suppress the immune response, the exact levels of expression necessary for a healthy immune system are unknown. This missing piece of information may hold the key to understanding and treating the widespread phenomena of allergic rhinitis.

**This experiment will test the hypothesis that a measurable threshold exists in the amount of TGFB1 released which changes the cytokine from an immunosuppressive cytokine to a pro-inflammatory cytokine.** This is based on the fact that allergic rhinitis is an inflammatory disease, and that elevated levels of TGFB1 are found in the tissues of patients with the disease. The overall **objective** of the study will be to determine some tipping point in expression of TGFB1 that changes the overall response from suppressive to inflammatory. This knowledge will be applied to the **long-term goal** of the research, which is to control the levels of TGFB1 with a drug or treatment and eliminate the allergic rhinitis response.

**1. Observe changes in TGFB1 expression in nasal tissue before during and after response.** Preliminary data suggests that TGFB1 is present in elevated amounts in the nasal tissue of allergic rhinitis patients, causing the pro-inflammatory allergic response. I will use RNA-seq to compare rates of TGFB1 expression before, during, and after an allergic response in a patient to determine when the gene is most highly expressed and what baseline looks like in the same individual. These results can then be compared to the expression of TGFB1 in a non-allergic individual.

**References**

**[1]**Pawankar, R., Mori, S., Ozu, C., & Kimura, S. 2011. Overview on the pathomechanisms of allergic rhinitis. Asia Pacific Allergy, 1(3), 157–167. [**http://doi.org/10.5415/apallergy.2011.1.3.157**](http://www.apallergy.org/DOIx.php?id=10.5415/apallergy.2011.1.3.157)

**[2]**Wan, Y. Y., & Flavell, R. A. (2007). “Yin-Yang” functions of TGF-β and Tregs in immune regulation. Immunological Reviews, 220, 199–213. [**http://doi.org/10.1111/j.1600-065X.2007.00565.x**](http://onlinelibrary.wiley.com/doi/10.1111/j.1600-065X.2007.00565.x/abstract;jsessionid=1C24368F5F0AC35DC6AB718CF9021265.f02t04)