miR-155 and SHIP-1 Inverse Relationship in Mast Cells Suggests a Mechanism Driving Chronic Skin Allergies

Huda N Daudpota[1,3], M2 medical student; Heather Caslin, Ph.D. [1,2]; and Gregorio Gomez, Ph.D. [1,3]

[3]Department of Biomedical Sciences, Tilman J. Fertitta Family College of Medicine, Houston, TX, USA; [2]Department of Health and Human Performance, College of Liberal Arts and Social Sciences, Houston, TX, USA; [1]University of Houston, Houston, TX, USA

Allergic disease is the 6th leading cause of chronic illnesses in the U.S., and atopic dermatitis alone affects ~16.5 million U.S. adults. Approximately 40-50% of sensitized individuals develop late-phase allergic reactions, a precursor to chronic allergic diseases. miRNAs are post-transcriptional negative regulators of gene expression that are believed to play a role in allergic disease. We demonstrated by RNAseq and quantitative real-time PCR that miR-155 is increased in *ex vivo* human skin mast cells following crosslinking of the IgE receptor. We further showed that miR-155 is necessary for FcεRI-induced cytokine production and cyclooxygenase-2 expression, but not degranulation. Our mechanistic studies revealed that miR-155 is required for IgE-dependent phosphorylation of Akt, a critical signaling protein required for cytokine production. Because miRNAs inhibit gene expression, we posited that miR-155 inhibits the expression of a currently unknown phosphatase that blocks the phosphorylation (activation) of Akt; thereby, enabling cytokine production. Our results show that expression of src homology 2 domain containing inositol polyphosphate 5-phosphatase 1 (SHIP-1), an Akt phosphatase encoded by the *Inpp5d* gene, was significantly inhibited (5-fold decrease in expression) in IgE-sensitized mouse bone marrow-derived mast cells (BMMCs) activated through the FcεRI. These findings demonstrate that expression of miR-155 and SHIP-1 following FcεRI crosslinking is inversely correlated in mast cells, thus, supporting our hypothesis that miR-155 positively regulates IgE-dependent cytokine production by inhibiting the expression of SHIP-1 to enable Akt phosphorylation. Therefore, our study indicates that miR-155 promotes late-phase allergic reactions and the development of chronic allergic disease by targeting phosphatase SHIP-1.