**Elucidating LRRC31 induction by IL-13**

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**Background:** Eosinophilic esophagitis (EoE) is an allergic inflammatory disease of the esophagus triggered by food and aeroallergens. The disease is associated with a Th2-type immune response with eosinophils infiltrating the esophagus, basal cell hyperplasia, disruption of the epithelium and increase expression of the cytokine IL-13. IL-13 signals through signal transducer and activator of transcription 6 (STAT6) to change gene expression and induce Th2-type immune response. Notably, IL-13 treatment of primary esophageal epithelial cells results in changes in gene expression that markedly overlap with a previously identified esophageal transcriptome. The transcriptome is a set of esophageal transcripts, referred to as the EoE transcriptome, that differentiates EoE from controls. We identified leucine-rich repeat containing protein 31 (LRRC31) as one of the top upregulated genes in both the EoE and IL-13 transcriptomes. In addition, previous reports show the cytokine IL-4, which also signals through STAT6, to stimulates LRRC31 expression.

**Hypothesis:** We hypothesize that Leucine Rich Repeat Containing 31 (LRRC31) induced by IL-13 following STAT6 binding to the LRRC31 gene promoter.

**Methods:** Caco2 colon cancer cells were stimulated with IL-13 (100 ng/ml) for 48 hours and gene expression of LRRC31 was evaluated by qRT-PCR. STAT6 was knocked down in Caco2 cells using stable shRNA lentiviral vector and gene expression of LRRC31 was evaluated with IL-13 (100ng/ml) stimulation. The LRRC31 gene promoter (2Kb upstream of transcription start site) was cloned, with predicted transcription factor binding sites sequentially deleted, into a luciferase reporter construct and luciferase activity was measured following IL-13 stimulation.

**Results:** We defined the kinetics of LRRC31 expression in Caco2 cells and determined that LRRC31 is induced 2.67 fold by IL-13 in Caco2 cells at 48 hours. In STAT6 shRNA knockdown Caco2 cells, the IL-13 response was diminished as measured by CCL26 expression, a gene induced by IL-13. LRRC31 gene expression was also diminished by 0.29 fold at baseline but not by IL-13 compared to control vector. Promoter and deletions constructs are pending and we predict that deleting the STAT6 binding site in the LRRC31 gene promoter will diminish promoter activity.

**Conclusion:** Our data suggest that LRRC31 is induced by IL-13 in EoE. We identified the kinetic expression profile of LRRC31 in Caco2 cells and found that LRRC31 is induced at 48 hours. Using a STAT6 shRNA knockdown approach, we showed LRRC31 expression is dependent in part on STAT6 expression at baseline.Finally, we identified predicted and conserved STAT6 binding sites within the LRRC31 gene promoter that may be controlling gene expression. Thus, LRRC31 may be induced by IL-13 to drive epithelial pathology in EoE.

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