

Testing specialized pro-resolving mediators on bacteria-derived inflammation in chronic rhinosinusitis

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Background and Hypothesis:

Chronic rhinosinusitis (CRS) is defined by chronic tissue inflammation, and prior work in the field implicates activation of the NF κ b pathway. This pathway is activated by pattern recognition receptors (PRRs), which recognize molecules associated with pathogens and cellular damage. In CRS subjects, particularly those with nasal polyps, dysregulated pro-resolving processes have been documented. Specialized pro-resolving lipid mediators (SPMs), including lipoxin A₄ and the resolvins, are prime targets for active resolution of the chronic tissue inflammation that defines the disease. We hypothesize that exaggerated pro-inflammatory responses to CRS tissues could be mitigated by application of SPMs in vitro.

Project Methods:

CRS polyp tissue was collected from surgical specimens, and submerged in cell culture conditions with 10 ug/ml lipopolysaccharide (LPS) or lipoteichoic acid (LTA) to mimic bacterial pathogens commonly observed in CRS (i.e., *P. aeruginosa* or *S.aureus*). Tissues were treated with 50 nM of SPMs, either lipoxin A₄, resolvin D₁, or resolvin D₂. RNA was isolated from treated tissues. RNA was analyzed with Taqman Microarray NF-kB human pathway RT-PCR panel to evaluate expression of NF-kB-associated genes. In tandem, supernatant was collected for analysis of cytokine and chemokine signaling proteins. Protein assays were performed using the Luminex Multiplex Assay to observe modulation of pro-inflammatory immune signaling molecules.

Results:

LPS and LTA exposures demonstrated robust and different pro-inflammatory responses in ex vivo nasal polyp tissue. Treatment with SPMs was able to at least partially reduce NF-kB activation and the associated inflammatory response at a molecular level.

Conclusion;

Inflammation is a complex, temporally precise physiologic process. In chronic inflammatory mucosal diseases such as CRS, repeated acute insults may lead to chronic tissue inflammation. A novel treatment approach leveraging endogenous tissue resolving processes, i.e., SPMs was tested here in vitro and demonstrates potential promise for CRS with nasal polyps.