Eosinophilic esophagitis (EoE) is a life-long disease involving allergic inflammation of the esophagus. This condition is marked by the invasion of white blood cells, termed eosinophils, into the esophagus. Long-standing inflammation causes the esophagus to become fibrotic (scarred tissue). Once fibrosis occurs, patients are at risk of swallowing difficulty, narrowing of the esophagus and trouble passing food that may become lodged in the esophagus. However, very little is known about the mechanisms that lead to fibrosis in EoE.

The cells responsible for fibrosis are activated myofibroblasts. These cells are responsible for deposits of collagen into the esophagus. The collagen causes the tissue to become stiff. The activated myofibroblasts are also responsible for tissue contraction and cellular migration during wound healing. All of these processes lead to decreased diameter, motility and overall function of the esophagus.

It is generally accepted that fibroblasts exposed to the inflammatory cells within the esophagus become activated myofibroblasts during inflammation. An alternative source of activated myofibroblasts is the esophageal epithelial cells. In the healthy state, esophageal epithelial cells act as the mucosal barrier of the esophagus. These cells may begin to take on the characteristics of activated myofibroblasts under inflammatory conditions in a process called epithelial to mesenchymal transition (EMT). In addition, the investigators hypothesized that cross-talk between esophageal epithelial cells and esophageal fibroblasts may be contributing to esophageal fibrosis via EMT.

They concluded that signals from the esophageal epithelium stimulate fibroblasts to produce TNFα and IL1-β cytokines (small cell-signaling proteins that are involved in inflammation). These cytokines, in turn, cause esophageal epithelial cells to have myofibroblast-like behavior. In order to verify our results, we then used media from fibroblasts stimulated with epithelial media and stimulated fresh epithelial cells. We observed that these epithelial cells began to produce smooth muscle actin and vimentin. Furthermore, chemically inhibiting the TNFα and IL1-β cytokines completely prevented the transition to a myofibroblast-like cell.

Finally, we analyzed the behavior of the cultured esophageal epithelial cells after undergoing EMT. We found that esophageal epithelial cells when stimulated with TNFα have enhanced contractility, migratory capabilities, and collagen production compared to unstimulated cells. We were able to use time lapse photography to watch the epithelial cells develop lamellipodia (a distinct region of the cell that facilitates cell movement) and migrate in a 24-hour time period.

We concluded that cultured esophageal epithelial cells have the ability to functionally behave like activated myofibroblasts. Furthermore, fibroblast derived TNFα may be the key effector cytokine of this transition. In order to determine the actual contribution of EMT to esophageal fibrosis in EoE, we have developed a mouse model of EoE in which prolonged exposure to ova-albumin leads to food impaction and fibrosis. We plan to perform lineage tracing experiments in this mouse model to determine if these pathways are relevant in vivo.

I am extremely grateful for the support of the APFED HOPE Award. This award has allowed me to continue investigating mechanisms of fibrosis in EoE and laid the foundation for future work which will look at therapeutic strategies to prevent and treat this devastating side effect.

Research Roundup

Highlights from recent research publications

Co-existing allergic conditions were found to common in patients with Eosinophilic Gastritis, Gastroenteritis, and Collitis, at significantly higher rates than in the average population (21.8%), though less common than observed in EoE. The most commonly reported condition was allergic rhinitis (28-30%). Asthma was reported in 16% of patients with EG, 19% of patients with EGE, and 15% of patients with EC. Allergic Comorbidities in Eosinophilic Gastritis, Gastroenteritis, and Collitis

Researchers found that unsedated transnasal endoscopy is an effective and lower cost way to monitor pediatric EoE, and yield results comparable to upper endoscopy (a.k.a. esophagogastroduodenoscopy). Unsedated Transnasal Esophagoscopy for Monitoring Therapy in Pediatric Eosinophilic Esophagitis

Researchers looking at microbial communities found in esophageal samples saw a rise in the number of bacteria in children and adults with EoE or GERD, including a jump in Haemophilus (a type of bacterium) in individuals with EoE. Esophageal Microbiome in Eosinophilic Esophagitis