

## **Intestinal flora directs infiltrate composition and disease severity in a novel zebrafish entero-colitis model**

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The pathogenesis of inflammatory bowel disease involves dysfunctional mucosal immune responses to commensal bacteria in genetically predisposed hosts. The complicated interactions between innate cells and bacteria however, have left researchers with exceeding difficulties to assess the relative contribution by each of these cells to the intestinal pathology. We altered the intestinal microbiota of zebrafish with antibiotics and assessed the effects on the mucosal infiltrate and severity of intestinal inflammation in a novel oxazolone-induced entero-colitis model. Intestinal inflammation was evaluated by histology, flow cytometry and cytokine profiling. Zebrafish oxazolone entero-colitis is microbiota-dependent and characterized by an influx of granulocytes, epithelial damage, Goblet-cell depletion and increased expression of pro-inflammatory cytokines. Vancomycin treatment diminished the intestinal microbial load and resulted in a bacterial composition dominated by Fusobacteria. Vancomycin conferred strong protection from entero-colitis associated with reduced percentages of infiltrating neutrophils. In contrast to vancomycin, administration of colistin sulphate resulted in a predominance of  $\gamma$ -proteobacteria in the intestine that correlated with reduced infiltration of eosinophils and lymphocytes and no significant reduction in entero-colitis. We conclude that components of the intestinal microbiota drive zebrafish oxazolone entero-colitis and directly affect the severity of disease and composition of the intestinal infiltrate.