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Single-cell transcriptome profiling of bronchoalveolar cells identifies a Th17 signature in severe equine asthma

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Objective: identify the immune signature of severe equine asthma (SEA) using single-cell mRNA sequencing (scRNA-seq)

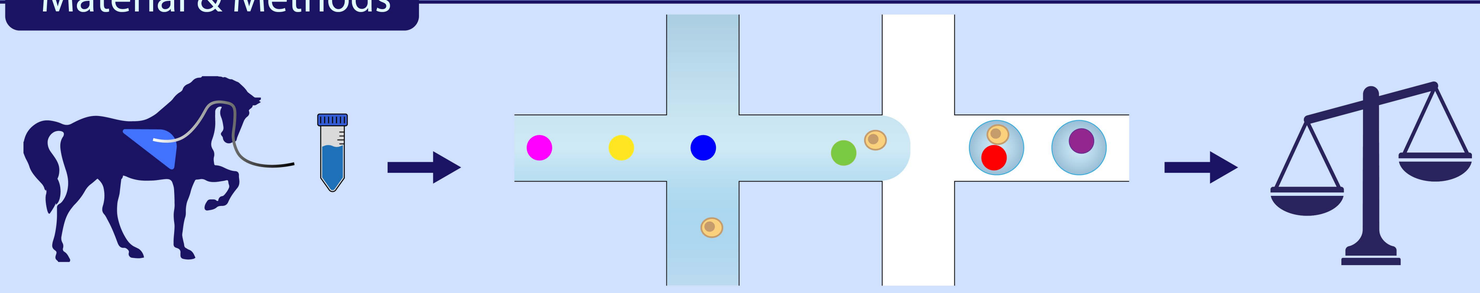
Population

Control
N = 5

SEA
N = 6

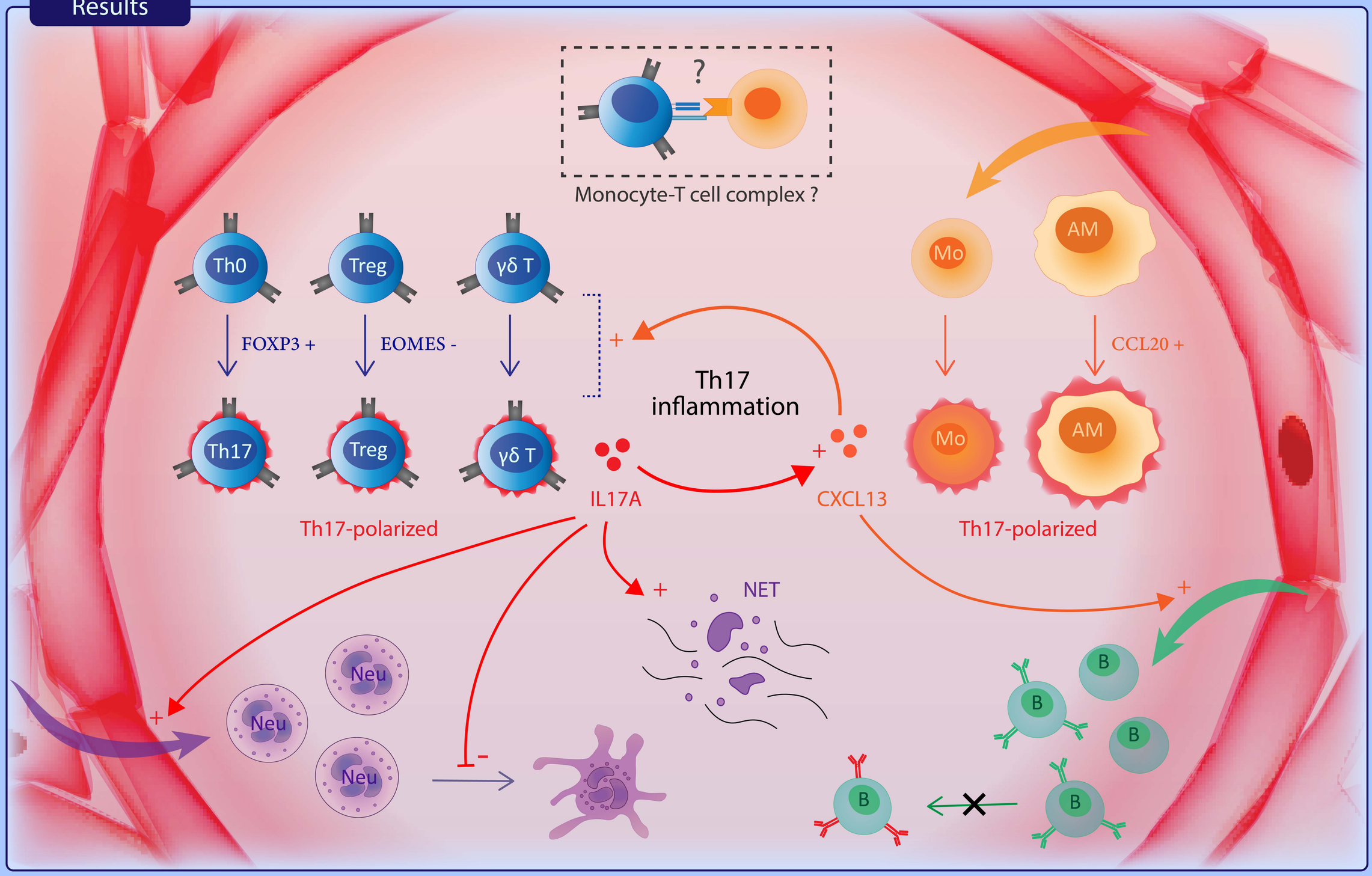
Swiss Warmbloods ≥ 6 years old
Control: • HOARSI = 1
• Normal BALF cytology
SEA: • HOARSI ≥ 3
• BALF neutrophils > 10%

Material & Methods



Bronchoalveolar lavage fluid (BALF) was subjected to 10X Genomics scRNA-seq, with approximately 6,000 cells per sample. Data preprocessing used Cell Ranger v6.0, followed by downstream analysis in R using Seurat. Cell types and subtypes relative proportions were compared between groups, and differential gene expression (DGE) analysis between the SEA and control groups was conducted using the Nebula package in R. *HOARSI, Horse Owner Assessed Respiratory Signs Index*

Results



ScRNA-seq analysis of bronchoalveolar cells reveals a Th17-polarization of the pulmonary immune response in SEA. Th17-polarized T cells and monocyte-macrophages fuel an inflammation loop where activated monocytes release CXCL13, promoting Th17 polarization of T cells. IL17A, released by activated T cells, further induces CXCL13 release. Reciprocal activation of T cells and monocytes may also occur via direct cell-cell contact (monocyte-T cell complexes). IL17A and CXCL13 recruit B cells and neutrophils, respectively, from peripheral blood. IL17A influences neutrophils by decreasing apoptosis and enhancing their capacity for NETosis. In SEA, there is a reduced activation of non-switched plasma cells, resulting in a decreased pool of activated plasma cells necessary for a Th2 response. *AM, alveolar macrophage; B, B cell; Mo, monocyte; Neu, neutrophil; NET, neutrophil extracellular trap; T, T cell; Th, T helper; Treg, regulatory T cell.*

Key Points

- **In BALF from SEA-affected horses:**
  - **DGE analysis supports a Th17 response**
  - **B cells are more abundant**
  - **Activated plasma cells are decreased**
- **Monocyte-lymphocyte complexes may be present in equine BALF**