**Results**

**Data Exploration and Cell Type Composition**

The dataset, comprising nasopharyngeal and bronchial samples from moderate and critical COVID-19 patients, was subset to focus on these two severity groups. The dataset dimensions were 16,355 genes across 132,618 cells. The distribution of samples across severity classes revealed 13 critical and 14 moderate patient samples. Thirteen distinct cell types were identified: B cells, Basal cells, Basophil/Mast cells, Ciliated cells, Dendritic cells, Fibroblasts, Goblet cells, Intermediate cells, Macrophages, Monocytes, Neutrophils, T cells, and unassigned cells. Major cell types included Neutrophils, Goblet cells, and T cells. The cell type composition within each sample was visualized to provide an overview of cellular heterogeneity across samples and severity groups (Fig. 1).

**Cell-Cell Communication Patterns Differ Between Moderate and Critical COVID-19**

Cell-cell communication (CCI) analysis was performed to infer interactions between cell types within individual samples. These interactions were then aggregated to compare overall communication patterns between moderate and critical patient groups.

Differential CCI analysis revealed distinct communication patterns between moderate and critical samples (Fig. 2). In moderate patients, there was a stronger interaction between Goblet cells (sender) and T cells (receiver). In contrast, critical patients exhibited a stronger interaction between Monocytes (sender) and Neutrophils (receiver).

**Key Ligand-Receptor Interactions in Moderate COVID-19 Patients**

Given the observed strong interaction between Goblet and T cells in moderate patients, we examined the specific ligand-receptor pairs mediating this communication. The top 20 ligand-receptor interactions, ranked by interaction probability, were identified (Table 1). The analysis revealed several notable interactions, including ANXA1-FPR1 (probability 0.491), HLA-B-CD8A (0.364), and HLA-A-CD8A (0.357).

**Key Ligand-Receptor Interactions in Critical COVID-19 Patients**

In critical patients, where Monocytes exhibited strong communication with Neutrophils, we investigated the key ligand-receptor interactions mediating this communication. The top 20 ligand-receptor interactions, ranked by interaction probability, were identified (Table 2). High probability interactions included ANXA1-FPR1 (0.346), CCL3-CCR1 (0.343), and CXCL3-CXCR2 (0.318).