PUBLICATION DIGEST

Dysbiosis of a microbiota-immune metasystem in critical illness is associated with nosocomial infections

Schlechte, J. et. al. *Nature Medicine* (2023)

INFECTIOUS DISEASE

Researchers at the **University of Calgary** demonstrated that intestinal dysbiosis is linked to increased frequency of nosocomial infections in critically ill patients. A systems-level analysis of microbiota dynamics and single-cell profiling of systemic immune and inflammatory responses by CyTOF® flow cytometry show the gut microbiota and systemic immunity function as an integrated system that can impact health outcomes and drive host defense and disease susceptibility.

Key Takeaways

- Imbalance of the gut microbiome is marked with increased *Enterobacteriaceae* during ICU stay.
- CyTOF flow cytometry enabled comprehensive and unbiased phenotypic and functional characterization of the immune landscape.
- Dysbiosis impairs host defense, creating a higher risk of hospital-acquired infections.
- Immune dynamics during acute critical illness were associated with dysregulated myeloid cell responses and amplified systemic inflammation.

Background

Critically ill patients in intensive care units are more susceptible to nosocomial infections that contribute to higher risk of mortality. Since severe infections correlate to impaired immunity, and the gut microbiome is known to influence immune homeostasis, the researchers hypothesized that the interaction between gut microbiota and systemic immunity could drive impaired host defense if thrown into dysbiosis during critical illness.

Study Design

The prospective study used integrated multi-omics analysis to examine fecal microbiota and systemic cellular immune and inflammatory responses in 51 critically ill adults, with samples analyzed at the time of ICU admission and then serially on days 3 and 7 of ICU admission using 16s rRNA gene amplicon sequencing.

The cellular immune and inflammatory landscapes in the bloodstream of each patient were tested with high-dimensional single-cell analysis using CyTOF flow cytometry.

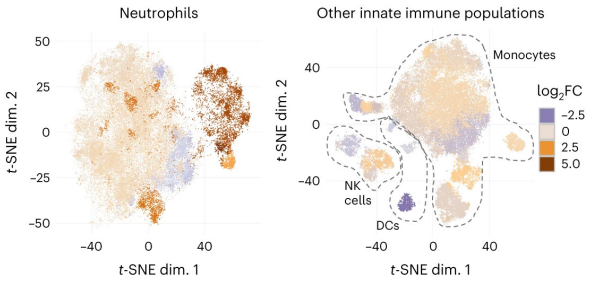

Figure 1. t-SNE plots of neutrophils (left) and all other innate immune cells (right; monocytes, dendritic cells and NK cell clusters as indicated), with heat map overlay showing the log2FC in abundance of each cell cluster between ICU patients with (n = 18) or without (n = 26) progressive enrichment of *Enterobacteriaceae* in their fecal microbiota

Results

- Intestinal dysbiosis was found to be present upon admission and progressively worsened over the illness, observed by reduced biodiversity, taxonomic richness and compositional shifts.
- Analysis showed depletion of T cells, B cells, NK cells, dendritic cells, mature neutrophils and classical/intermediate monocytes, along with an increase of immature and dysfunctional neutrophils and non-classical monocytes, with cytokine storm syndrome.

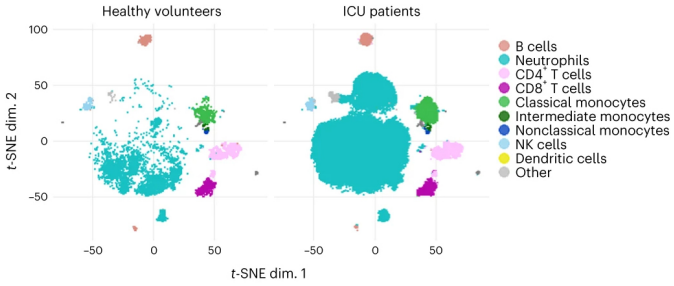

Figure 2. The cellular immune landscape of blood: t-SNE dimensionality reduction of the single-cell immune landscape between healthy volunteers and ICU patients