

The Selective Cytopheretic Device Induces Monocyte Phenotype Switching Towards an Anti-Inflammatory, Reparative Phenotype

James D. Odum, MD, MEd¹; Christopher Pino, PhD^{2,3}; Taylor Mendendorp³; H. David Humes, MD^{2,3}

¹University of Alabama at Birmingham, ²University of Michigan, Nephrology / Internal Medicine,

³Innovative BioTherapies (Ann Arbor, MI)



Introduction

- The **Selective Cytopheretic Device (SCD)** is an immunomodulatory therapy integrated into a continuous renal replacement therapy circuit that was developed to abrogate the inflammatory state associated with sepsis.
- The SCD is thought to **cause direct immunomodulation of circulating activated neutrophils (NE) and monocytes (MO)**.
- Previous work (Sci.Rep.14,12747,2024) has demonstrated that SCD processing of NE promotes apoptosis and return towards homeostasis. However, **the precise mechanisms responsible for MO immunomodulation have yet to be identified**.
- Given the role of MO in the pathogenesis of acute kidney injury and repair, **this study leverages single cell RNA sequencing (scRNAseq) of MO exposed to an in vitro SCD circuit to elucidate the role of SCD therapy on MO phenotype shifting.**

Methods and Materials

- Whole blood from 4 healthy donors was circulated through an in vitro closed-loop circuit containing a miniaturized SCD (Figure 1).
- We collected MO at 4 timepoints (**Fig 1**): (1) baseline (BSL) after isolating PBMCs from the fresh human donor blood; (2) after 2h of circulation through the in vitro circuit (Circ); (3) post-elution of SCD-adherent cells via plasma chase (Plasma); and (4) post final elution of remaining SCD-adherent cells using 0.2% EDTA in PBS (Elute).
- MO were enriched using the Miltenyi Pan-MO kit and magnetically isolated, fixed in 4% formaldehyde, and stored in 50% glycerol at -80°C per 10x Flex guidelines (**Fig 2**).
- Single-cell RNA sequencing was performed on an Illumina NovaSeq 6000, and standard downstream analyses were conducted in R.

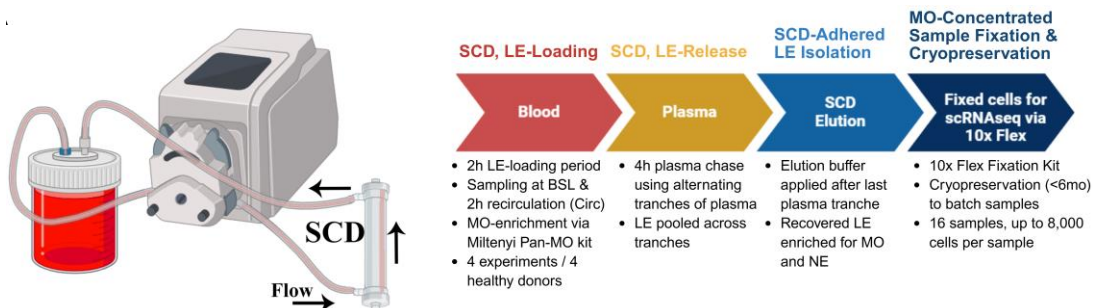


Figure 1: In Vitro miniaturized Selected Cytopheretic Device platform and outline of experimental timepoints.

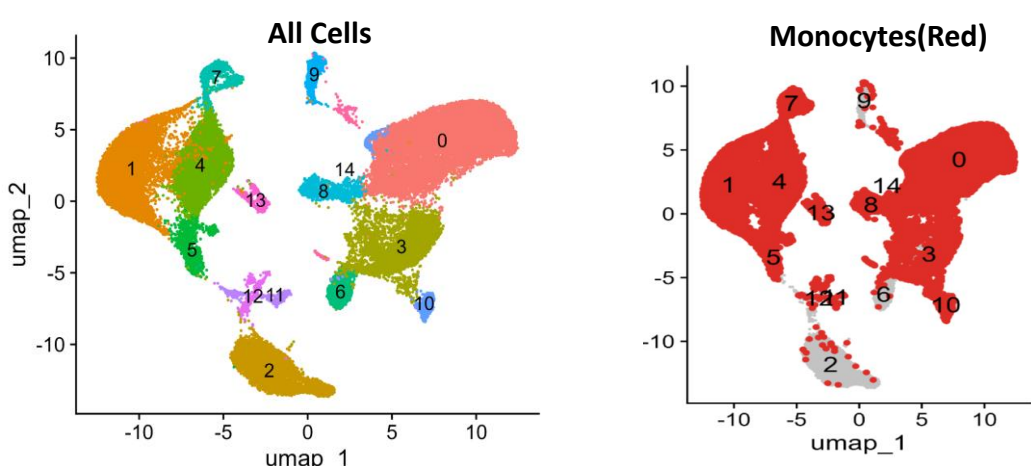


Figure 2: UMAP of all cells subjected to single cell RNA sequencing confirms successful enrichment of monocytes from peripheral blood mononuclear cells.

Results

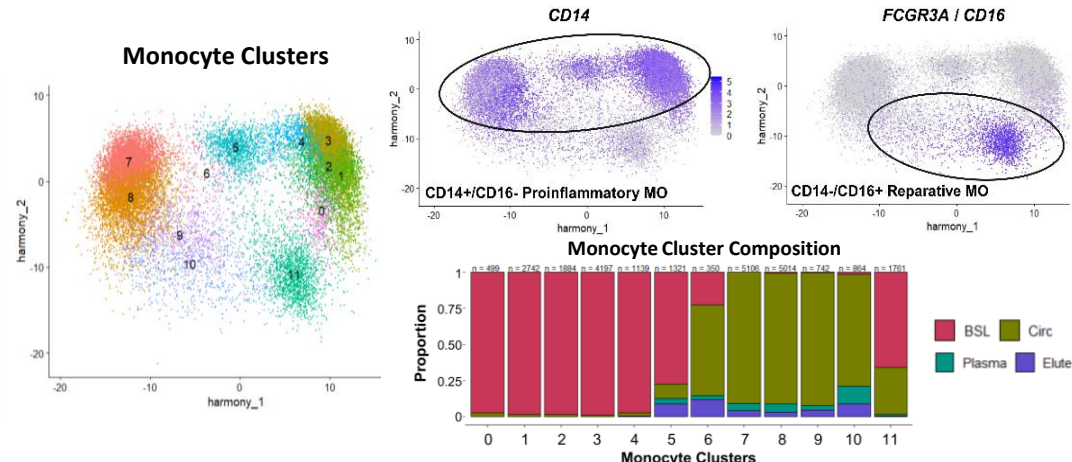


Figure 3: Monocyte clusters (left) and feature plots (top right) demonstrate expression of CD14+/CD16- Proinflammatory monocytes separate from CD14-/CD16+ Reparative monocytes in single cell UMAP space. Monocyte cluster composition by experimental phase demonstrates increases in Circ-Monocytes by cluster 7 (bottom right).

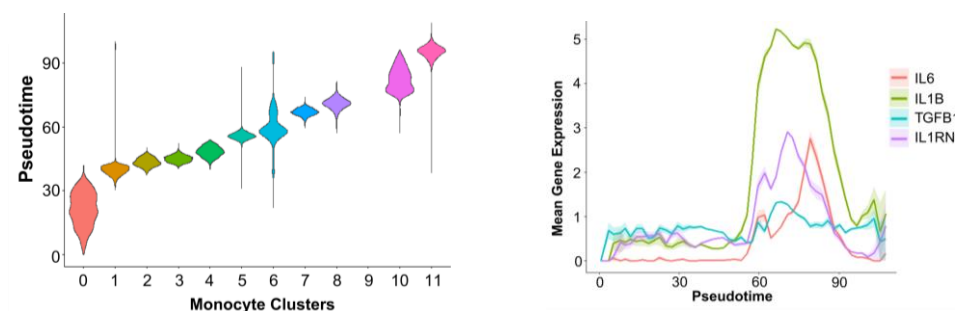


Figure 4: Pseudotime highlights the computationally derived temporal relationship across monocyte clusters during experiment by assigning a pseudotime value (0-100) to each monocyte (left). Genes corresponding to proinflammatory (IL6, IL1B) and anti-inflammatory (TGFB1, IL1RN) cytokines plotted by expression across pseudotime (right).

Targeted Gene Ontology Pathway Analysis: Inflammatory Pathways

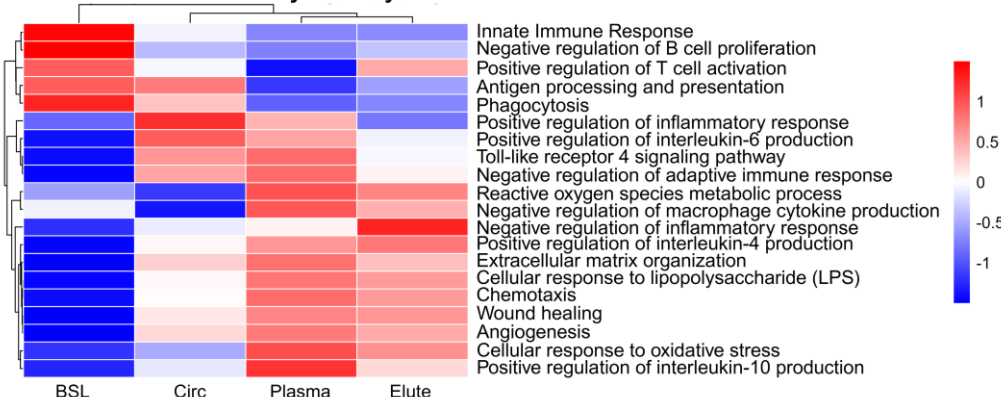


Figure 5: Heatmap of pro- and anti-inflammatory Gene Ontology biological process pathways across experimental phases shows that monocytes associated with SCD processing in the plasma phase upregulate pathways related to interleukin-10 regulation, wound healing, and suppression of macrophage cytokine production, while retaining responsiveness to new inflammatory stimuli.

Conclusions

- Exposure to a miniaturized *in vitro* peristaltic pump induces inflammatory changes in circulating monocytes (Circ; Monocyte clusters 5-6; pseudotime values 50-70).
- The Selective Cytopheretic Device induces monocyte phenotype shifting towards an anti-inflammatory, reparative transcriptomic profile (Plasma; Monocyte clusters 7-10; pseudotime values 70-90).
- Pathway analysis indicates that the Selective Cytopheretic Device directly modulates innate and adaptive immune responses while maintaining their ability to respond to pathogenic stimuli (lipopolysaccharide) and participate in chemotaxis and wound healing.

THE 31ST INTERNATIONAL CONFERENCE ON
ADVANCES IN CRITICAL CARE NEPHROLOGY

AKI & CRRT 2026

MARCH 29 - APRIL 1, 2026

SAN DIEGO, CALIFORNIA