

## Introduction

### Cardiopulmonary Bypass (CPB)

- CPB is a common procedure used in cardiac surgeries to repair congenital heart diseases (CHDs) in pediatric patients<sup>1</sup>.
- CHDs are the most common birth defects and main cause of death in neonates in US<sup>2</sup>.
- Out of the 40,000 neonatal patients suffered from CHDs annually, 25% of them required immediate surgical intervention with CPB<sup>3</sup>.

### Problem with Pediatric CPB

- Current CPB conditions are not well-designed for pediatric patients<sup>4</sup>.
- Smaller size of patients vs. larger foreign material surface, such as PVC, in the CPB circuit<sup>4</sup>.
- High shear stress induces inflammatory response and mechanical trauma to the blood components, especially monocytes<sup>5</sup>.

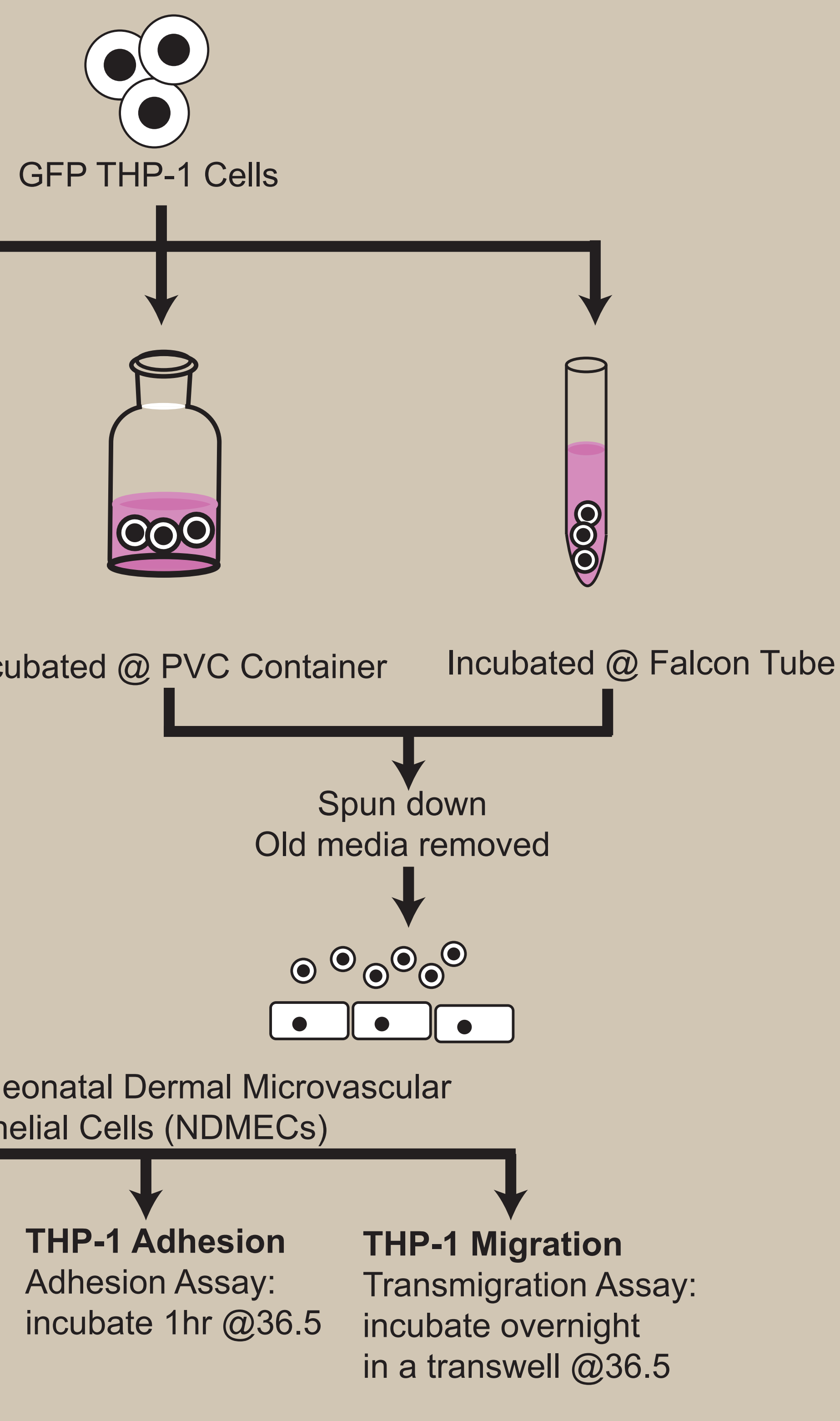
### Impact of Shear Stress on Monocytes

- CPB Shear in PVC tubing specifically upregulates TNF- $\alpha$  and IL-8 in human monocyte-like THP-1 cells through calcium-dependent signaling pathway *in vitro*<sup>6</sup>.
- TNF-alpha-mediated necroptosis was found in a subpopulation of sheared monocytes<sup>6</sup>.
- The cause of inflammatory response in endothelium associated with CPB shear remains unclear.

## Objective

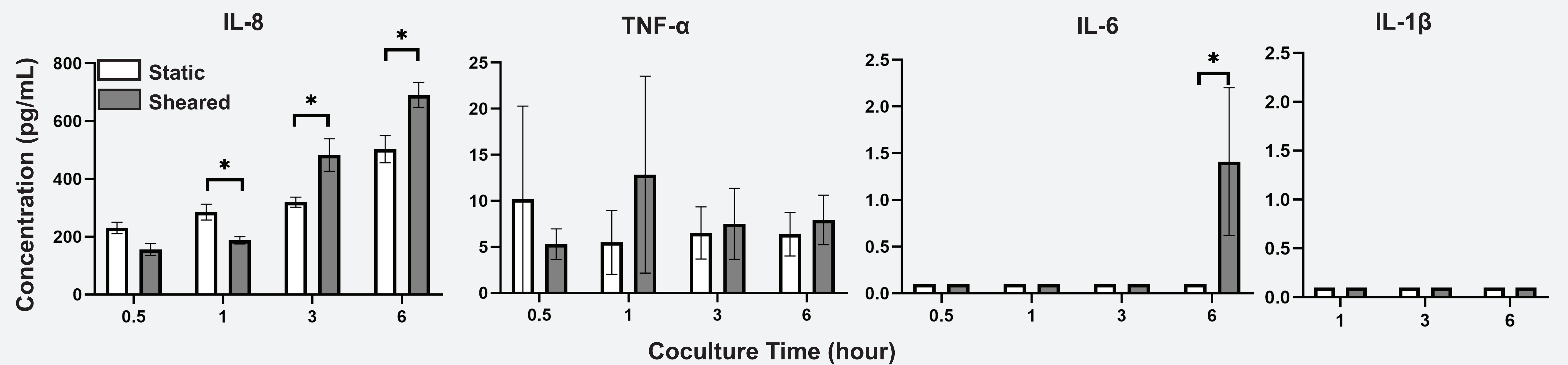
To investigate the interaction between endothelium and monocytes sheared in PVC tubing using an *in vitro* model

## Methods and Experiment Design

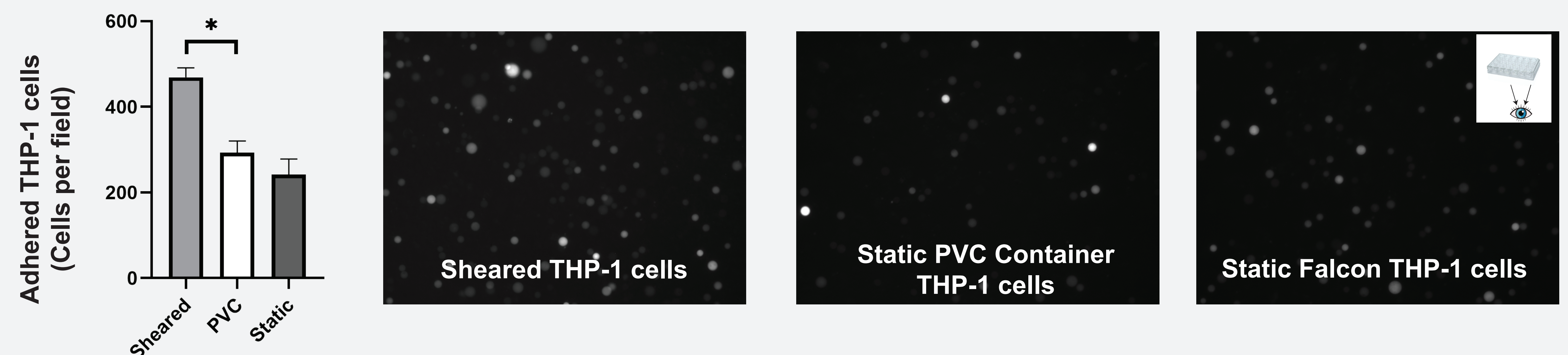


## Results

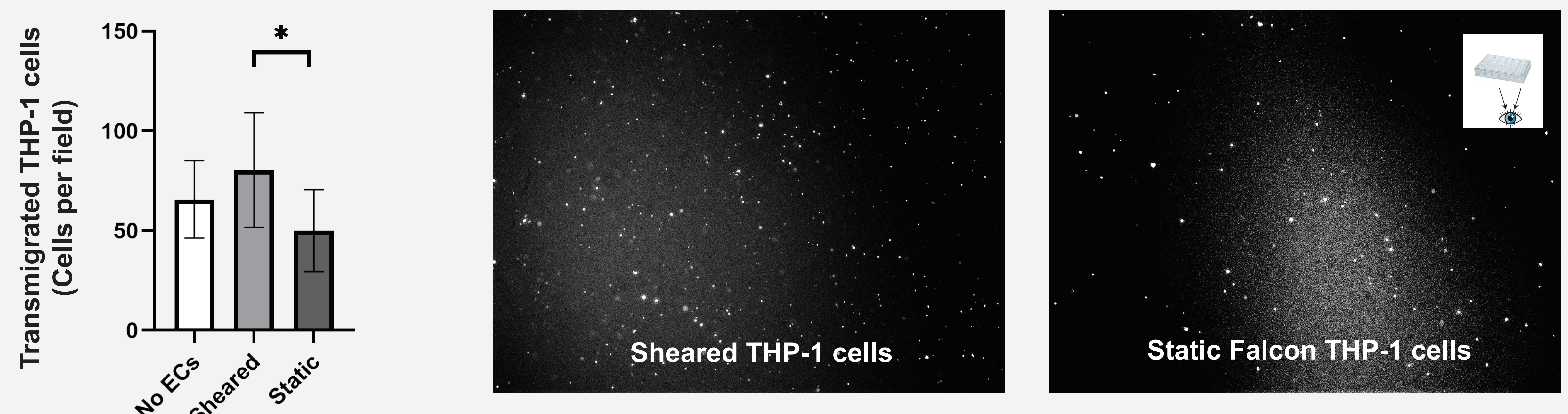
### 1. Interaction between sheared THP-1 cells and NDMECs resulted in increased IL-8 release, but not other cytokines.



### 2. Shear stress in PVC tubing increased the adhesion of THP-1 cells on EC monolayer.



### 3. Shear stress in PVC tubing promoted the transmigration of THP-1 cells through EC monolayer.



## Discussion and Conclusion

- THP-1 monocyte-like cells activated by shear stress and PVC tubing in the *in vitro* CPB circuit are more likely to adhere to microvascular endothelial cells and infiltrate the endothelial monolayer.
- These inflammatory events may be specifically driven by IL-8, which increases the endothelial permeability by disrupting the VE-cadherin at cell junctions (Data not shown, need further investigation).
- Future experiment will probe the phenotypical change of the HNDMECs in response to the insult of shear stress and PVC tubing on THP-1 cells using single cell RNA sequencing.

## Significance

This study aims at revealing the mechanism of inflammatory response after neonatal CPB and developing regenerative medicine to prevent and repair the damage to neonatal patients

## Acknowledgement

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