

## B7

### **Title: HIV-Induced Podocyte Pyroptosis Contributes to Proliferation of Parietal Epithelial Cells**

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#### Background

The lack of or abundance of proliferating parietal epithelial cells (PECs) in Bowman's space determines the glomerular phenotype in focal segmental glomerulosclerosis. Proliferating PECs in Bowman's space characterize the HIV-associated nephropathy. The involved mechanism of PECs proliferation in HIV milieu is not understood. Interleukin (IL)-1  $\beta$  has been reported to stimulate PECs proliferation. We hypothesize that massive injury of HIV-infected podocytes would stimulate PECs proliferation.

#### Methods

Immortalized human podocytes were differentiated and transduced with either vector (V-PDs) or HIV (NL4-3, HIV-PDs) and evaluated for pyroptosis. PECs were incubated in 10% of control (V-PDs), and experimental (HIV-PDs) conditioned media for 48 hours. Also, PECs were incubated in 10% control and experimental media with or without IL-1 $\beta$  (neutralizing) antibodies for 48 hours. Cells were evaluated for proliferation by MTT cell viability assay. To establish an interaction, PECs were grown in outer wells, and V-PDs/HIV-PDs were seeded into inner wells (Trans-well plates). After 48 hours, PDs were assayed for IL-1 $\beta$  by ELISA. Additionally, PECs grown on coverslips were treated with 10% control and experimental media for 48 hours, followed by immunolabeling for PCNA/Ki67.

#### Results

HIV-PDs showed a higher percentage of pyroptosed cells ( $P < 0.01$  vs. V-PDs). Cellular lysates and incubation media of HIV-PDs showed increased ( $P < 0.05$  vs. V-PDs) generation of IL-1 $\beta$ . Conditioned media of HIV-PDs stimulated PECs proliferation; however, anti-IL-1 $\beta$  antibody partially inhibited HIV-PDs conditioned media-mediated proliferation. PECs growing in outer wells of trans-well plates containing HIV-PDs showed increased proliferation. PECs treated with HIV-PDs conditioned media showed a higher percentage ( $P < 0.01$  vs. V-PDs) of PCNA/Ki67 +ve cells.

#### Conclusion

HIV-induced podocyte pyroptosis contributes to PECs proliferation.