Abstract: **P149**

**Angiotensin-II enhances neutrophil extracellular trap formation in an AT1R and NADPH oxidase-dependent manner**

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**Background**

Arterial hypertension is a major risk factor for coronary artery disease (CAD). By formation of neutrophil extracellular traps (NETs), neutrophils release their nuclear content into the extracellular space, fighting pathogens. NETs have been implicated in CAD. In preliminary studies of CAD patients, we observed a positive correlation between blood pressure and NETosis ex vivo, implicating blood pressure modulating NETosis. Angiotensin-II (Ang-II) mediates blood pressure via its potent vasoconstrictive properties, but also exerts pro-inflammatory functions via the angiotensin type 1 receptor (AT1R). AT1R is expressed on neutrophils. We thus hypothesized that Ang-II might influence NETosis.

**Methods**

We stimulated isolated neutrophils with ionomycin ex vivo. NETosis was measured using Sytox Green, a dye that exclusively stains extracellular DNA, a hallmark feature of NETs. The detergent Triton served as positive control. To assess the role of the Ang-II pathway, we pre-incubated neutrophils with Ang-II, AT1R antagonist losartan or NADPH oxidase inhibitor diphenyleneiodonium (DPI).

**Results**

We observed a dose-dependent NET release by ionomycin. Irrespective of ionomycin concentration, pre-treatment with Ang-II significantly enhanced NETosis to 80-90% of positive control. Losartan abolished this effect, suggesting an AT1R-dependent pathway. NADPH oxidase is crucial for NETosis due to release of reactive oxygen species. DPI abolished the effect of Ang-II on NETosis.

**Conclusion**

Our results implicate that via Ang-II, arterial hypertension aids neutrophils to undergo NETosis by increasing intracellular ROS production, which makes neutrophils more susceptible to pro-NETotic stimuli. This provides new insight in how effective blood pressure lowering might lead to more favorable outcomes in CAD.