

## MEETING ABSTRACTS

# PARAOXONASE-2 DEPENDENT REDOX CONTROL OF PLATELET PHYSIOLOGY

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**Background and Objective:** Platelets are not only central players in hemostasis and thrombosis but also important modulators of immune responses, inflammation and cancer. Activated platelets generate reactive oxygen species (ROS) that modulate platelet function through redox signaling and oxidative stress. The anti-oxidative enzyme paraoxonase-2 (PON2) is known to counteract inflammation and atherosclerosis. Recently, we showed that PON2-deficient mice exhibit tissue factor-dependent hypercoagulability<sup>1</sup>. Here, we investigated the role of PON2 in ROS production, phenotype and activation of platelets from PON2-deficient mice.

**Methods:** Platelet count and mean platelet volume (MPV) were determined by a cell counter. Flow cytometry was used to quantify platelet surface receptors, intracellular ROS and platelet function in diluted citrate-anticoagulated platelet-rich plasma. Platelet aggregation was analyzed by light transmission aggregometry in platelet-rich plasma.

**Results:** Platelets from PON2-deficient mice displayed increased basal and agonist-induced ROS levels accompanied by decreased platelet count but increased MPV compared to wildtype platelets. PON2-deficient platelets showed increased surface expression of the von Willebrand receptor (vWF) GPIb $\alpha$ , vWF-binding, P-selectin surface expression, but no  $\alpha$ IIb $\beta$ 3 integrin/fibrinogen receptor activation *ex vivo*. Botrocetin induced enhanced binding of vWF to PON2-deficient platelets in vitro. However, agonist-induced  $\alpha$ IIb $\beta$ 3 integrin activation, P-selectin surface expression and platelet aggregation were impaired compared to wildtype platelets. Interestingly, addition of 0.5 mM Ca<sup>2+</sup> to platelet-rich plasma normalized platelet hyporeactivity.

**Conclusion:** Our data demonstrate that PON2 plays a crucial role in platelet ROS production, phenotype and function. Reactivity of platelets from PON2-deficient mice depends on extracellular Ca<sup>2+</sup>-concentration.

*Keywords:* Paraoxonase-2; Reactive oxygen species; Platelets; Hemostasis; Ca<sup>2+</sup> homeostasis

## References

1. Julia Ebert et al.. "Paraoxonase-2 regulates coagulation activation through endothelial tissue factor." *Blood*, no. (2018): blood-2017-09-807040. Accessed May 14, 2018. doi: 10.1182/blood-2017-09-807040.