LDL uptake and neutrophil effector function

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BACKGROUND

The number of activated neutrophils in the circulation of hyperlipidemic patients is correlated with levels of low density lipoprotein (LDL).¹ Activated neutrophils can expel their chromatin, forming net-like structures.² These neutrophil extracellular traps (NETs) constitute important risk factors for acute myocardial infarction (AMI).³ Pro-protein convertase subtilisin/kexin 9 (PCSK9) is a regulator of LDL receptor (LDLR) expression and has gained attention in the treatment of hyperlipidemia.⁴

RESULTS

Figure 1. CV risk factors and lipid profile of AMI patients.

Figure 2. Ionomycin (IM) induced NET formation is (a) higher in AMI patients compared to healthy controls (HC). (b) Pre-conditioning of neutrophils of AMI patients with PCSK9 attenuates stimulated NET formation in a dose-dependent manner.

Figure 4. Expression of LDL binding receptors is (a) differentially influenced by stimulation, increasing CD36 and LOX-1, but decreasing LDLR. (b) Neutrophil stimulation induces uptake of labeled LDL. BL, baseline; stim. stimulated

AIM

We aimed to investigate the influence of LDL and PCSK9 on neutrophils and NET formation in patients with AMI.

METHODS

25 consecutive AMI patients were enrolled to assess cardiovascular (CV) risk factors, *ex vivo* NET formation in response to PCSK9 and ionomycin (IM), and neutrophil surface receptor expression by flow cytometry

Figure 3. Basal NET formation is correlated with (a) CD11b expression of neutrophils and (b) LDL levels of AMI patients. BL, baseline; NQA, NET quantification

CONCLUSION

- LDL primes neutrophils, elevating their propensity to undergo NET formation, while PCSK9 reduces NET formation
- Our data indicate a role of LDL uptake for neutrophil effector function during cell activation.

REFERENCES

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