

PREDICT-EV; The Role of Extracellular Vesicles in Platelet Adhesion: Implications Following Transient Ischaemic Attack

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INTRODUCTION

Platelet adhesion to endothelial cells is a fundamental step in the development of thrombosis, a leading cause of ischemic stroke.

Transient Ischemic Attack (TIA) patients are at a 25% higher risk of experiencing an ischemic stroke in the next 12 months.

Previous research from this group and the literature shows that endothelial-derived Extracellular Vesicles (EVs) are increased after exposure to hypoxic conditions (e.g. TIA, Ischemic stroke), and these EVs exhibit pro-thrombotic potential.

Aim: To investigate the impact of pre-incubating endothelial cells with hypoxia-derived extracellular vesicles and assess platelet adhesion.

METHODS

Static and **fluidic-based** novel model systems were set up to assess platelet adhesion to endothelial cells.

The fluidic model mimics the endothelium in vivo conditions, applying a controlled flow rate that **mimics the pressure and shear stress** experienced in capillaries.

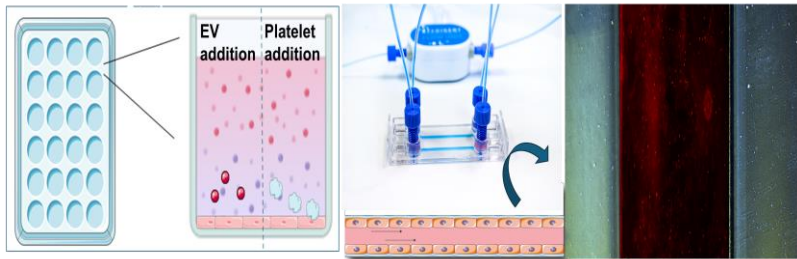


Figure 1. Visual representation of 'Static' and 'Fluidic-based' experiments. Cells were seeded on a 48 well plate (static) or microfluidic chip (fluidic), grown to confluence, and treated with EVs, and then fluorescently labelled platelets.

RESULTS

Pre-treatment with EV derived from TIA patients showed significantly increased platelet adhesion to healthy endothelium compared to healthy controls and no EV.

This increase was comparable with the TNF- α positive control.

Interestingly, a similar effect was observed with pre-incubation with EV from the TIA-mimic group in static experiments, but not in the fluidic model.

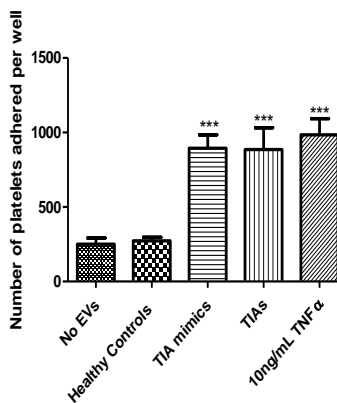


Figure 2. Platelet adhesion to the endothelium in static conditions. Results represent N=10.

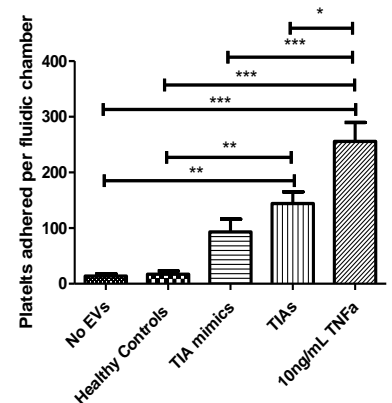


Figure 3. Platelet adhesion to the endothelium under the flow of liquid. Results represent N=4.

The QR code links to a video showing platelets adhering to endothelial cells under a controlled flow rate

CONCLUSIONS

Key finding: TIA EVs mediate increased platelet adhesion to endothelial cells, a key step in thrombus formation.

Increased platelet adhesion in TIA patients indicates increased thrombotic potential that may predispose these patients to subsequent ischemic events. Static data from the TIA-mimic group suggests patients exhibiting cardiovascular disease risk factors are also prothrombotic. Fluidic experiments produced contrasting information.

Future works: How TIA EVs mediate platelet adhesion is yet to be determined.