complication. Increasing evidence suggests that immune-thrombotic mechanisms may critically contribute to persistent microvascular obstruction. This study aimed to determine whether platelet-driven myeloid immune remodelling contributes to no-reflow.

Methods: Single-cell RNA sequencing (scRNA-seq) was performed on intracranial arterial blood from stroke patients undergoing thrombectomy to identify no-reflow-specific immune signatures. Findings were validated in a C57BL/6 mouse tMCAO model, classified into no-reflow and good-reflow groups by laser Doppler imaging. Platelet-myeloid interactions, CXCL4 levels, neutrophil extracellular traps (NETs), and metabolic-stress markers were assessed by flow cytometry, ELISA, and histology.

Results: Clinical scRNA-seq revealed that no-reflow involves a 'structural remodelling' of the myeloid compartment rather than simple cell expansion. Myeloid cells in no-reflow patients displayed distinct states characterised by metabolic inhibition and oxidative stress uncoupling. Notably, cell-cell communication analysis identified amplified platelet-myeloid crosstalk, with **CXCL4 emerging as a key driver**.

Consistent with clinical findings, no-reflow mice exhibited impaired microcirculation and larger infarcts. This was accompanied by significantly increased platelet–neutrophil/monocyte aggregates and elevated serum CXCL4 (PF4) levels. Furthermore, the no-reflow brain showed enhanced NET formation, oxidative damage (4-HNE/8-OHdG upregulation), and dysregulated metabolic-stress signalling (e.g., PRDX6, GMPR), mirroring the transcriptional signatures observed in patients.

Conclusions: These findings define no-reflow as an immune-driven disorder characterised by **platelet-CXCL4-amplified myeloid remodelling** and metabolic-oxidative stress imbalance. Targeting the CXCL4-myeloid axis represents a promising translational strategy to restore microvascular perfusion.

Conflict of interest: Xiaoyi Jiang, Yue Zhang, Zhiyu Leng, Ming Yuan, Qinxue Sun, Yuhualei Pan, Gang Li:nothing to disclose

Abstract citation ID: aakag023.989

ABSTRACT NUMBER: ESOC2026A2138

PLATELET-DERIVED CXCL4 DRIVES MYELOID IMMUNE REMODELLING IN CEREBRAL NO-REFLOW: A TRANSLATIONAL STUDY INTEGRATING CLINICAL SINGLE-CELL TRANSCRIPTOMICS AND MURINE MODELS

Xiaoyi Jiang[1], Yue Zhang[1], Zhiyu Leng[1], Ming Yuan[1], Qinxue Sun[1], Yuhualei Pan[1], Gang Li[1]

[1] *Department of Neorology, Shanghai East hospital,Tongji University school of medicine, Shanghai, China*

Background and aims: No-reflow after reperfusion therapy remains a major determinant of poor outcome in ischaemic stroke and is traditionally regarded as a haemodynamic