

C5B9 DEPOSITS ON ENDOTHELIAL CELLS FOR THE EVALUATION OF COMPLEMENT FUNCTION IN THROMBOTIC MICROANGIOPATHIES OF DIFFERENT ORIGIN & THERAPY MONITORIZATION

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INTRODUCTION:

Atypical haemolytic uremic syndrome (aHUS) is a rare, progressive, life-threatening form of thrombotic microangiopathy (TMA). aHUS is caused by dysregulation of the alternative complement pathway over the cell surfaces. Nonetheless, there is wide evidence that complement activation has a role in other causes of TMA.

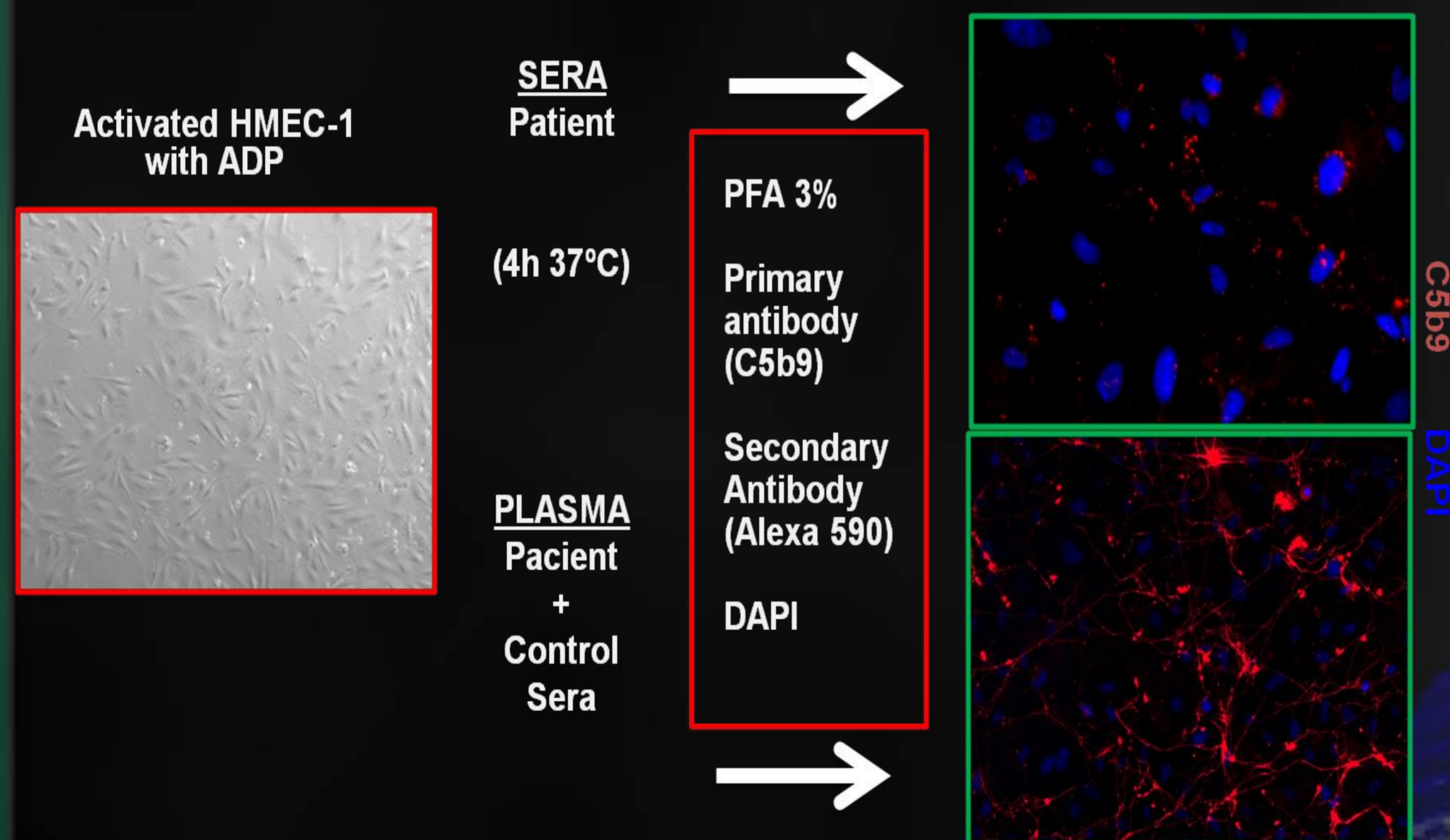
AIMS:

A reliable method is needed to evaluate terminal complement activation over cell surfaces in aHUS patients (early diagnosis, identify remissions & recurrences, individualized treatment). This method could also explore possible implications of complement mediated damage in other TMAs and evaluate the possible indication of complement blockage.

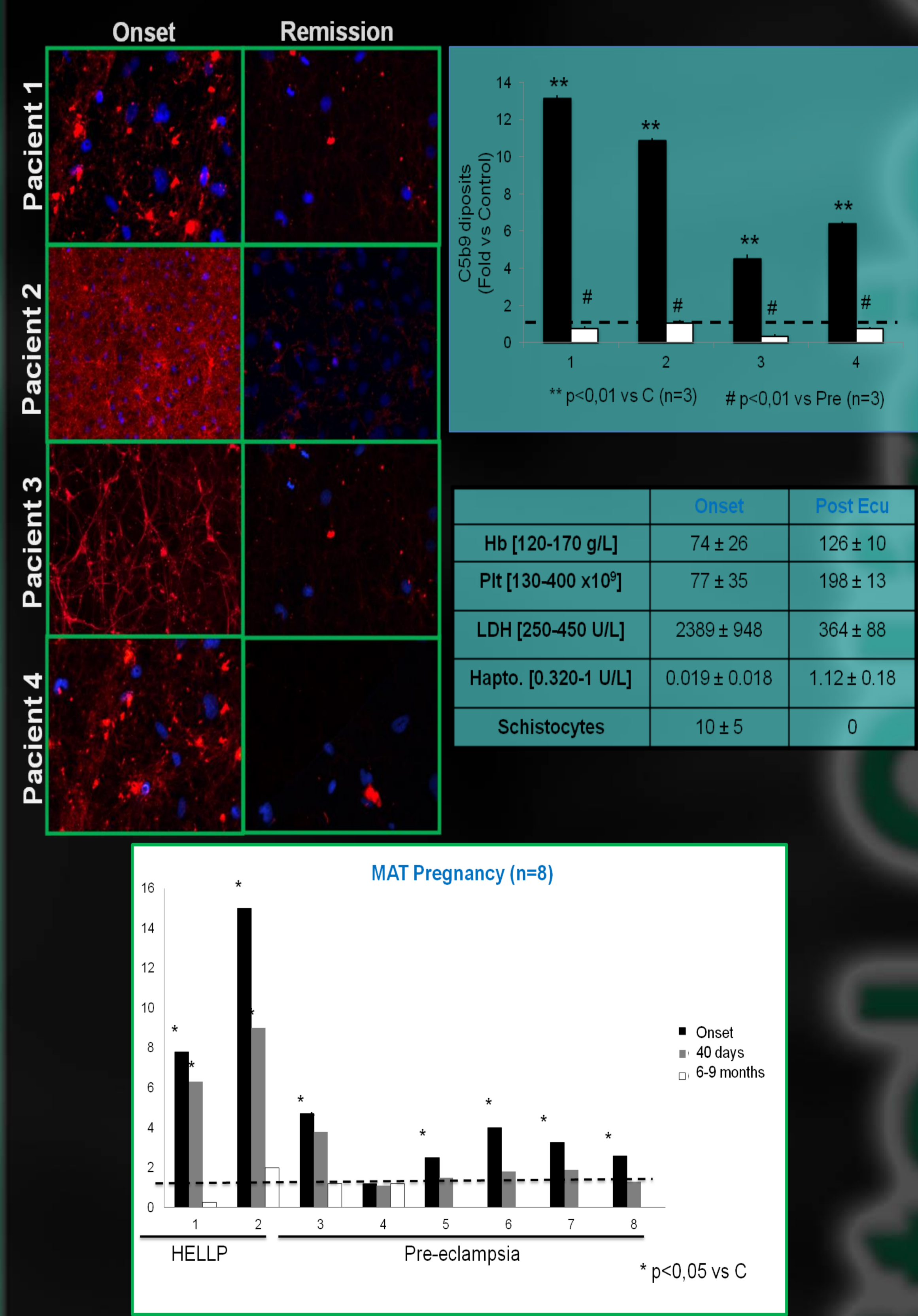
METHODS:

Complement activation was assessed by exposing endothelial cells (EC) to patients' sera or to patients' plasma samples mixed with a control sera pool (1:1). C5b9 deposits on EC were analyzed through immunofluorescence and expressed as fold increase vs control samples.

EX VIVO INDUCTION DEPOSITION OF C5B9 OVER EC



RESULTS:



Exposure of EC to aHUS patients plasma during the onset of the disease resulted in a significant increase in C5b9 deposits (8 ± 2 , $n=4$, $p<0.01$), which was prevented in samples from the same patients treated with E (0.7 ± 0.1) [See Image]. Significant fibrin formation was observed together with C5b9 deposition. Notably, results obtained using plasma samples were much more remarkable and reproducible than those obtained with sera. C5b9 deposition was also increased using samples from HELLP syndrome & pre-eclampsia patients (at acute phase, 6 ± 2 , $n=8$, $p<0.01$) and 40 days later (3.2 ± 1 , $p<0.01$). Complement activation was at control levels when analyzing samples from patients with malignant hypertension (0.8 ± 0.2 , $n=5$) or aHUS patients in remission after treatment with regular doses of E ($n=5$) and lower doses ($n=2$).

CONCLUSIONS:

This method could be useful for the diagnosis of aHUS patients and to monitor therapy response. It also could explore the possible implications of complement mediated damage in other TMAs with consequent potential indication of complement blockage. Further research is needed to clarify the basis for the colocalization of C5b9 and fibrin on EC surface.

