Can Blood-Brain Barrier Disruption and Active Inflammation in Multiple Sclerosis be Monitored by EVs in Plasma?

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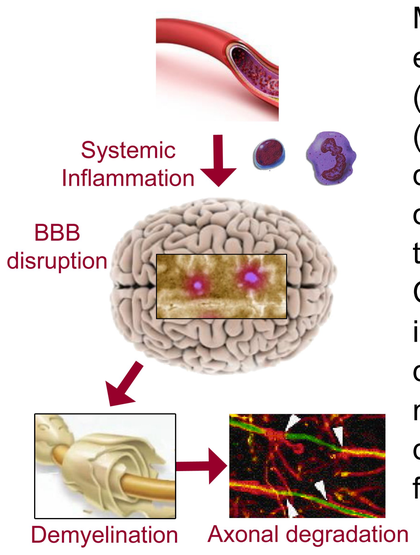
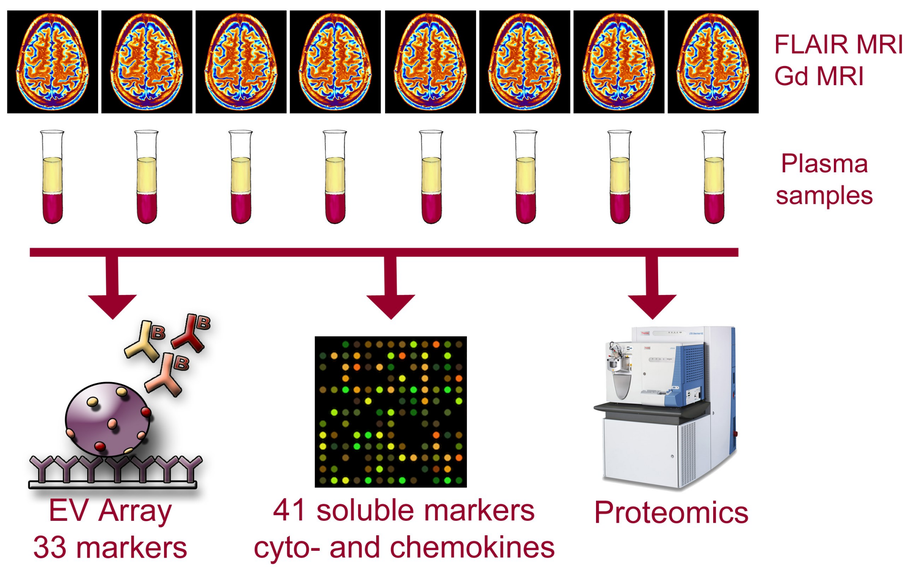
Introduction



Multiple sclerosis (MS) is an inflammatory demyelinating disease of the central nervous system (CNS). Disruption of the blood-brain barrier (BBB) plays a major role in disease activity and damage of the BBB may be initiated by systemic or CNS inflammation and contribute to escalation of pro-inflammatory responses within the CNS. We hypothesized that damage of the BBB is reflected in the appearance of endothelium-derived extracellular vesicles (EVs) in the plasma, and correlate with soluble biomarkers of endothelial stress and regulators of systemic inflammation.

Five patients with untreated MS were followed by weekly MRI scanning and blood sampling for seven weeks. Plasma samples were analyzed for 41 soluble biomarkers by Mesoscale V-PLEX whereas EVs were analyzed by the EV Array as depicted in the study design below.

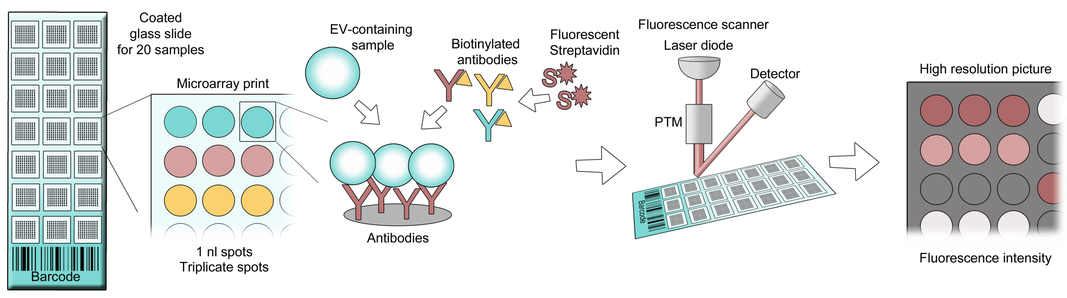


Method

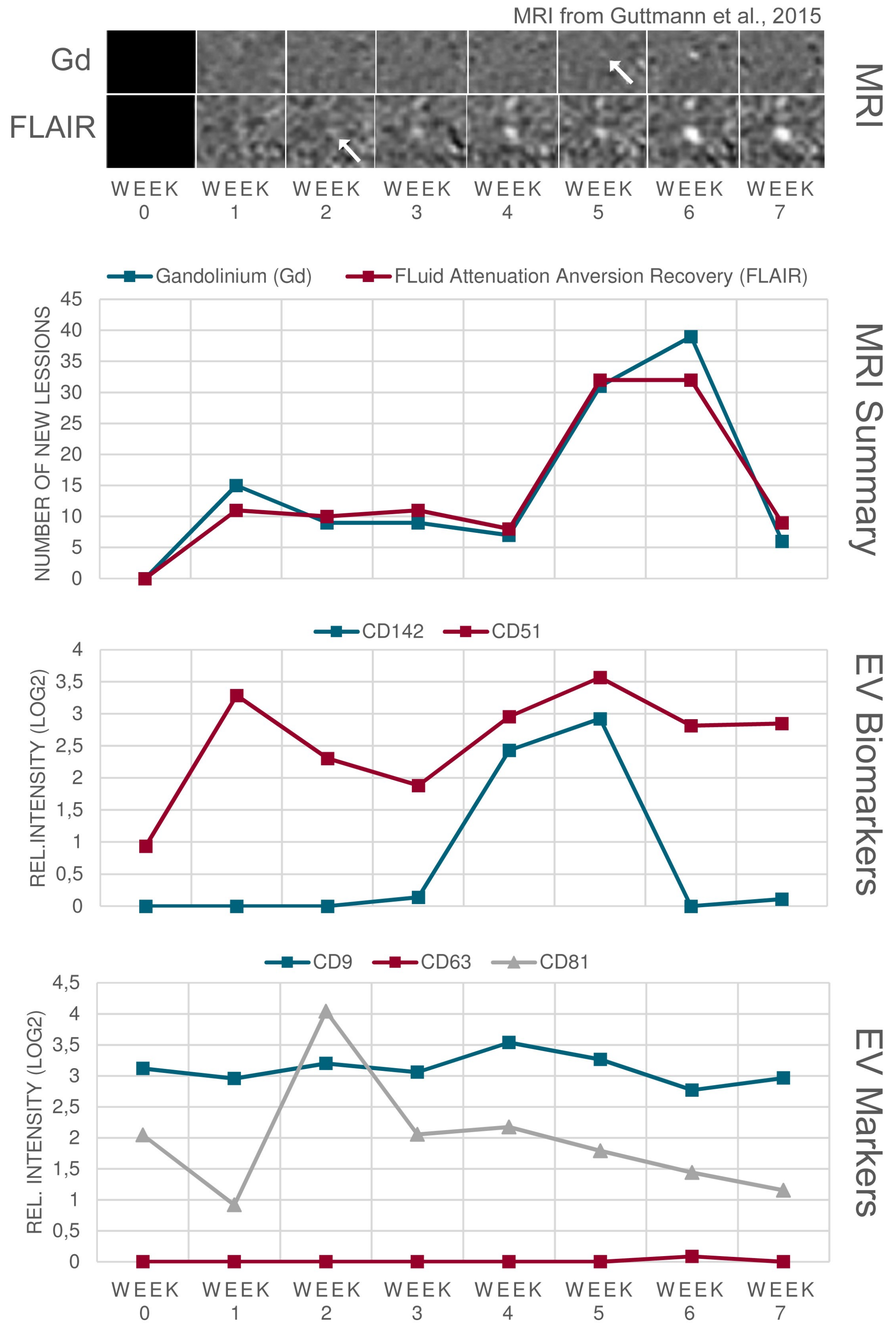
The EV Array was customized by known EV markers and endothelial stress induced EV markers as determined by quantitative proteomics to include 33 different antibodies against EV markers involved in immune responses, inflammation and endothelial stress (as indicated below). For detection of EVs, a cocktail of antibodies against CD9, CD63, and CD81 was used.

EV	Immune	Endothelial	Platelet	Other
Annexin V	CD3	CD31	CD42a	LAMP2
CD9	CD8α	CD51	CD62 E	TNF RII
CD63	CD19	CD146	CD62 E/P	Tspan8
CD81	CD28	tPA	CD142	AKAP3
CD82	CD80	Thrombospondin-1		CD106
TNF RI	MIC A/B	VE-Cadherin		CD151
TSG101	CTLA4			
Alix	ICAM-1			
	HLA DR/DP/DQ			

The EV Array Principle:



Results



The results from one patient is illustrated. Two types of MRI scanning (Gd and FLAIR) were analyzed and the number of newly appearing lesions were counted for each week.

The EV contents of the plasma samples were investigated by the EV Array and a selection of markers are shown. The amount of the two biomarkers CD142 and CD51 was found to increase prior (week 4 and 5) to the major increasement of lesions (week 5 and 6). This increasement was not found in the amount of general EV markers (CD9, CD63 and CD81).

Perspectives

Using the EV Array technology, we demonstrate for the exemplified patient how plasma EVs can serve as a potential diagnostic and predictive tool in detection of inflammation and possible BBB disruptions. Further multivariate correlation analyses for all patients, time points, EV markers and soluble markers will reveal the best predictive marker or combination of markers.

Scanning of the QR code will lead to more information of the technology, the people behind, and the complete publication list.

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