

Extracellular vesicles: what's blood plasma made of?

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Blood plasma contains extracellular vesicles (EVs), derived from activated or apoptotic cells. Intense research focuses on EVs because of their various physiopathological roles and potential biomedical applications. However, our current knowledge on EVs is still limited, mainly due to their small size and to the limitations of characterization methods.

Our aim is to provide a comprehensive description of EVs in physiological and pathological situations, and to answer basic questions such as: How do they look? What is their size distribution? How many of them expose phosphatidylserine? How many of them derive from erythrocytes? From platelets? What is their concentration? We focused first on EVs present in blood plasma from healthy subjects, with the objective to provide a reference catalogue for further studies in pathological situations.

To address these questions, we used two electron microscopy techniques, combined with receptor-specific gold labeling:

- Cryo-transmission electron microscopy allowed us to determine the structure, size and phenotype of EVs.
- Direct on-grid sedimentation of EVs on EM-grids permitted us to quantify them.

In parallel, we developed a novel approach of flow cytometry for determining the concentration of the major EV populations in plasma.

This study led to several important new findings, revealing the presence of EVs of various morphologies and sizes, showing that only a minority of EVs expose PS and providing an estimate of EV concentrations in healthy blood plasma.

[1] Arraud, N et al. *J. Thromb. Haemost.* 2014 12: 614–627.

[2] Arraud, N et al. *J. Thromb. Haemost.* 2015 13: 237-247.