Binding of Neurotransmitters to Lipid Membranes

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Published in:
Biophysical Journal

Link to article, DOI:
10.1016/j.bpj.2013.11.2562

Publication date:
2014

Document Version
Publisher's PDF, also known as Version of record

Link back to DTU Orbit

Citation (APA):
Microvesicles (MVs) are cell-derived membrane fragments which are present in plasma and other body fluids. In plasma, MVs participate in physiological processes of hemostasis and inflammation. MVs contain cell-specific molecules and are present at elevated levels in various diseases, which has raised the hypothesis of their potential application as disease biomarkers. The characterization of MVs is however hampered by their small size, estimated from 50 nm to 1 μm, and by limitations of the methods currently used for their analysis. Our aim is to provide a comprehensive description of MVs from plasma of healthy individuals and answer basic questions concerning MVs: 1) What do MVs from plasma look like?; 2) What is their size distribution?; 3) How many of them derive from erythrocytes?, from platelets?; or 5) What is their concentration? By combining cryo-Electron Microscopy (EM) and receptor-specific gold labeling, the morphology, size and phenotype of MVs from normal plasma were characterized. MVs present three morphologies, consisting of spherical vesicles, of 40 nm – 1 μm in diameter, tubular vesicles, of 1-5 μm in length, and large membrane fragments, 1-8 μm wide. The sub-population of pro-coagulant MVs that expose PS, identified by labeling with Annexin-A5-conjugated gold nanoparticles, was found to form a minority of MVs, about 25%, in contrast with the current theory of MV formation. MVs derived from the main blood cell populations, erythrocytes, platelets and leukocytes, were identified by immuno-gold labeling. Finally, concentrations of MVs were determined by a novel quantitative approach based on MV sedimentation on EM grids. This study (in revision) provides a detailed description of MVs from normal plasma, novel insights on mechanisms of MV formation, and will serve as a reference for further studies of MVs in pathological situations.