

Off-the-shelf: stable, ready-to-use, pre-labeled human plasma and urine-derived EVs

Britta A. Bettin^{1,2}, K. Maaninka³, C. Hau^{1,2}, P. Siljander³, E. van der Pol^{1,2,4}, R. Nieuwland^{1,2}

¹ Department of Clinical Chemistry, ² Vesicle Observation Center Amsterdam UMC, University of Amsterdam, Amsterdam, the Netherlands

³ Department of Biosciences, Division of Biochemistry and Biotechnology and Division of Pharmaceutical Biosciences, Faculty of Pharmacy, University of Helsinki, Helsinki, Finland

⁴ Department of Biomedical Engineering and Physics, Amsterdam UMC, University of Amsterdam, Amsterdam, the Netherlands

E-mail: b.a.bettin@amsterdamumc.nl

Background

Human body fluids contain extracellular vesicles (EVs)

Background: EVs are being explored as biomarker for diseases. Exploiting EVs as biomarkers requires reliable measurements.

Flow cytometer (FCM)

Problem: EV concentration measurements are incomparable between instruments.

Solution: To standardize EV concentration measurements by developing reference materials and biological test samples.

Biological test sample requirements

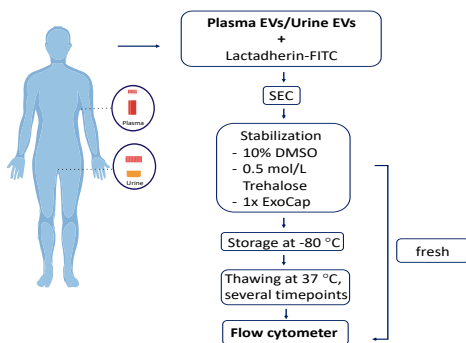
- Stable
- Ready-to-use
- Traceably characterized
- Flow cytometry compatible
- Validate newly developed reference materials and methods

Aim

To develop stable, ready-to-use, and well-characterized biological test samples containing EVs to test new standardization procedures for EV concentration measurements.

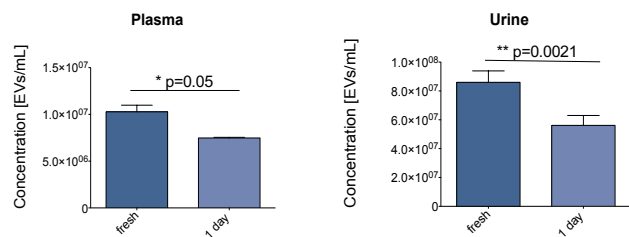
Methods

Experimental setup



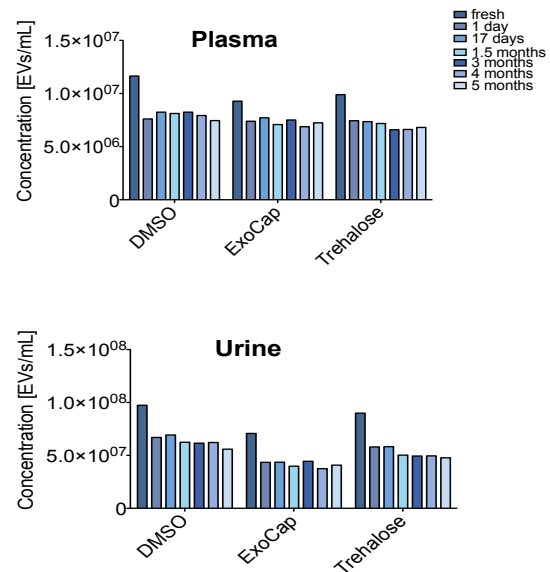
Results

Stability of lactadherin labelled plasma and urine EVs



* significant at the 0.05 level, ** significant at the 0.01 level

The plasma and urine EV concentrations decreased 27% and 35% after one day of storage.



After five months of storage, the concentration of plasma EVs decreased 2.0% (DMSO and ExoCap) and 8.5% (trehalose) compared to day one, while the concentration of urine EVs decreased 6-18%.

Conclusion & Discussion

- Pre-labeled plasma-derived EVs can be stored for up to (at least) 5 months when using cryopreservation agents.
- Urine-derived EVs seem less stable compared to plasma-derived EVs during storage.
- These optimized biological test samples will be used to validate newly developed reference materials and methods.