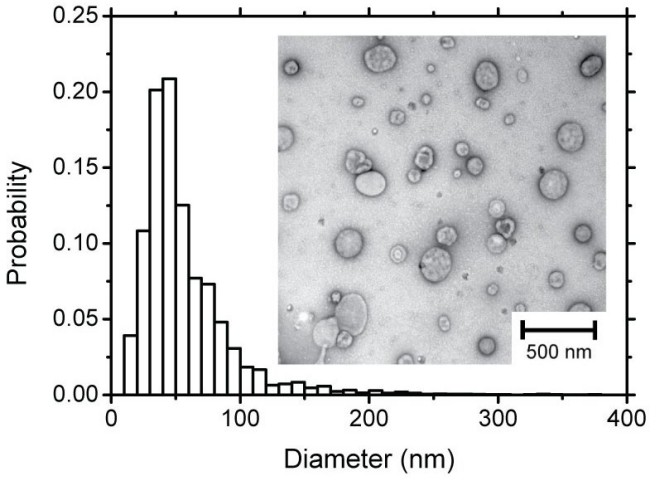
Developing a new method to isolate extracellular vesicles from human blood plasma for biomarker exploration

An internship position is available at the Amsterdam Vesicle Center, part of the Amsterdam UMC. Research will be performed in a multidisciplinary team including biologists, chemists and physicists.

Background: All body fluids contain small cell-derived extracellular vesicles (EVs; Figure 1). EV research is booming, because EVs offer a potential treasure cove for novel and non-invasive biomarkers. To gain full access to the unique biochemical composition of EVs, however, isolation is a must.



Problem: Human blood plasma is the most commonly studied 'starting material' for EV biomarker research. EVs are a small fraction of plasma, and plasma itself is a highly challenging matrix. Especially the presence of lipoprotein particles (lipoproteins) causes problems when isolating plasma EVs, because their size and density overlap. Consequently, at present there is not a single method available to selectively isolate EVs from plasma.

Solution: Upon cell stress, cells produce increased concentrations of stress proteins, also known as "heat-shock proteins" (HSPs). During cell stress, also the concentration of HSPs increases in released EVs, which is thought to promote cell survival. Recently, HSPs were found to be present on the EV surface, and a commercial kit was developed to capture EVs exposing HSPs. This kit has been successfully used to capture EVs from human urine for downstream RNA analysis. Based on the finding that human urine-derived EVs apparently expose HSPs, we hypothesize that also human plasma-derived EVs may expose HSPs. Since the biogenesis of lipoproteins differs completely from EVs, it seems unlikely that also lipoproteins expose HSPs. If so, this would offer a unique opportunity to selectively isolate human plasma EVs.

Tasks: Your aim is to test whether this commercial kit specifically captures EVs, either directly from human plasma or after size-based isolation of plasma EVs by size-exclusion chromatography (SEC). The efficacy to selectively capture EVs will be monitored by high-throughput single particle detection

methods as flow cytometry, (fluorescence) microfluidic resistive pulse sensing, by biochemical approaches, and by electron microscopy.

Contact: dr. Rienk Nieuwland (r.nieuwland@amsterdamumc.nl), dr. Jillian Bracht (j.w.p.bracht@amsterdamumc.nl) and dr. Edwin van der Pol (e.vanderpol@amsterdamumc.nl)

Websites: www.metves.eu and www.edwinvanderpol.com