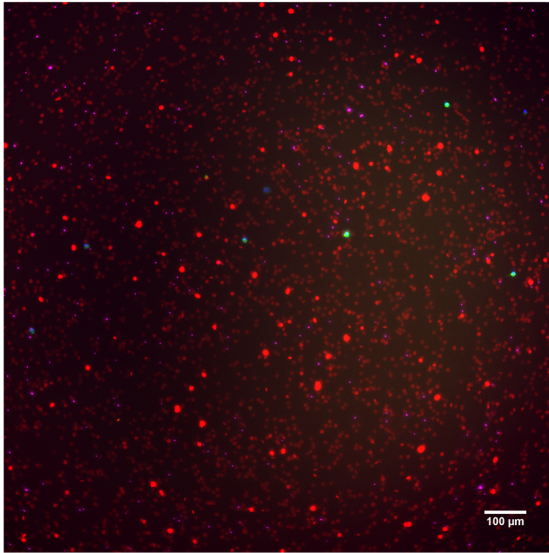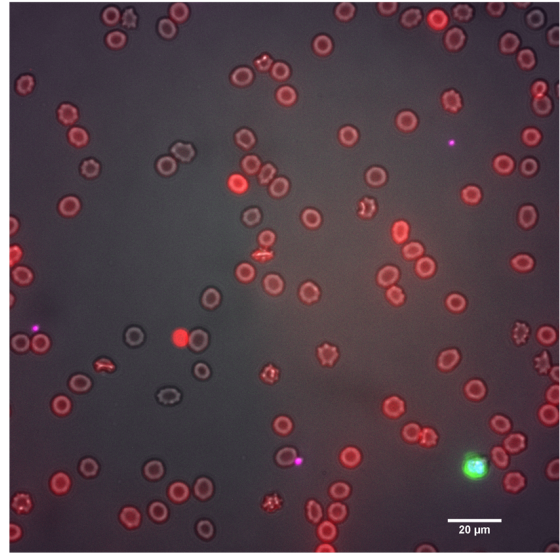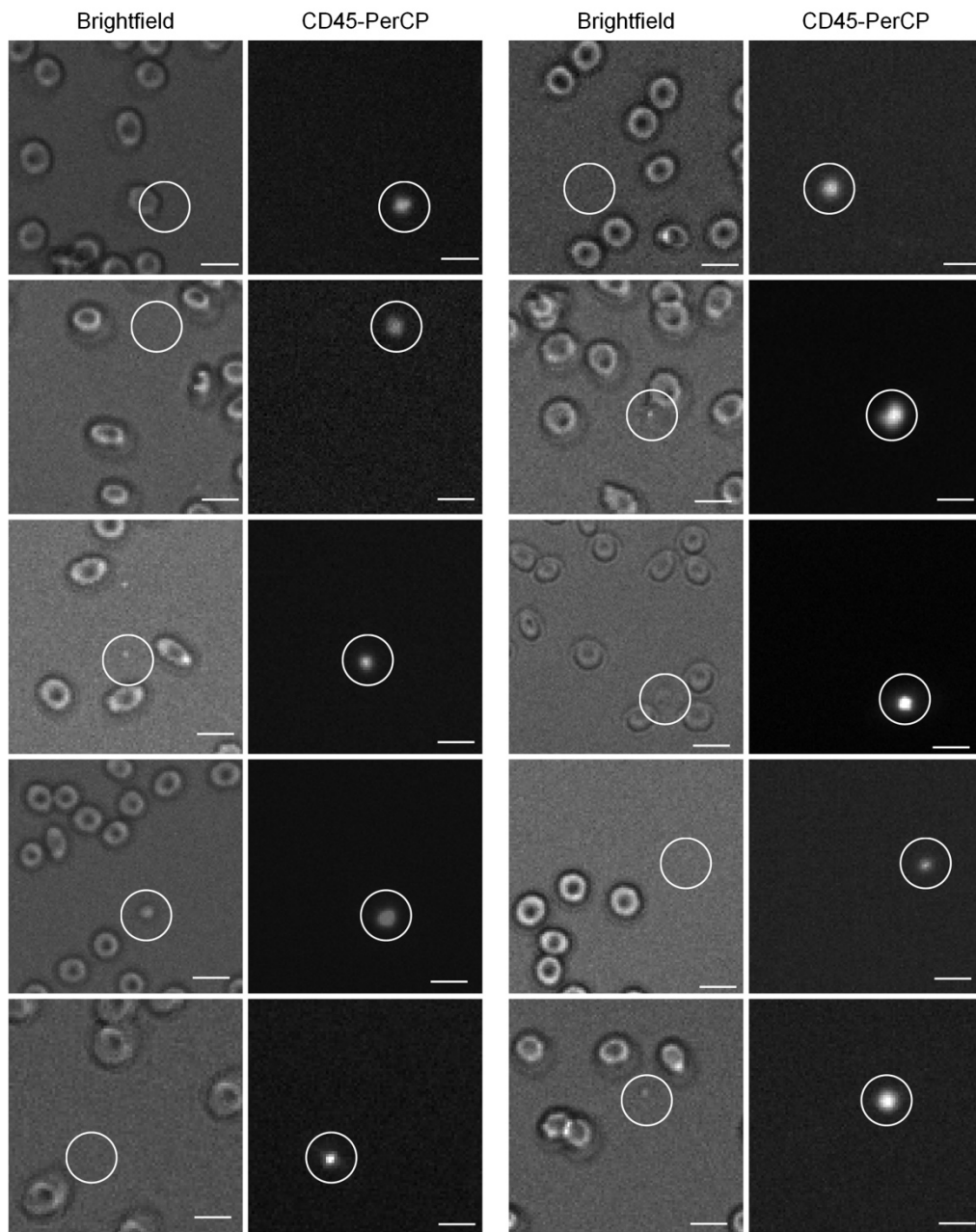**A. 10x/0.45 NA objective**

Hoechst, CD235a, CD61, CD45

B. 60x/0.7 NA objective

Hoechst, CD235a, CD61, CD45, brightfield

Supplementary Figure S1: Examples of composite immunofluorescence images of blood samples without EpCAM enrichment, obtained with an inverted scanning fluorescence microscope using a 10×/0.45 NA (Panel A) and a 60×/0.7 NA objective (Panel B). The images that were obtained with the 10× objective were used as an input in the open-source ACCEPT software for the automated enumeration of the different cell and EV populations.

Leukocyte-derived EVs in whole blood

Brightfield	CD45-PerCP	Brightfield	CD45-PerCP

Supplementary Figure S2: Examples of brightfield and immunofluorescence images of leukocyte-derived Extracellular Vesicles, enclosed within circles. Scale bars indicate 10 μm.