

Response to reviewers:

We would like to thank all reviewers for assessment of our work and thoughtful comments.

Reviewer 1:

Helmke A and von Vietinghoff S reported review article on extracellular vesicles (EVs) as mediators of vascular inflammation in kidney disease. Inflammation in kidney diseases is important for the development of pathology. Examining EVs in the processes should be valuable and the approach may open up a new field. However, since physiological implications of EVs are not well known, it is difficult for readers to understand pathological implications of EVs in the setting of each kidney disease. Please mention possible physiological roles of EVs in general.

Response:

EV are already present in normal body fluids. We have now included this information as requested. Given the extent of the topic, we refer to a very recent extensive review (page 4, paragraph 1).

Reviewer 2:

This is a very well-written, comprehensive review and the authors should be congratulated for their efforts. My only comment to the authors is if they would be kind enough to provide limitations in the use of extracellular vesicles.

Response:

The limitations of current EV assessment are now introduced in more detail as suggested (page 5, paragraph 1) and clearly stated in the brief conclusion section (page 16).

Reviewer 3:

The authors reviewed about the functional roles of extracellular vesicles (EV) on vascular inflammation in kidney disease (in particular renal vasculitis) and atherosclerosis. Although the review is vast, I recommend to put in perspective a very recent review about the EVs in renal diseases (Erdbügger U & Le TH, JASN 2015). Besides the analysis of the circulating EVs, the analysis of urinary EVs may serve as a novel diagnostic approach for different clinical renal syndromes, including AKI and glomerular and tubular diseases.

Response:

We have now included the new review by Erdbügger et al. that also summarizes current knowledge on urinary EV (page 6, paragraph 2). While this is an interesting diagnostic approach, our manuscript focuses on vascular functional consequences of EV as stated by the reviewer.

Although there is a clear association between EVs and vascular inflammation in kidney disease and atherosclerosis, I suggest the authors to highlight at the concluding remarks section, the need of newer detection techniques, the establishment of a methodologic and nomenclature consensus and a clearer understanding of the composition of the EVs (Witwer KW et al J Extracell Vesicles 2013; 2:20360; Yáñez-Mó M et al. J Extracell Vesicles 2015; 4:27066).

Response: The limitations of current EV assessment are now introduced in more detail with both references as suggested (page 5, paragraph 1) and the recent comprehensive overview by Yáñez-Mó inserted as a reference also in the introduction (page 4, paragraph 1). The limitations of EV research are also clearly stated in the brief conclusion section (page 16).

Replace "Classification of EV" by Characterization of EV.

Response: The wording of the title was changed as requested.