The Journal of Physiology

Extracellular vesicles - markers and mediators of pregnancy complications: gestational diabetes, pre-eclampsia, preterm birth and fetal growth restriction

Rachel Farrelly, Margeurite Gina Kennedy, Rebecca Spencer, and Karen Forbes
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The referees have opted to remain anonymous.

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Dear Ms Farrelly,

Re: JP-TR-2022-282849 "Extracellular vesicles - markers and mediators of pregnancy complications: macrosomia, pre-eclampsia, preterm birth and fetal growth restriction" by Rachel Mary Farrelly, Margeurite Mary Kennedy, Rebecca Spencer, and Karen Forbes

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Yours sincerely,

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EDITOR COMMENTS

Reviewing Editor:

The authors state that most of the work presented here focuses on small EVs. To be complete please include a section about larger EVs (microvesicles) as they contain different cargo and likely have different functions. Also, please explain if small EVs are more relevant than other EVs in common, non-obstetric conditions - cancer, heart disease, inflammation, etc.

REFEREE COMMENTS

Referee #1:

In this paper, Farrelly et al. review the biology of extracellular vesicles (EVs) in common obstetric complications - preterm birth, fetal growth restriction, preeclampsia, and gestational diabetes. The primary findings they review are: 1) maternal EVs induce placental dysfunction in gestational diabetes cases; 2) placental EVs cause increased blood pressure in preeclampsia cases; 3) circulating EVs play a role in the initiation of labor at term; 4) the number of circulating placental EVs is reduced in the first/second trimesters in preterm birth cases; and 5) the ratio of placental-to-total EVs is reduced in cases of fetal growth restriction. The findings the authors review are derived from mouse and human studies.

The paper is written well - easy to understand and comprehensive for EV studies in regard to obstetrical outcomes. The figures are helpful. The question to be considered is whether the Journal of Physiology is the appropriate forum for this paper. The background data ("Introduction" and "The Placenta") review basic information that is known by reproductive biologists, while the background sections on EVs and EV cargo will already be known by other investigators studying EVs. Interestingly, the authors state that most of the work presented here focuses on small EVs, but they do not explain if small EVs are more relevant than other EVs in common, non-obstetric conditions - cancer, heart disease, inflammation, etc.

The strength of the paper is the compilation of data regarding EVs in relation to the four obstetric complications. I believe the data are comprehensive through most of 2022, and I believe this review paper may inspire additional research in these areas. The paper is likely to be cited frequently.

Referee #2:

Nicely written review that covers the basics well.

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Referee #2:
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Responses
I would like to thank the two reviewers for their kind words. All suggested changes have been included. They can be found highlighted within the highlighted manuscript.

Rachel F

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Reviewing Editor:

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