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REVIEW | EXTRACELLULAR VESICLES

Advances in therapeutic applications of extracellular vesicles

Oscar P. B. Wiklander[1,2,*], Meadhbh Á. Brennan[3,4,5], Jan Lötvall[6], Xandra O. Breakefield[4] and Samir EL Andaloussi[1,2,*]

+ See all authors and affiliations

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RE: Amniotic Exosomes and Pregnancy

Pascal J. Goldschmidt-Clermont, Co-Founder of REGENiSELF, REGENiSELF

Other Contributors:
Darcy L. DiFede, Chief Operating Officer of REGENiSELF, REGENiSELF

Ian A. White, Chief Scientific Officer, REGENiSELF

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In their article, Advances in therapeutic applications of extracellular vesicles, Wiklander et al. provide an instructive review of recent progress made in the field of extracellular vesicles (EVs), and exosomes in particular, they concluded “EVs act as important mediators of intercellular communication that influence both physiological and pathological conditions”. With this e-letter, we provide an example of the formidable role of extracellular vesicles in human biology: the case of pregnancy.

One physiological condition where extracellular vesicles are essential is pregnancy (1). The growth of the human embryo/fetus, in the womb is one of the most rapid situations of tissue growth for humans. It is likely that such growth is facilitated through the paracrine impact

of amniosomes, considering the need for massive amounts of information and basic materials (lipids, proteins, complex sugars, nucleic acids, etc.) required to generate a mature human fetus. Actually, the concentration of amniosomes in the amniotic fluid has been reproducibly assessed at 250 billion exosomes per milliliter (1), thus, perhaps, amniotic fluid might be the most exosome rich fluid within the human body.

It is highly likely that the pregnant mother is also heavily impacted by amniosomes. Amniosomes are small enough (150 nm or less) to pass through the placental barrier. The heart of pregnant women undergoes formidable transformation during pregnancy (2). The stroke volume for a heart (the amount of blood pushed into the circulation by each heart beat) is, perhaps, the most critical measure of cadiac performance. Instructively, the stroke volume of the heart of a woman at the end of the fifth month of pregnancy, and thereafter, is equivalent to that of a competition super-athlete (swimmer or runner) (3,4). However, the heart rate of a pregnant woman is about twice that of a super-athlete at rest (3,4), meaning that at baseline the heart of a pregnant woman is producing a massive amount of work compared to non-pregnant humans. It's difficult to reconcile such cardiac transformation within the context of our current knowledge of heart physiology, and it is tempting to speculate that amniosomes, rich in pro-growth proteins, microRNAs and cellular nutrients, could contribute to this transformation in a substantial, and yet unrecognized, way.

Preeclampsia is a hypertensive condition that affects woman in late stages of pregnancy exclusively, and impacts 7% of all pregnancies (5). As the leading cause of fetal and maternal morbidity and mortality worldwide, the only treatment for preeclampsia is urgent delivery of the baby. Amniosomes have been shown to be abnormal in preeclampsia, and thus such abnormal amniosomes could contribute to this condition (5). The mother can be affected also in a pregnancy specific fashion with other conditions like peri-partum cardiomyopathy (PPCM) and post-partum depression. These conditions too could be secondary to a specific deficit for certain species of amniosomes, a deficiency that we named Amniosome Deficiency Syndromes (ADS). A novel homologous-use therapy could involve the administration of allogeneic amniosomes harvested from normal pregnancies to pregnant women diagnosed with an ADS as in PPCM. While PPCM may be a rather rare form of exhaustion of the specific amniosomes required for cardiac performance during pregnancy, there might be a more generalized role for amniosomes in many cases of human cardiomyopathies. And this novel approach could be a significant application of "EVs…as potential therapeutic agents" as suggested by Wiklander et al.

By: Pascal J. Goldschmidt-Clermont, Darcy DiFede, Ian A. White
Regeniself, University of Miami Life Science and Technology Park, 1951 NW 7th Avenue, Miami, Florida 33136.

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Competing Interests: The company REGENiSELF is focused on the science of Stem Cell and Extracellular Vesicles for the prevention and treatment of human illnesses.