EXTRACELLULAR VESICLES (EV) SIZE IN SHALLOW TROPHOBLAST INVASION IN OLD WORLD NON-HUMAN PRIMATES

Marcel Chuecos, BS[1], Edward Dick[2], Gene Hubbard[3], Cathy Perez[2], Soumyalekshmi Nair[4], Carlos Palma[4], Vyjayanthi Kinhal[4], Carlos Salomon[4] and Natalia Shlabritz-Loutsevitch, MD, PhD[1].

[1]OB/GYN - Research, TTUHSC-Permian Basin, Odessa, Texas, United States. [2]Southwest National Primate Center, Texas Biomedical Research Institute, San Antonio, Texas, USA . [3]University of Texas Health Sciences Center at San Antonio, San Antonio, Texas, USA. [4]Exosome Biology Laboratory, Centre for Clinical Diagnostics, University of Queensland Centre for Clinical Research, Royal Brisbane and Women's Hospital, The University of Queensland, Brisbane, QLD, Australia. [5]Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, Ochsner Clinic Foundation, New Orleans, Louisiana USA; Department of Clinical Biochemistry and Immunology, Faculty of Pharmacy, University of Concepción, Concepción, Chile

natalia.schlabritz-lutsevich@ttuhsc.edu

Introduction

Extracellular vesicles are playing a critical role in pathophysiological responses. Pregnancy-related changes in extracellular vesicles (EV) compositions, and the presence of trophoblast debris in maternal tissues, are well described in human normal and pathological pregnancies. Extracellular vesicles, including exosomes are playing a critical role in cell-to-cell and organ communication However, the concentration of circulating vesicles in baboons, which is a model to study pregnancy-related physiology, has not been established yet.

Objective

We previously suggested the absence of the trophoblast debris in the maternal circulation in baboon (*Papio spp.)* (SRI, March 2012, San Diego, CA, USA), based on the evaluation of the available lung samples from the pregnant animals. It was proposed that shallow trophoblast invasion in *Papio spp*. (as compared to human placentation) does not result the trophoblast shedding. We further analyzed placental samples from the stillbirths in the baboons and in humans and found, that syncytiotrophoblast thickness is decreased in the placenta from the stillborn baboons, similar to the finding in humans.

Materials and Methods

We evaluated plasma from three non-pregnant, four pregnant, and one fetal baboon at 130-165 days of gestation. The total numbers of EV were quantified by nanoparticle tracking analysis (NTA). The different population of vesicles was determined based in their size and classified as <50, 50-150, 150-200 and >200nm. Additionally, we performed the analyses of microphotographs, obtained from baboon placenta at the end of gestation, which were originally analyzed in Placenta 2009 Sep;30(9):752-60. In approximately 80 microphotographs the intervillous space and fetal capillaries were identified and examined for the presence of the extracellular vesicles, which in turn were measured using Image-Pro Premier 9.3 program. The largest diameters are reported.

Results and Discussion

The total concentration of EVs was ~8-fold higher in the peripheral circulation in maternal compared with fetal plasma. EVs <50 nm were not present in the peripheral circulation of the non-pregnant animals. Concentrations of EV of 50-150nm and >200 nm were approximately two times higher in pregnant compared to the non-pregnant animals, with no difference in the concentration 150-200mn.

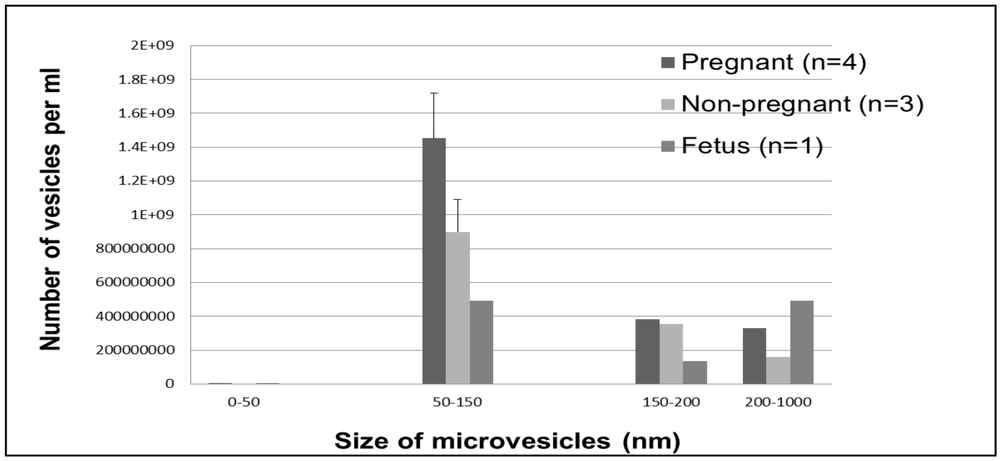

Figure 1. Serum extracellular vesicles distribution in baboons (*Papio spp.*) : non-pregnant female (n=3), pregnant females (n=4) and fetus at term.

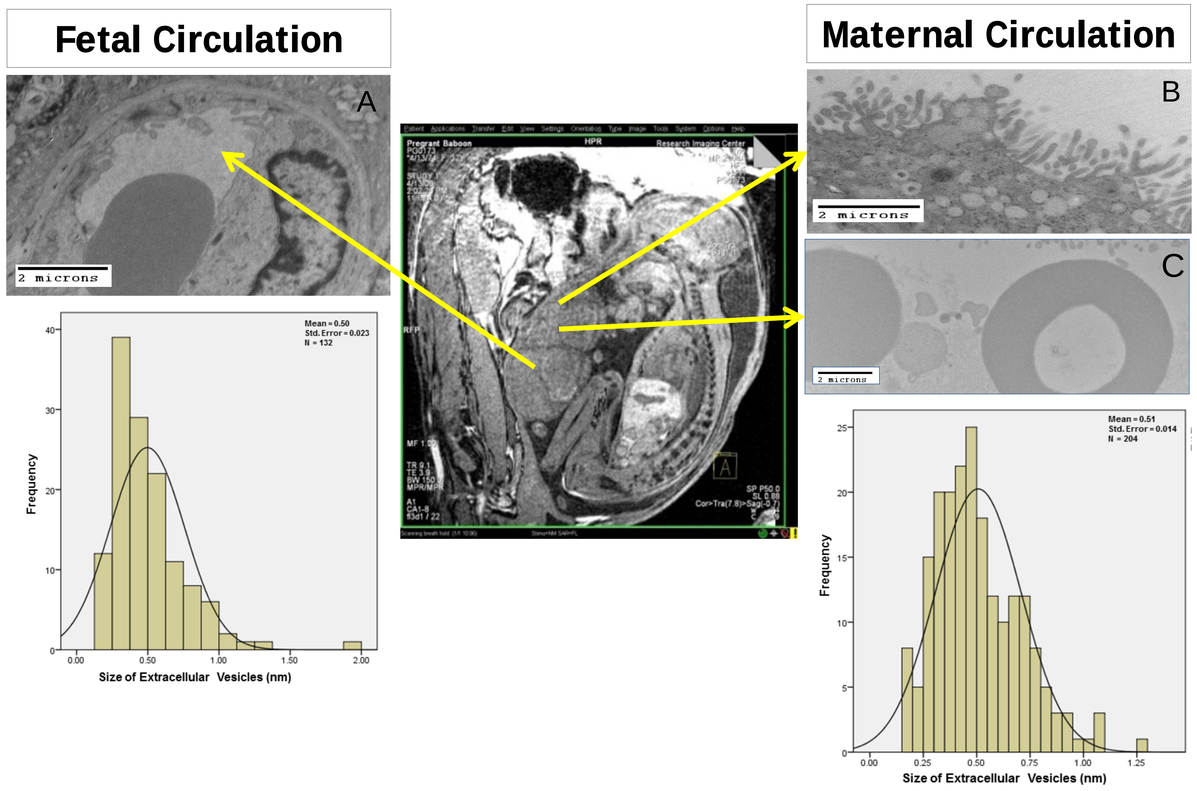

Figure 2. Extracellular vesicles size distribution in fetal placental capillaries (A), intervillous space (B), and maternal placental capillaries (C), determined by evaluation of electron microscopy images (n=80).

Discussion

The comparison of the numbers of exosomes in the peripheral circulation revealed some differences, despite similar in both species increase in pregnant compared to the non-pregnant females concentrations of EV. However, the number of the exosomes in baboons per ml of serum was 1000 times lower, compared to humans. While the differences of concentrations of exosomes between pregnant and non-pregnant women were in the magnitude of 50 times while in the baboons in our study was 2. Interestingly, the number of exosomes dramatically increased in pre-eclampsia, the pathology, which has not been documented in Papio spp. The mechanisms, leading to placental shedding in *Papio spp.* remain to be elucidated.

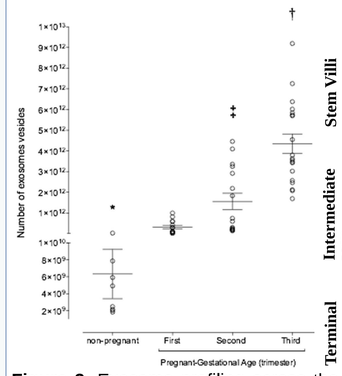

Figure 3. Exosome profiling across the pregnancy. Number of exosomes across the pregnancy. Data are presented as aligned dot plot and values are mean ± SEM.

Extracted from: C. Salomon, *et al.* A gestational profile of placental exosomes in maternal plasma and their effects on endothelial cell migration PLoS One, 9 (2014), p. e98667.

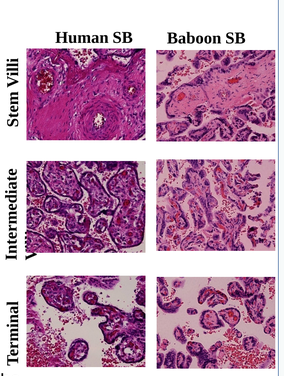

Figure 4. Comparable histology of human and baboon placentas.

Extracted from: The Syncytiotrophoblast (ST) Volume Is Critical for Human, but Not Non- Human Primates (NHP) Stillbirths (SB) at Term. SRI meeting, 2012).

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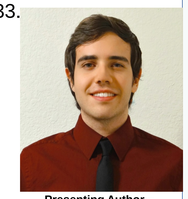

Presenting Author – Marcel Chuecos