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ISEV2021 Abstract Book

About ISEV

The International Society for Extracellular Vesicles is the leading professional society for researchers and scientists involved in the study of microvesicles and exosomes. With nearly 1,000 members, ISEV continues to be the leader in advancing the study of extracellular vesicles. Founded in 2012 in Sweden, ISEV has since moved its Headquarters to the United States. Through its programs and services, ISEV provides essential training and research opportunities for those involved in exosome and microvesicle research.

Mission Statement

Advancing extracellular vesicle research globally.

Vision

Our vision is to be the leading advocate and guide of extracellular vesicle research and to advance the understanding of extracellular vesicle biology.

ISEV2021 Annual Meeting

The International Society for Extracellular Vesicles is the is the premier international conference of extracellular vesicle research, covering the latest in exosomes, microvesicles and more. With an anticipated 1,000 attendees, ISEV2021 will feature presentations from the top researchers in the field, as well as providing opportunities for talks from students and early career researchers.

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PS19.14 | Tumor-derived microRNA-378a-3p-containing extracellular vesicles induce osteoclastogenesis by activating Dyrk1a/Nfatc1/Angptl2 axis to promote the metastasis of prostate cancer

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Introduction: The majority of the deaths of prostate cancer (PCa) are caused by progression to bone metastatic PCa. The importance of extracellular vesicles (EVs) in the formation of the pre-metastatic niche has been demonstrated in recent years. However, whether and how tumor-derived EVs interact with pre-osteoclasts to release EV-delivered microRNAs to activate pre-metastatic niche formation and prostate cancer bone metastasis remain unclear.
Methods: Bioinformatics and qRT-PCR analyses were used to screen and identify the expression of miR-378a-3p in both serum and tissue derived EVs from primary or metastatic PCa patients. Biological function assay studies in vitro and in vivo were implemented to identify the functions of miR-378a-3p during PCa progression. Dual-luciferase reporter assay, co-IP assay, western blot assay, IF staining, RIP and ChIP assays were conducted to investigate the underlying mechanism.
Results: We found that EV-mediated release of miR-378a-3p from tumor cells is upregulated in bone-metastatic PCa for maintenance of a low intercellular concentration of miR-378a-3p to promote proliferation and anti-apoptosis of PCa cells and a MAOA-mediated epithelial-to-mesenchymal transition (EMT) for migration as well. Furthermore, we demonstrated that the enrichment of miR-378a-3p in tumor delivered EVs was induced by overexpression of hnRNPA2B1, a RNA binding protein, as a transfer chaperone. After miR-378a-3p enriched EVs was absorbed by pre-osteoclasts, elevated intercellular concentration of miR-378a-3p in pre-osteoclasts promotes osteoclastogenesis by targeting Dyrk1a/Nfatc1 signaling pathway. Moreover, inhibition of Dyrk1a by miR-378a-3p attenuated its sequestration to Nfatc1 so that the nuclear translocation of Nfatc1 was increased to promote expression of the downstream target gene Angptl2. As a feedback, increased secret of Angptl2 into the environment was found to be capable to improve PCa progression.
Summary/Conclusion: Our findings indicate that tumor-derived miR-378a-3p-containing EVs plays a significant role in promoting prostate cancer bone metastasis by activating Dyrk1a/Nfatc1/Angptl2 axis in pre-osteoclasts to induce osteoclastogenesis, which implicates that miR-378a-3p may be a potential predictor of metastatic PCa. Moreover, reducing the release of miR-378a-3p-containing EVs or blocking the function of miR-378a-3p in pre-osteoclasts might be a potential therapeutic strategy for PCa metastasis.

PS20 | EVs and Our Non-Human Friends

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PS20.01 | Comparative proteome profiling in exosomes derived from porcine colostrum versus mature milk

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Introduction: Colostrum and milk have high nutritional value and provide a complete diet for neonates, along with bioactive substances which modulate various functions such as immune defense. The mechanisms by which milk components can prime the infant's active immunity are not entirely clear, and EVs are suggested to be essential for the infant's physiological development.
Methods: We assessed the exosomal proteome profile from milk samples obtained from 10 healthy sows, at day 0 (colostrum), day 7, and 14 post partum. Exosomes were isolated by ultracentrifugation coupled with size exclusion chromatography, and were characterized by nanoparticle tracking analysis, transmission electron microscopy and Western blotting for exosome markers. Isolated exosomes were in-gel digested and after TMT-labelling of the peptides, they were subjected to LC-MS/MS. The statistical analyses were performed in R using an in-house developed workflow. Non-unique peptides, single-hit proteins, and fractions with low intensity per protein were filtered out. The data were transformed and normalized using the VSN package and then aggregated to protein-level by Tukey's median polish procedure. The P-values were adjusted for multiple testing by Benjamini-Hochberg method.
Results: After exclusion criteria were applied, a total of 319 proteins in each timepoint were statistically analyzed. Exosomes from colostrum presented 162 differentially abundant proteins (DAP) (82 increased and 80 decreased) as compared to exosomes from milk at day 7, and 170 DAP (81 increased and 89 decreased) from milk at day 14, respectively. Comparison between milk exosomes at day 7 and day 14 showed no DAP. The DAP identified were related to biological functions such as uptake of metabolites, regulation of hemostasis and cellular development.
Summary/Conclusion: Colostral exosomes have different proteome profiles than exosomes from mature milk, with significance not only for the physiological understanding of EV's impact on the interaction between mother and newborn, but also for the prospective use of supplements with high economic potential such as milk and colostrum replacers.

PS20.02 | Comparison of extracellular vesicles and proteins as a source of small RNA biomarkers in canine urine

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Introduction: Urinary extracellular vesicles (EVs) and their RNA cargo are a novel source of biomarkers, however non-vesicular RNA is also present within urine. Here, we compared the small RNA profiles of the EV and protein fractions of canine urine, to determine their potential as a source of small RNA biomarkers.
Methods: EV and protein fractions were obtained by size-exclusion chromatography (SEC) of 0.22μm filtered urine from five healthy control (HC) dogs and five dogs with urinary tract infections (UTI). RNA from both fractions was analysed using the Agilent Bioanalyzer small RNA chip and small RNA sequencing. The raw sequences were compared to examine the fraction-specific profiles. EV and protein fractions from HC and UTI samples were compared to identify differentially expressed sequences.
Results: In HC samples, the protein fractions included more small RNA compared to EV fractions (30.4-307.2 vs 2.6-20.3 ng/ml of starting urine, respectively). After sequencing, 11000–20000 and 17000–73000 different raw sequences (>5 copies) were identified from the HC protein and EV fractions respectively, 700–5000 of which were shared. When UTI samples were compared to HC, no sequences were differentially expressed in the EV fractions (adjusted p-value < 0.05) and 172 were differentially expressed in protein fractions. Principle component analysis separated the UTI and HC groups based on the small RNA profiles of the protein fractions, but not based on the small RNA profiles of EV fractions.
Summary/Conclusion: EV and protein fractions obtained after SEC of 0.22 um filtered dog urine have distinct small RNA profiles. When HC and UTI samples were compared, differentially expressed RNA sequences were identified in the protein fractions, but no significant differences in the EV fractions were demonstrated. These results suggest that UTI does not lead to changes in the small RNA profile of small EVs in urine.