culture experiments. Then, we preliminarily validated exosomal miRNAs in 2 serum sample sets (25 healthy controls and 22 lung cancer patients) by quantitative real-time RT–PCR. Every research subject signed a prior informed consent that was approved by the Human Research Ethics Committee from Southern Medical University.
Results: The small RNA profile of exosomes was changed following EMT. Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analysis revealed that the specific miRNA profile of M-exosomes has the potential to drive signal transduction networks in EMT and cancer progression. Co-culture experiments confirmed that M-exosomes can enter epithelial cells and promote migration, invasion and expression of mesenchymal markers in recipient cells. Exosomal miR-7a, miR-21 and miR-320 expression levels in serum were significantly increased in patients with lung cancer as compared with healthy individuals.
Conclusion: Our research has provided a new insight into the role of exosomes produced by mesenchymal cells, the specifically expressed miRNA in which was associated with the function of EMT and metastasis, and may promote transfer of the malignant phenotype (mesenchymal phenotype) to epithelial recipient cells. These miRNAs differently expressed between healthy individuals and lung cancer patients, and may serve as source of new biomarkers in lung cancer.

PT10.08

Quantitative proteomics of exosome derived from isogenic metastatic and non-metastatic breast cancer in mouse model reveal differential expression of intravasation factors

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Introduction: Breast cancer is a malignant carcinoma which metastasises anywhere in body but mainly metastasises to bone, lungs, regional lymph nodes, liver and brain. The spread of cancer usually happens through following steps. Firstly, cancer cells invade nearby healthy cells, and the cancer cells penetrate into the circulatory or lymph system, this is called as intravasation.
To investigate physiological roles of exomes in the breast cancer metastasis, it is crucial to reveal the key factor of intravasation from exosomal proteins. Previous studies showed that exosome is significant in metastasis.
Methods: We studied two isogenic breast tumour cell lines, highly metastatic 4T1 and nonmetastatic 67NR, to identify differences in the exosomal proteins. To isolate exosome in *in vivo* environment, 4T1 cells and 67NR cells were injected to BAlB/c mice. Primary cells from the induced tumours by 4T1 and 67NR were isolated and subcultured. The cultured cell media from primary cell cultures were used for exosome isolation by size exclusion chromatography.
We performed quantitative proteomic analysis of prepared exosomes derived from breast cancer in mouse model using isobaric tag based tandem mass tag (TMT) and liquid chromatography coupled with tandem mass spectrometry (LC-MS/MS).
Results: We identified 1254 exosomal proteins and significantly 53 up-regulated proteins and 93 significantly down-regulated proteins in exosomes from 4T1 ($p < 0.05$). Interestingly, migration related pathways and factors are specifically up regulated in exosomes from 4T1. These results suggest that migration factors from exosomes play critical roles in intravasation through specific migration pathways.
Conclusion: Taken together, our exosomal proteome analyses showed key factors of intravasation were enriched in exosomes isolated from metastatic breast cancer.

PT10.09

Tumour exosome-mediated promotion of adhesion to mesothelial cells in gastric cancer cells

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Introduction: Peritoneal metastasis consists of a highly complex series of steps, and the details of the underlying molecular mechanism remain largely unclear. In this study, the effects of tumour-derived exosomes (TEX) on the progression of gastric cancers were investigated in peritoneal metastasis.
Methods: TEX were extracted from cell-conditioned medium by ultracentrifugation. The effects of TEX on the malignant potential of gastric cancer were investigated in adhesion, invasion, and proliferation assays. PCR array as well as western blotting were performed to determine the underlying molecular mechanisms. The molecular changes in mesothelial cell after internalisation of TEX derived from malignant pleural effusion were also con rmed.
Results: TEX were internalised in both mesothelial and gastric cancer cells in a cellular origin non-speci c manner. Internalisation of TEX into mesothelial cells promoted signi cant adhesion between mesothelial and gastric cancer cells, and TEX internalisation into gastric cancer cells signi cantly promoted migratory ability, while internalisation of mesothelial cell-derived exosomes did not. Expression of adhesion- related molecules, such as bronectin 1 (FN1) and laminin gamma 1 (LAMC1), were increased in mesothelial cells after internalisation of TEX from gastric cancer cell line and malignant pleural effusion.
Conclusion: TEX may play a critical role in the development of peritoneal metastasis of gastric cancer, which may be partially due to inducing increased expression of adhesion molecules in mesothelial cells.

PT10.10

Tumour microenvironment affects the composition of endothelial cell-derived extracellular vesicles: impact in tumour progression

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The tumour microenvironment plays a crucial role in the progression of tumour growth and metastasis by deregulating various physiological processes including angiogenesis and inflammation. Several studies have previously demonstrated that tumour-derived extracellular vesicles (EVs) are actively involved in the mediation of tumorigenesis by "reprogramming" target cells (e.g. endothelial cells (ECs)) through transfer of pro-angiogenic microRNAs. But the function of EVs released by target cells is poorly studied. Consequently, we sought to determine the composition of EVs released by ECs under tumour microenvironment, and to assess whether these vesicles present different functional properties. Using RNA-seq approaches, we demonstrated that EVs released by ECs in tumour microenvironment context present a specific repertory of microRNAs associated to tumour angiogenesis and inflammatory pathways. Interestingly, some of the dysregulated microRNAs are differently expressed at the cellular and exosomal levels. Furthermore, we showed that these vesicles were able to deregulate angiogenesis pathway by transferring several dysregulated microRNAs to target cells. Currently, we are identifying the molecular targets and pathways modulated by EC-derived EVs under tumour microenvironment.

PT10.11

A role of exosomal miR-10a in bone marrow stromal cells obtained from patients with multiple myeloma

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