P072-T | Artificial microvesicles from human cells: production, biological properties and potential therapeutic use

A. Rizvanov; M. Zhuravleva; L. Tazetdinova; V. Vorobev; S. Kletukhina; S. Kurbangaleeva; O. Neustroeva; M. Gomzikova
Kazan Federal University, Kazan, Russian Federation

Background: The risk of oncological transformation and tumor growth associated with stem cell therapy led to the development of a concept of cell-free therapy, the most promising tool of which are microvesicles – membrane vesicles shed from the cell surface. The main obstacle to the development of pharmaceutical drugs based on microvesicles is limited yield. Here we used the method of cytochalasin B treatment of human cells to increase generation of microvesicles. The purpose of our work was to characterize and evaluate the biological activity of cytochalasin-B-induced microvesicles, or artificial microvesicles (CIMVs), on mesenchymal stem cells (MSC).

Materials and methods: The size of CIMVs was characterized by scanning electron microscopy (SEM, Merlin Carl Zeiss). The angiogenic activity of CIMVs was evaluated by subcutaneous injection in the mixture with Matrigel in Rattus norvegicus. Histological examination of Matrigel implants was conducted 8 days after transplantation.

Results: We found that the size of CIMVs MSC vary from 100 nm to 2600 nm with a peak in the region of 200–1000 nm. After subcutaneous injection in the mixture with Matrigel in vivo CIMVs induced sprouting of $3{\cdot}84 \pm 0{\cdot}16$ blood vessels per mm^2, whereas in negative control (subcutaneous injection of Matrigel) was $0{\cdot}67 \pm 0{\cdot}15$ vessels per mm^2. CIMVs statistically significant (value $P < 0{\cdot}01$) stimulated sprouting of blood capillaries 5·7 times higher than the control sample.

Conclusions: We established that the size of obtained CIMVs is comparable with the size of natural microvesicles. Observed angiogenic activity of CIMVs confirms the perspective of therapeutic application of CIMVs derived from stem and progenitor cells. Pretreating of cells by cytochalasin B increases the yield of CIMVs and makes them perspective pharmaceutic drug.

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P001-F | Redox status of a metastatic microenvironment in the liver of patients with colorectal cancer

K. Usachev*; A.P. Burlaka†; A.A. Burlaka‡; A.V. Vovk†; I.I. Ganusevich†; S. Lukin†,§; S.V. Virko†; K. Iskhakova*; M. Gafurov*
**Kazan Federal University, Kazan, Russian Federation; †R.E. Kavetsky Institute of Experimental Pathology, Oncology and Radiobiology, NAS of Ukraine, Kyiv 03022, Ukraine, Kyiv, Ukraine; ‡Ukrainian National Cancer Institute, Kyiv, Ukraine; §V.E. Lashkaryov Institute of Semiconductor Physics NAS of Ukraine, Kyiv, Ukraine*

Background: Defects in the mitochondrial electron transport chain (ETC) are considered as the major players in tumorigenesis. Redox state of liver tissues (LT) after the surgery treatment of patients with colorectal cancer (CRC) around the metastasis (Mts) was studied.

Material and methods: LT adjacent to Mts and remote species (5 cm from Mts) from 25 patients with metachronous liver metastases were studied by electron paramagnetic resonance (EPR) with spin-trapping for quantification of the activity of N2 iron-sulfur proteins, levels of NO-N2 complexes, labile iron pool (LIP), lactoferrin (LF), superoxide and NO radicals. Activity of metalloproteinase MMP-2 and MMP-9 were determined by the polyacrylamide gel electrophoresis.

Results: In adjacent and remote LT low activity of N2 in ETC (EPR signal with $g = 1{\cdot}94$), loss of functions of detoxification system (cytochrome P-450, $g = 2{\cdot}25$), appearance and growth of NO-N2 complexes ($g = 2{\cdot}007$) are obtained. Intensive EPR signals from LIP ($g = 2{\cdot}2$–$2{\cdot}4$) and LF ($g = 4{\cdot}3$) are registered. Superoxide generation rates are of up to 5 times higher than in the reference material. NO levels are of 1·7 times higher for the adjacent LT. Activity of MMP-2 and MMP-9 was registered both in adjacent and remote tissues while be higher in 1·7–2·0 times in the adjacent LT.

Conclusions: Formation of the Mts microenvironment in liver is accompanied by superoxide and NO activation of MMP, by the remodeling of the extracellular matrix as well as by the accumulation of LIP and increase of level of LF. Our findings can be used to estimate the functional state of LT with distant metastasis.

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