EFFECTS OF MELANOMA DERIVED EXOSOMES ON PERITUMORAL STROMAL CELLS

Tünde Buknicz¹, Barbara Gubán¹, Beáta S. Bolla¹, Krisztina Buzás^{2,3},
Mária Harmati², Árpád Bálint², Péter Horváth², Zsuzsanna Bata-Csörgő¹, Lajos Kemény^{1,4}, István Németh¹

1 Department of Dermatology and Allergology, University of Szeged, Szeged, Hungary

2 Biological Research Center, Institute of Biochemistry

3 Faculty of Dentistry, University of Szeged, Hungary

4 MTA-SZTE Dermatological Research Group, University of Szeged, Szeged, Hungary

BACKGROUND AND AIMS

Recently great attention is given to the role of tumor-stroma interactions mediated by melanoma derived exosomes as well as to their interaction with peritumoral stromal cells for tumor supporting microenvironment.^(1,2) Therefore we aimed to investigate the effects of human melanoma-derived exosomes on peritumoral stromal cells and their role in spontaneous cell fusion, previously described by our research group.

MATERIALS AND METHODS

- We used freshly isolated normal human dermal fibroblasts, myofibroblasts and adipose derived mesenchymal stem cells (Ad-MSC) for our experiments.
- Exosomes were obtained with differential filtration and ultrafugation.
- To assess proliferation and viability we used xCELLigence system and MTT assay according to the manufacturer's protocol.
- Wound healing model was performed to assess migratory capacity of cells.
- Immunofluorescent staining was performed with monoclonal mouse anti-human smooth muscle actin (SMA) antibody, samples were examined in epifluorescent microscope.

RESULTS

Melanoma-derived exosomes increase cell index

Melanoma-derived exosomes increase migratory capacity

Average speed [micrometer/minute]

Average angle direction from origin [degree]

Melanoma-derived exosomes enhance SMA expression

Melanoma-derived exosomes attenuate metabolic activity of cells

Melanoma-derived exosomes did not influence spontaneous cell fusion rate

SUMMARY

Based on our results we conclude that melanoma-derived exosomes can influence normal stromal cells. They affect the functions of normal stromal cells, their proliferation, viability, and may convert them into cells that provide a tumor promoting niche. However, in this experimental setup exosome treatment did not have a significant effect on spontaneous cell fusion rate. Further investigations are needed to study the viability of parental cells as well as of spontaneous hybrids by different exosome treatments.

REFERENCES

1. David W. Greening, Shashi K. Gopal, Rong Xu, Richard J. Simpson, Weisan Chen: Exosomes and their roles in immune regulation and cancer. <https://doi.org/10.1016/j.semcd.2015.02.009>
2. Joshua L. Hood, Roman Susana San, Samuel A. Wickline: Exosomes Released by Melanoma Cells Prepare Sentinel Lymph Nodes for Tumor Metastasis. DOI: 10.1158/0008-5472.CAN-10-4455 Published June 2011
3. Lajos V. Kemény, Zsuzsanna Kurgys, Hilda Pólyánka, Thomas Dittmar, Lajos Kemény, István B. Németh: Melanoma cells can adopt the phenotype of stromal fibroblasts by spontaneous cell fusion. 44th ESDR meeting Copenhagen, oral 003. (2014)

ACKNOWLEDGEMENTS

Renáta Bozó, Monika Kohajda and Zsuzsanna Palotás for technical assistance. This study was supported by scholarship of Bolyai, Hungarian Academy of Sciences. Email: buknicztunde@gmail.com

The project is supported by the European Union and co-financed by the European Social Fund.