

## The development of biosafety tool for stimulating angiogenesis based on microvesicles from cells with enhanced ability to stimulate angiogenesis

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To date, ischemic disease represents one of the major problems of modern medicine. We offer an effective and safe tool for clinical applications - artificial microvesicules from cells that can promote angiogenesis but could not be used because of high risk of unlimited growth (genetically modified cells, cells after long-term culture *in vitro* or tumor cells).

It is known that the most promising approach for the treatment of ischemic tissue damage is cell therapy with genetically modified cells, with whom therapeutic ability were enhanced. However, the following problem arises: the genetic modification and / or long-term culture of human cells *in vitro* propose the risk of malignant transformation.

In this context, to find ways for secure use of the cells with an increased risk for malignant transformation properties is our aim. For this purpose, as a reliable model, we have used cells that can promote angiogenesis and have risk of unlimited growth - the tumor cells (cell line SH-SY5Y). In our present work we present a strategy to overcome possible risks - production of artificial microvesicules (aMVs). Microvesicles have advantages that make them promising vector system: their bi-lipid structure protects it's cargo; efficient delivery to the cytosol of target cells by process of membrane fusion; they are comprised of natural non-synthetic and non-viral components; microvesicles can be engineered to express a surface receptor for target delivery.

We showed that microvesicles from tumor cells with angiogenic properties are comparable with native cells proangiogenic activity *in vitro* (capillary like tube formation assay on Matrigel) and *in vivo* (subcutaneous injection to *Rattus norvegicus*). This tool is safe and biocompatible as our *in vivo* experiments indicated.