

MOLECULAR CYTOLOGY

Application of carbon nanoparticles in hypericin-mediated photodynamic therapy

supervisor: prof. RNDr. Peter Fedoročko, CSc. (peter.fedorocko@upjs.sk)

consultant: RNDr. Rastislav Jendželovský, PhD. (rastislav.jendzelovsky@upjs.sk)

study form: full time

Annotation: Nanoparticles are increasingly being studied for their interesting properties and potential exploitation in nano-oncology. The effectiveness of some anticancer drugs may be affected by decreased aqueous solubility, poor cell permeability, and high cell efflux. For this reason, various types of nano-drug carriers (e.g. liposomes, polymeric micelles, dendrimers, superparamagnetic iron oxide crystals and colloidal gold) have already been tested in practice to increase drug selectivity and thus minimize the side effects of anti-cancer drugs. A suitable subject in combination with nanoparticles appears to be hypericin, a natural photosensitizer, characterized by high production of oxygen radicals, but due to its hydrophobicity also reduced systemic availability. The aim of the dissertation thesis will be to find out whether the application of carbon-based nanoparticles is safe for a healthy cell and how the use of nanotechnology can influence the amount of hypericin and the effect of photodynamic therapy in tumour cells and micro-tumours.

The main scope of employment will be:

cultivation of cancer cell lines

ex ovo cultivation of *Coturnix japonica* embryos

preparation of solid micro-tumours on CAM

analysis of the nanoparticle effect on chosen parameters of fibroblasts and CAM

analysis of the nanoparticle effect on chosen parameters of cancer cells

identification of nanoparticles ability to bind up in hypericin and influence hypericin transport into the cells

analysis of hypericin content in cancer cell lines and cells and cells of micro-tumors using the methods of flow cytometry and confocal microscopy

analysis of the combination therapy of nanoparticles and photoactivated hypericin on chosen parameters of cancer cells

References:

Sharma K. S., Chiang Y. L., Hamblin R. M. Photodynamic therapy with fullerenes in vivo: reality or a dream? *Nanomedicine* (Lond.), 2011, vol. 6, p. 1813-1825.

Huang Y-Y., Sharma K. S., Dai T., Chung H., Yaroslavsky A., Garcia-Diaz M., Chang J., Chiang Y. L., Hamblin R. M. Can nanotechnology potentiate photodynamic therapy? *Nanotechnology Reviews*, 2012, vol. 1, p. 111-146.

Gurunathan S., Kang M-H., Qasim M., Kim J-H. Nanoparticle-Mediated Combination Therapy: Two-in-One Approach for Cancer. *International Journal of Molecular Sciences*, 2018, vol. 19, 3264, p. 1-37.

Jendželovská Z., Jendželovský R., Kuchárová B., Fedoročko P. Hypericin in the light and in the dark: two sides of the same coin. *Frontiers in Plant Science*, 2016, vol. 7, p. 1-20.

Jendželovský R., Jendželovská Z., Kuchárová B., Fedoročko P. Breast cancer resistance protein is the enemy of hypericin accumulation and toxicity of hypericin-mediated photodynamic therapy. *Biomedicine and Pharmacotherapy*, 2019, 109, p. 2173-2181.

Majerník M., Jendželovský R., Babinčák M., Košuth J., Ševc J., Gombalová T. Z., Jendželovská Z., Buríková M., Fedoročko P. Novel insights into the effect of hyperforin and photodynamic therapy with hypericin on chosen angiogenic factors in colorectal micro-tumors created on chorioallantoic membrane. *International Journal of Molecular Sciences*, 2019, vol. 20, 3004, p. 1-24.

Presensitization of cancer cells by activation of death receptor

supervisor: prof. RNDr. Peter Fedoročko, CSc. (peter.fedorocko@upjs.sk)

consultant: RNDr. Rastislav Jendželovský, PhD. (rastislav.jendzelovsky@upjs.sk)

study form: full time

Annotation: Skyrin is a likely precursor in the synthesis of hypericin. Based on the similarity in the chemical structure, it is believed that, like photoactivated hypericin, it could inhibit tumour cell proliferation and induce cell death. Our preliminary results suggest that, in addition to its antiproliferative activity, skyrin induces DR5 death receptor expression not only under normoxic but also under hypoxic conditions. The aim of the dissertation thesis will therefore be to verify the potential of skyrin to activate the extrinsic apoptosis receptor pathway and to use it in favour of the subsequently applied experimental anti-tumour procedure.

The main scope of employment will be:

cultivation of cancer cell lines

ex ovo cultivation of *Coturnix japonica* embryos

preparation of solid micro-tumours on CAM

analysis of mRNA and protein levels of extrinsic apoptosis death receptor pathway

analysis of the DR5 activation effect on chosen parameters of fibroblasts and CAM

analysis of the combination therapy of DR5 activation and subsequently applied potential anticancer agents (TRAIL, resveratrol, sulforaphane) on cell proliferation and cell death induction of cancer cells and cells from micro-tumors using the methods of flow cytometry and confocal microscopy

References:

Elrod H. A., Sun S. Y. Modulation of death receptors by cancer therapeutic agents. *Cancer Biol Ther*, 2008, vol. 7, p. 163-173.

Koul M., Meena S., Kumar A., Sharma P. R., Singamaneni V., Riyaz-Ul-Hassan S., Hamid A., Chaubey A., Prabhakar A., Gupta P., Singh S. Secondary Metabolites from Endophytic Fungus *Penicillium pinophilum* Induce ROS-Mediated Apoptosis through Mitochondrial Pathway in Pancreatic Cancer Cells. *Planta Medica*, 2016, vol. 82, p. 344-355.

Wang C., Jin Q., Yang S., Zhang D., Wang Q., Li J., Song S., Sun Z., Ni Y., Zhang J., Yin Z. Synthesis and Evaluation of ¹³¹I-Skyrin as a Necrosis Avid Agent for Potential Targeted Radionuclide Therapy of Solid Tumors. *Molecular Pharmaceutics*, 2016, vol. 13, p. 180-189.

Majerník M., Jendželovský R., Babinčák M., Košuth J., Ševc J., Gombalová T. Z., Jendželovská Z., Buríková M., Fedoročko P. Novel insights into the effect of hyperforin and photodynamic therapy with hypericin on chosen angiogenic factors in colorectal micro-tumors created on chorioallantoic membrane. *International Journal of Molecular Sciences*, 2019, vol. 20, 3004, p. 1-24.

Role of extracellular matrix in the formation of microenvironment in the subependymal region of rat spinal cord during the development.

supervisor: doc. RNDr. Zuzana Daxnerová, CSc. (zuzana.daxnerova@upjs.sk)

study form: full time

Annotation: The aim of the study is to uncover the changes in extracellular matrix and its role in subependymal region of rat spinal cord during the perinatal development of CNS using the molecular and ultrastructural methods.