# TOWARD UNDERSTANDING THE INTERPLAY BETWEEN CANCER CELLS TREATED BY AMINOLEVULINIC ACID-PHOTODYNAMIC THERAPY AND IMMUNE CELLS

# B. Čunderlíková<sup>1,3</sup>, K. Klučková<sup>2</sup>, P. Mlkvý<sup>3,4</sup>, T. Teplický<sup>1</sup>

<sup>1</sup>Institute of Medical Physics, Biophysics, Informatics and Telemedicine and <sup>2</sup>Institute of Immunology, Faculty of Medicine, Comenius University, Bratislava, SR <sup>3</sup>International Laser Centre, Slovak Centre of Scientific and Technical Information, Bratislava, SR <sup>4</sup>St. Elisabeth Cancer Institute Hospital, Bratislava, Slovakia

# Introduction

Effective anticancer therapy seems to require stimulation of antitumour immune system [1]. Evidence shows that photodynamic therapy is able to induce immunogenic cell death that activates antitumour immunity. This, however depends on many factors, such as dose, treatment schedule, cancer genetic background, cancer cell death pathway [2,3] as well as potential immune cell modifications induced by factors released by dying cancer cells. The aim of our study was to test capacity of aminolevulinic acid-photodynamic therapy (ALA-PDT) to induce cancer cell death that could lead to activation of immune cells.

#### **Material and Methods**

Effects of ALA-PDT were studied in *in vitro* models utilizing established human cell lines by confocal fluorescence microscopy and ELISA assays. The treatment was applied on cancer cells cultured either under conventional culture conditions or in collagen matrices.

#### Results

Application of ALA-PDT resulted in both death pathway and release of factors from esophageal cancer cells that are consistent with immunogenic cell death. Human macrophages were able to engulf remnants of cancer cells subjected to ALA-PDT under conventional culture conditions. However, when treatment was applied on cellular clusters embedded in collagen matrices, no interactions between cancer cells and macrophages, irrespective of their polarization phenotype, were observed.

#### Conclusion

Our results show capacity of ALA-PDT to induce immunogenic cell death judged by *in vitro* assays and indicate modifying effect of microenvironmental factors on the interplay between cancer cells and immune cells.

This publication was created thanks to support within the Operational Program Integrated Infrastructure for the project: Research and development in medical sciences - the way to personalized treatment of serious neurological, cardiovascular and cancer diseases 313011T431, co-financed from the resources of the European Regional Development Fund and funding from Laserlab-Europe V (European Union's Horizon 2020 research and innovation program under grant agreement no 871124).

# Literature

- Fabian K.P., Wolfwon B., Hodge J.W.: From immunogenic cell death to immunogenic modulation: Select chemotherapy regimens induce a spectrum of immune-enhancing activities in the tumor microenvironment. Front Oncol 11/2021, 728018.
- [2] Zhu M. et al.: Immunogenic cell death induction by ionizing radiation. Front Immunol 12/2021, 705361.
- [3] Vanmeerbeek I., et al.: The interface of tumour-associated macrophages with dying cancer cells in immuno-oncology. Cells 11/2022, 3890.