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## RESEARCH AREA

Regulation of signaling pathways is largely achieved by dynamic chemical modification of proteins. The focus of our research lies on protein modifications through ADP-ribosylation during interaction between tumors and the immune system. As of present, one in six deaths worldwide is still due to malignant tumors. Today's medicine is pinning its best hopes on targeted molecular therapy and immunotherapy to fight cancer. An effective immune response can, indeed, eradicate malignant cells and curb metastasis. However, tumors have a number of processes that inhibit immune cell function. One of the most abundant cells in the tumor stroma are macrophages (Mφ), phagocytes that are part of the innate immune system and also play an important role in directing the adaptive immune response. Paradoxically, their presence in the tumor is usually associated with a poor prognosis, as their interaction with tumor cells results in the acquisition of a phenotype that enhances tumor vascularisation, cancer cell proliferation and resistance to chemotherapy. Both others' and our own preliminary results suggest that protein ADP-ribosylation events are involved in this reprogramming of Mφs. In the laboratory, we are using proteomic methods to identify ADP-ribosylome changes in Mφs as they switch phenotype in association with tumor cells. We are using 2D and 3D tumor cell-Mφ co-culture models to study this. We aim to identify the signaling proteins, transcription factors, metabolic enzymes that undergo modification and the ADP-ribosyltransferase enzymes responsible for their modification. We envision that targeted interference with the identified signaling pathways by manipulating ADP-ribosylation will alter the behavior of tumor Mφs in a favorable direction, which may provide the basis for new cancer therapies.

## TECHNIQUES AVAILABLE IN THE LAB

Conventional 2D and 3D spheroid cell culture. Gene transfer by lentiviral transduction. Gene silencing, genome editing in cell lines using Crispr/Cas9 methodology. Flowcytometry. Respirometry and metabolic analysis. Recombinant DNA techniques, mutagenesis, PCR, RT-qPCR. Recombinant protein expression and protein purification. Immunofluorescence, immunohistochemistry. Confocal microscopy, microirradiation, FRAP. High-content automated microscopy.

## SELECTED PUBLICATIONS

Guti, E., Regdon, Z., Sturniolo, I., Kiss, A., Kovács, K., **Demény, M.**, Szöőr, Á., Vereb, G., Szöllősi, J., Hegedűs, C., Polgár, Z., Virág, L. (2022) The multitargeted receptor tyrosine kinase inhibitor sunitinib induces resistance of HER2 positive breast cancer cells to trastuzumab-mediated ADCC. **Cancer Immunol Immunother** doi: 10.1007/s00262-022-03146-z. Online ahead of print.

**Demény, M,.A.**, Virág, L. (2021) The PARP Enzyme Family and the Hallmarks of Cancer Part 1. Cell Intrinsic Hallmarks. **Cancers 13:** 2042.

**Demény, M,.A.**, Virág, L. (2021)The PARP Enzyme Family and the Hallmarks of Cancer Part 2: Hallmarks Related to Cancer Host Interactions. **Cancers 13:** 2057.

Regdon, Z., **Demény, M,.A.,** Kovács, K., Hajnády, Z., Nagy-Pénzes, M., Bakondi, E., Kiss, A., Hegedűs, C., Virág, L. (2021) High-content screening identifies inhibitors of oxidative stress-induced parthanatos: cytoprotective and anti-inflammatory effects of ciclopirox. **Br J Pharmacol 178:** 1095-1113.

Sharma, R.*, **Demény, M.***, Ambrus, V., Király,, S.B., Kurtán, T., Gatti-Lafranconi, P., Fuxreiter, M. (2019) Specific and Fuzzy Interactions Cooperate in Modulating Protein Half-Life. **J Mol Biol 431:** 1700-1707.