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RESEARCH AREA

The main profile of our research group is to investigate the relationship between oxidative stress and poly-ADP-ribosylation of proteins in different cellular systems and animal models. A common feature of living organisms is the generation of various free radicals and other reactive intermediates from the oxygen consumed during cellular respiration. These oxygen derivatives may have an important cellular regulatory role, but in pathological conditions, such as inflammation, ischemia-reperfusion injuryn (e.g. in myocardial infarction or stroke), their overproduction cannot be counteracted by the antioxidant system and they cause tissue damage. In addition to the peroxidation of lipids and the oxidation of proteins, oxidative damage also leads to DNA breaks, which are mainly recognized by the enzyme poly(ADP-ribose) polymerase-1 (PARP1), which marks DNA breaks with NAD-derived ADP-ribose polymers to initiate DNA repair. Through its role in DNA damage sensing, the enzyme is a survival factor, but when DNA damage is irreparably severe, PARP1 overactivation triggers a poly(ADP-ribose)-dependent cell death pathway termed parthanathos. In addition to this dual role in cell death, PARP1 also has several functions independent of DNA breakage e.g. in transcriptional regulation. ADP-ribosylation by the 17-members of the PARP enzyme family regulates almost all cellular functions. Our research group is working on diverse and multifaceted research projects, including the study of redox balance and the role of PARP enzymes in tissue macrophages, therapeutic resistance of tumor cells, cell death models, inflammatory processes and tumor-host interactions. An integral part of our research program is the identification of molecules with high-throughput screening that interfere with the above processes.

TECHNIQUES AVAILABLE IN THE LAB

The techniques we use cover almost the entire spectrum of biochemistry, cell and molecular biology and pharmacology. Morphological and functional assays for the characterization of cell death, confocal microscopy, gene inactivation, stem cell cultures, tumor cell-immune cell (e.g. natural killer cell, macrophage) cocultures, 3D cell cultures are all part of our repertoire. We are working on reprogramming macrophages and designing and expressing chimera antigen receptors on macrophages to exploit the anti-tumor effects of these cells. We also screen compound libraries to identify potential drug candidates using HTS (high-throughput screening) and imaging-based HCS (high-content screening) technologies.

SELECTED PUBLICATIONS

Garcia,Soriano, F*.,**Virág, L*.,** Jagtap, P., Szabó. E., Mabley, JG., Liaudet, L., Marton, A., Hoyt, DG., Murthy, KG.,Salzman, AL., Southan, GJ., Szabó, C. (2001) Diabetic endothelial dysfunction: the role of poly(ADP-ribose)polymerase activation. **Nat Med. 7:** 108-13.(*shared first authors)

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Kiss, A., Ráduly, A.P., Regdon, Z., Polgár, Z., Tarapcsák, S., Sturniolo, I., El-Hamoly, T., **Virág, L*.,** Hegedűs, C*. (2020) Targeting Nuclear NAD+ Synthesis Inhibits DNA Repair, Impairs Metabolic Adaptation and IncreasesChemosensitivity of U-2OS Osteosarcoma Cells. **Cancers 12:** 1180. (*shared corresponding authors)

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 andanti-inflammatory effects of ciclopirox. **Br J Pharmacol 178:** 1095-1113.