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A persulfide analog of the nitrosothiol SNAP, D-P*, induces apoptotic cell death in Jurkat leukemia T-cells

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Background/Aim: Many studies have reported about the controversial role of hydrogen sulfide (H_2S) in cell survival, proliferation and apoptosis. In the present work, two H_2S -releasing compounds, sodium hydrogen sulfide (NaHS) and D-P*, a novel persulfide analog of the nitrosothiol S-nitroso-N-acetyl-D,L-penicillamine, were selected for evaluation of their antiproliferative and pro-apoptotic potential in Jurkat leukemia T-cells.

Materials and Methods: Jurkat leukemia T-cells were stimulated with phorbol 12-myristate 13- acetate and the calcium ionophore A23187 in the absence or presence of different concentrations of NaHS or D-P* (0.125 – 1 mM). Interleukin-2 (IL-2) production was analyzed by enzyme-linked immunosorbent assay. Proliferation and cell viability were monitored by 2,3-bis-(2-methoxy-4-nitro-5-sulfophenyl)-2H-tetrazolium-5-carboxanilide assay, annexin-V/7-amino-actinomycin D staining and western blot.

Results: Both H2S donors effectively blocked IL-2 synthesis in Jurkat T-cells. In contrast to NaHS, D-P* dramatically reduced proliferation and cell viability of Jurkat T-cells. D-P* induced cleavage of caspase-3/-7, poly (ADP-ribose) polymerase, myeloid cell leukemia-1 and β -catenin. High concentrations of the anti-oxidant N-acetyl-cysteine could completely block programmed cell death.

Conclusion: In contrast to the "classic" H2S donor NaHS, the novel and slow-releasing H2S donor D-P* showed potent antiproliferative and pro-apoptotic activities in Jurkat leukemia T-cells suggesting that D-P* led to an imbalance in the redox system (GSH depletion?) which in turn induced apoptosis.

Biography

Burkhard Kloesch has completed his PhD at the age of 31 years from Karl-Franzens University Graz and postdoctoral studies from General Hospital Graz, Austria and Ludwig Boltzmann Institute for Experimental and Clinical Traumatology in Vienna, Austria. He is the director of the Ludwig Boltzmann Institute for Rheumatology. He has published more than 10 papers in reputed journals and is a member of the Austrian Society of Rheumatology (OEGR).

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