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Development of protective agents against necrotic cell death

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Necrotic cell death leads to severe tissue damage in many clinical conditions. The molecular mechanisms underlying necrosis are poorly elucidated, and no drugs are available for its treatment or prevention. We identified key steps in the molecular pathway of necrosis. Necrosis induced in vitro by various reagents caused an early significant increase in intracellular proteolytic activity. We demonstrated selective inhibition of the necrotic process by specific protease inhibitors both in vitro and in vivo. The results indicate that activation of a protease pathway plays a regulatory key role in necrosis. We identified an additional approach for treatment of necrosis. Humanin (HN) is a 24-residue peptide known for its protective effect against Alzheimer's disease related apoptosis. Recently, peripheral effects of humanin were observed. We have shown that HN derivatives have a protective effect against necrosis. Among the HN derivatives tested, HN17 was the most active against necrosis. HN peptides also induced an elevation of cellular ATP levels in cells challenged with necrosis. Most importantly, we have shown that the anti-necrotic effects of the HN derivatives were enhanced synergistically by combination with anti necrotic or pro-survival agents. Thus, the new strategies may serve as basis for the development of drug therapies for necrosis-related diseases, e.g. traumatic brain injury, stroke, myocardial infarction and other conditions for which no efficient drug-based treatment is currently available.

Biography

Ilana Nathan has completed her PhD at Ben-Gurion University of the Negev, Beer-Sheva, Israel. Visiting Scientist at NCI, NIH, Bethesda, MD. Professor, Department of Clinical Biochemistry, Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer Sheva. Israel. Head of the Hematology Research Laboratory, Soroka University Medical Center, Beer Sheva. Israel. Served as a consultant of biotechnology companies. Delegate of Israel in the Biomedicine and Molecular Sciences domain in the European Organization for Cooperation in the field of Scientific and Technical Research. Published over 90 papers and has 12 patents.

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