Molecular Mechanisms and Biological Role of Eryptosis in Human Health and Disease

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Abstract:

Eryptosis is the programmed death of erythrocytes, a physiological process analogous to the apoptosis of nucleated cells. It plays a crucial role in eliminating defective red blood cells, preventing haemolysis and the consequent release of toxic haemoglobin into the circulation. However, excessive eryptosis can contribute to anaemia and impair microcirculatory functions. Eryptosis has been observed in numerous clinical conditions, including diabetes, chronic kidney disease, haemolytic uraemic syndrome, sickle cell anaemia, thalassaemia, and glucose-6-phosphate dehydrogenase deficiency. However, molecular mechanisms underlying eryptosis are still under investigation. We aimed to study the molecular events of eryptosis by using *in vitro* models of erithrocytes exposed to different xenobiotics. Results suggest that certain xenobiotics trigger eryptosis by inducing critical molecular processes, such as increased membrane permeability to Calcium, activation of caspase and of non-selective cation channels, formation of ceramide, and modulation of some kinases activity. Among these latter, Janus-activated kinase 3, AMP-activated protein kinase, casein kinase 1α, and p38 MAP kinase seemed to be involved. Data suggest that eryptosis is an active and regulated process and it may be pharmacologically controlled for clinical applications. A deeper understanding of the signaling pathways governing eryptosis may open new perspectives for therapeutic interventions in haematological and infectious diseases.

Keywords:

eryptosis, *in vitro* models, cell membranes, intracellular signaling, xenobiotics, programmed erythrocyte death, red blood cells.