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THE IMPORTANCE OF PYROPTOSIS IN CELL PATHOLOGY

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Pyroptosis is an inflammatory form of programmed cell death that usually occurs when intracellular pathogens are recognized in immune cells (Liu et al., 2019). Inflammasomes are innate immune mechanisms that promote inflammation by activating the protease caspase-1. Active caspase-1 induces pyroptosis, a necrotic form of regulated cell death, which facilitates the release of intracellular proinflammatory molecules, including IL-1 family cytokines. The *aim* of the review of our work is to make a scientific search for new reliable information on aging and cell death.

The research was carried out in the specialized laboratory of immunology of reproduction of mammals. The immune status of the cows was determined using the developed immunocard (Yablonskyi & Zhelavskyi, 2014). Immunological studies examined the cellular, humoral, and innate immunity of mammary gland.

Recent studies identified mediators of inflammasome-associated cell death and suggested that inflammasomes induce not only pyroptosis, but also apoptosis. Caspase-1 has the potential to induce pyroptosis and apoptosis in a manner that is dependent on the expression of the pyroptosis mediator gasdermin D. Caspase-1-induced apoptosis is mediated by Bid and caspase-7. Caspase-8 is also activated following the formation of inflammasomes and may induce apoptosis (Zhelavskyi, 2004; Wang at al., 2019). Because inflammasomes contribute to the pathogenesis of inflammatory disorders and host defenses against microbial pathogens, a more detailed understanding of the mechanisms underlying inflammasome-associated cell death may contribute to the development of novel therapeutic strategies for inflammasome-related diseases (Zhang et al., 2019; Zhou et al., 2020). Pyroptosis can be assessed by quantifying released cytoplasmic LDH, visualizing the loss of membrane integrity by fluorescence microscopy, detecting interleukin (IL) -1β, caspase activation, and gasdermin D cleavage by Western blotting (Wu et al., 2021). Neutrophils are located in the peripheral bloodstream only for 6 – 10 hours, and then get into the tissue where they perform their effector function. Priming phagocytic cells are capable of destroying pathogenic agents both in the immediate attack (killing) as well as by absorption and digestion (Jorch & Kubes, 2017). Phagocytes are also able to realize its function by activating metabolic reactivity, followed by the extracellular release of antimicrobial compounds. This phenomenon has been called in the scientific literature as a respiratory burst. In the phagocytes occurs biochemical activation of the hexose monophosphate shunt and NADPH oxidase of phagosome cell

(Papayannopoulos, 2018). This metabolic reaction occurs against the backdrop of increasing (in ten times) consumption of cell glucose and Oxygen. NADPH oxidase converts O^2 – superoxide anion (O^{2-}) and formation NETs (Yablonskyi & Zhelavskyi, 2009; Zhelavskyi, 2017; Cahilog et al., 2020). Cell death is commonly segregated into necrosis and apoptosis; apoptosis being programmed cell death, for instance during development and physiological cellular turnover, whilst necrosis predominantly takes place in an unregulated manner. NETosis, like necrosis, is a mode of cell death that involves the loss of membrane integrity. During NETosis, decondensation of chromatin is thought to be initiated by peptidyl arginine deiminase 4 (PAD4); its subsequent release together with granule contents is vital in the innate immune response to infection and inflammation (Zhelavskyi et al., 2020). This suggests that in the bloodstream of healthy animals, the formation of NETs should not occur, as this may lead to occlusion of small flakes of DNA. Many authors have shown that the formation of NETs in the bloodstream mechanically disrupts blood circulation in the tissues and organs (Rebordão et al., 2017; Papayannopoulos, 2018). Blood inhibitory factors have been found to have a humoral nature. Autologous serum and blood plasma inhibit extracellular DNA release by neutrophils isolated from peripheral blood. Thus, in the systemic blood flow, in the absence of inflammation, the formation of NETs is suppressed. Neutrophils of patients with chronic granulomatous disease are known to be unable to generate ROS due to a deficiency of the NADPH oxidase enzyme. In turn, the neutrophils of these patients were unable to form NETs. However, at least in part, the glucose oxidase enzyme compensated for the functional failure of NADPH oxidase to produce hydrogen peroxide (Jorch & Kubes, 2017). Neutrophils are, above all, tissue cells involved in inflammatory and antimicrobial reactions. They also function actively in the mucous membrane. It is obvious that disorders of mucosal immunity contribute to the recurrent course and chronicity of local inflammatory processes (Kambara et al., 2018; Zhelavskyi et al., 2020).NETosis, a unique form of cell death, is initiated by the presence of pathogens or their components and most often occurs in immune cells, especially neutrophils (Zhelavskyi, 2017; Linkermann, 2019). After recognition of pathogens in neutrophils, cells undergo histone modification, chromatin decondensation, and a neutrophilic extracellular trap. NET comprising chromatin and antimicrobial components. This process is facilitated by superoxide produced by NADPH oxidase 4 (NOX4), autophagy and dependent on peptidylarginine deziminase 4 (PAD4) citrated histones. Staining of co-localized proteins derived from neutrophils and extracellular DNA, as well as citrullinated histones is used to assess NETosis. In addition, cell-free DNA and DNA neutrophils, the resulting protein complexes can be detected using PicoGreen® and ELISA. Both morphology and cell-related components of NETosis can be detected by flow cytometry (Zhelavskyi, 2012; Rijal et al., 2018).

Modern research is aimed at deepening the study multiple mechanisms and phenotypes compose programmed. Cells. will certainly be taken into account by the Nomenclature Committee on Cell Death. Cellular regulation is associated with a variety of physiological mechanisms of development, and is also important in processes such as inflammation, immune response, embryogenesis maintenance of tissue homeostasis.