INVESTIGATION OF THE MECHANISMS OF PYROPTOSIS: PRACTICAL AND SCIENTIFIC SIGNIFICANCE

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Pyroptosis is a form of programmed cell death. This is a non-specific defense mechanism of the body that protects against the introduction of the pathogen. Pyroptosis is different from other cell death forms (such as apoptosis, necrosis, autophagy) in morphological features, occurrence mechanism, and mechanism of action [1]. When a cell undergoes pyroptosis, the nucleus condenses to form a pyroptotic body, pores appear in the cell membrane, the cell swells and ruptures, releasing its contents.

Caspase family is a homologous and structurally similar proteolytic enzyme in cytoplasm, which selectively recognizes and cleaves peptide bonds behind downstream target aspartic acid residues. In normal cells, caspase protein usually exists in the inactive pro-caspase state, and only after hydrolysis of amino acid sequence into active caspase can play its role. Gasdermin also plays an important role in pyroptosis. Gasdermins (GSDMs) are a family of functionally diverse proteins expressed in a variety of cell types and tissues. The gasdermin family includes 6 members, of which gasdermin D is the executor of pyroptosis due to its ability to form membrane pores [2]. Upon cleavage by activated caspase-1,4,5,11, gasdermen D can be divided into N and C segments. Among them, the N fragment can form pores in the cell membrane, leading to cell swelling, rupture, outflow of cytokines, triggering the body's immune response, and leading to pyroptosis.

The occurrence of pyroptosis can be divided into the classical pathway (depends on caspase-1) and the non-classical pathway (depends on caspase-4,5 or caspase-11) [3]. Both pathways cause the release of IL-1β and IL-18, which are involved in inflammasome activation. IL-1β induces tissue inflammation, vasodilation, and extravasation of immune cells, and also plays a role in adaptive immune response [4]. IL-18 can promote the production of INF-γ by Th1 cells, NK-cells and enhance local inflammatory response [5]. Inflammasomes and cytokines produced in the process of pyroptosis can trigger an inflammatory response in the body, and can lead to diseases, such as neurological diseases, cardiovascular diseases, and tumors. Pyroptosis is closely associated with infectious diseases. Pyroptosis has been found in Shigella, Brucella infection, anthrax, tuberculosis.

M. Adams, B. Young, A. Riestra (San Diego University, USA) hypothesize that pyroptosis of cells contribute to *Trichomonas vaginalis*-associated comorbidities. Pyroptosis is executed via inflammatory caspase cleavage of the gasdermin D protein.

To study the involvement of caspase-1 in mediating host-cell death after *Trichomonas vaginalis* infection, they assayed for the loss of membrane integrity leading to release of cytosolic lactate dehydrogenase (LDH). Results provide evidence of gasdermin D processing indicative of pyroptotic host cell death being activated in epithelial cells during *T. vaginalis* infection. Understanding this mechanism of protist-induced pyroptosis as a cytopathic and pathogenic inflammatory response is crucial for development of anti-inflammatory targeted therapies.

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