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Ekspresja receptora P2X7 w pierwotnych liniach ludzkich melanocytów i komórkach czerniaka

Rozprawa na stopień doktora nauk medycznych i nauk o zdrowiu w dyscyplinie nauki medyczne

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Abstract

Title of dissertation: P2X7 receptor expression in primary human melanocyte cell lines and melanoma cells.

Purinergic signaling comprises a complex network of cell-surface receptors present in nearly all cell types and plays a key role in diverse signaling pathways, regulating cellular responses under both physiological and pathological conditions. Within this family, the P2X7 receptor is notable for its unique properties. It is activated by extracellular ATP, which can be released into extracellular environment as a damage-associated molecular pattern (DAMP). Under normal conditions P2X7 functions as an ion channel, but prolonged or intense stimulation drives the opening of a large non-selective membrane pore, a process that can trigger cell death. Because of these distinctive properties, P2X7 has become an intensive focus of research worldwide. Nevertheless, findings to date are inconsistent, implicating the receptor in both pathological processes and protective physiological functions. Its function in skin cells, the largest organ in the body and an essential regulator of systemic homeostasis, remains poorly explored.

This study aimed to examine P2X7 receptor expression in primary human skin cells, with particular emphasis on melanocytes and melanoma cells, including both established cell lines and primary cultures. A comparison of P2X7 expression in cells isolated from human skin revealed significantly higher expression in melanocytes than in keratinocytes and fibroblasts, suggesting an important role for this receptor in the physiology of melanocytes. Furthermore, the receptor on melanocyte surfaces exhibited ion-channel activity in response to stimulation with the specific agonist BzATP, confirming its functionality. Activation of the receptor also modulated the expression of certain pro-inflammatory cytokines in melanocytes, and sustained stimulation inhibited their proliferation, indicating the involvement of P2X7 in melanocyte cellular responses. A comparative analysis of P2X7 expression in primary melanocyte lines and melanoma cells demonstrated that melanoma cells exhibit significantly lower P2X7 expression than primary melanocytes and display much weaker activation in response to BzATP. The mechanisms underlying this down-regulation remain to be elucidated, but reduced receptor levels may contribute to the malignant transformation of melanocytes. Additional factors, such as the presence of non-functional receptor isoforms or extracellular conditions that limit agonist availability or modify receptor sensitivity could also account for the diminished response, highlighting the need for further investigation. Taken together, these findings provide the first

direct comparison of P2X7 receptor expression across human skin cells, melanocytes, and melanomas, clearly demonstrating elevated receptor levels in primary human melanocytes.