Role of kinin receptors in skin pigmentation

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Introduction: Changes in skin pigmentation can be the result of abnormalities at a certain stage of melanin formation, destruction of melanocytes or a defective degradation of melanin. Previous studies have shown that all kinin system constituents are expressed in the normal and pathological skin, suggesting that kinin peptides may be involved in important primary function of the skin and pathological events. However, there are no studies reporting the participation of the kinin system in skin pigmentation process. In this context, the present study was designed to determine the role of kinins in the monobenzone (MBEH)-induced vitiligo-like model.

Methods: Briefly, female and male C57BL/6 wild type (WT) and knockout for kinins receptors (KOB1, KOB2 and KOB1B2) mice received daily topical application of 40% MBEH cream or vehicle (non-ionic cream) for 50 days. At the end, skin samples were collected for analysis. All procedures were approved by the Animal Use Ethics Committee of the Biological Sciences Section of the Federal University of Paraná (CEUA/BIO-1355).

Results: The obtained results showed that KOB1, KOB2 and KOB1B2 mice presented higher local skin depigmentation than WT. Lower levels of melanin content was detected in the epidermis and dermis of KOB1 and KOB2 mice treated with MBEH. Of note, KOB1B2 mice treated with vehicle displayed significant less melanin in the skin when compared to WT-vehicle, but MBEH treatment did increase depigmentation. Comparably, the genetic ablation of B1 and B2-kinin receptors led to reduced ROS generation in MBEH -treated mice. Again, the KOB1B2 mice presented lower ROS levels in vehicle-treated skin. Both KOB1 and KOB2 show increased dermal cell infiltrate in vitiligo skin, when compared to WT-MBEH. Lack of B1 receptor was associated with greater skin accumulation of IL-4, IL-6 and IL-17 by MBEH, while the double knockout mice presented lower levels of TNFα and IL-1α when compared to WT-MBEH.

Conclusions: Taken together, the lack of kinin receptors caused more severe depigmentation in the skin, as well as genetic deletion of both B1/B2 receptors seems to be linked with changes in levels of constitutive melanin levels. Thus, we suggest the participation of both kinin receptors in the modulation of important pathways that lead to skin pigmentation. We also noticed changes in the inflammatory response related to the release of cytokines, which may also influence the vitiligo phenotype. To better understand how and to what extent kinins are important for melanogenesis, further studies are needed.

Keywords: B1 receptors, B2 receptors, vitiligo, melanin, skin, cytokines

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