Synopsis of Original Research Paper

# Study of the Role of Eicosanoids in Melanocyte-stimulation in Post-in-flammatory Pigmentation

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Skin pigmentation after inflammation is a well recognized phenomenon, but its mechanisms have bee unknown yet. A number of substances are considered to contribute to post-inflammatory pigmentation, and eicosanoids are one of the most important mediators. Eicosanoids, prostaglandins (PGs) or leukotrienes (LTs), show a potent pharmacological activity in various tissues, and actively synthesized and degraded in the skin, and contribute to the pathogenesis of a number of skin diseases such as UV-dermatitis, atopic dermatitis, urticaria and psoriasis. We examined the synthesis of leukotrienes in human melanoma cells in order to assess the function of leukotrienes in human melanocytes. The enzyme activity of $LTA_4$ hydrolase, which catalyzes the conversion of $LTA_4$ to $LTB_4$, was detected in the supernatant of cultured human melanoma cells (MeWo cells) and melanoma cells obtained from patients. Immunoblotting analysis using an anti-human LTA, hydrolase antibody demonstrated LTA, hydrolase as a 70-kDa protein in both MeWo and melanoma cells. Considerable enzyme activity of $LTC_4$ synthase, which catalyzes the conversion of LTA4 to $LTC_4$, was detected in the microsomal fraction of both MeWo and melanoma cells. The HPLC profile of the $LTC_4$synthase reaction products revealed that $LTC_4$ was the main product. $LTD_4$ was not detected under these conditions, indicating that the microsomal fraction of human melanoma cells lacks the membranebound g-glutamyl transferase that converts $LTC_4$ to $LTD_4$. $LTC_4$ synthase activity was inhibited by the addition of MK-886, and was not altered by treatment with N-ethylmaleimide (NEM) or 1-chloro-2,4-dinitrobenzene (CDNB). These results indicate that the enzyme responsible for the conversion of LTA4 to LTC4 in human melanoma cells is $LTC_4$ synthase rather than a nonspecific or microsomal glutathione-s-transferase. These results also suggest that human melanoma cells can generate $LTB_4$ and $LTC_4$ from $LTA_4$, and that this process is catalyzed by two enzymes: $LTA_4$ hydrolase and $LTC_4$ synthase.