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MEETING ABSTRACTS

MICROPHTHALMIA-ASSOCIATED TRANSCRIPTION FACTOR REGULATES ACETYLCHOLINESTERASE EXPRESSION DURING MELANOGENESIS OF B16F10 CELLS: A CHOLINERGIC REGULATOR IN PIGMENTATION

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Acetylcholinesterase (AChE) hydrolyses acetylcholine that functions as a neurotransmitter in neurons. The non-neuronal functions of AChE have been proposed in different cell types. Here, we revealed the expression of AChE in melanocyte and melanoma, in which the tetrameric (G4) form was the major isoform. In the melanogenesis of cultured B16F10 murine melanoma, the amount of AChE was markedly decreased. The differentiation of melanoma led to: (i) increase of melanin and its synthesis enzyme tyrosinase; (ii) change of intracellular cAMP level; and (iii) decrease of microphthalmia-associated transcription factor (MITF). The regulation of AChE during melanogenesis was hypothesized to be mediated by two transcriptional factors: cAMP responsive element binding protein (CREB) and MITF. In cultured melanoma, application of cAMP suppressed the expression of AChE, as well as the promoter activity of human *ACHE* gene. This suppression was shown to be mediated by a cAMP responsive element (CRE) located on the *ACHE* promoter, and mutation of this site eliminated the suppression. In melanoma, over expression of MITF induced the transcription of ACHE gene, and mutation of E-box site of the promoter blocked the induction. In parallel, application of an AChE inhibitor in vitro greatly enhanced acetylcholine-mediated responses of melanogenic gene expressions; but the enhancement was not revealed in the present of agonists of muscarinic acetylcholine receptor. Therefore, our results indicated that AChE transcription is specifically regulated by cAMP-dependent signaling pathway during melanogenesis of B16F10 cells, suggesting a potential role of AChE being played in this differentiation process.

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