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Defective eyelid leading edge cell migration in C57BL/6-corneal opacity mice with an “eye open at birth” phenotype

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ABSTRACT. Development of the eyelid requires coordination of the cellular processes involved in proliferation, cell size alteration, migration, and cell death. C57BL/6J-corneal opacity (B6-Co) mice are mutant mice generated by the administration of N-ethyl-N-nitrosourea (100 mg/kg). They exhibit the eyelids open at birth phenotype, abnormal round cell shape from tightened F-actin bundles in leading edge keratinocytes at E16.5, and gradual corneal opacity with neovessels. The tip of the leading edge in B6-Co mice did not move forward, and demonstrated a sharp peak shape without obvious directionality. Analysis of the biological characteristics of B6-Co mice demonstrated that abnormal migration of keratinocytes could affect eyelid development, but proliferation and apoptosis in B6-Co mice had no effect. Mutant gene mapping and sequence analysis demonstrated that in B6-Co mice, adenosine was inserted into the untranslated regions,

between 3030 and 3031, in the mRNA 3'-terminal of Fgf10. In addition, guanine 7112 was substituted by adenine in the Mtap1B mRNA, and an A2333T mutation was identified in Mtap1B. Quantitative real-time polymerase chain reaction analysis showed that expression of the Hbegf gene was significantly down-regulated in the eyelids of B6-Co mice at E16.5, compared to B6 mice. However, the expression of Rock1, Map3k1, and Jnk1 genes did not show any significant changes. Abnormal keratinocyte migration and down-regulated expression of the Hbegf gene might be associated with impaired eyelid development in B6-Co mice.

Key words: B6-Co mouse; Leading edge; Keratinocyte migration; Eyelid development; Gene expression