

Coupling of cell migration with neurogenesis by proneural bHLH factors.

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After cell birth, almost all neurons in the mammalian central nervous system migrate. It is unclear whether and how cell migration is coupled with neurogenesis. Here we report that proneural basic helix-loop-helix (bHLH) transcription factors not only initiate neuronal differentiation but also potentiate cell migration. Mechanistically, proneural bHLH factors regulate the expression of genes critically involved in migration, including down-regulation of RhoA small GTPase and up-regulation of doublecortin and p35, which, in turn, modulate the actin and microtubule cytoskeleton assembly and enable newly generated neurons to migrate. In addition, we report that several DNA-binding-deficient proneural genes that fail to initiate neuronal differentiation still activate migration, whereas a different mutation of a proneural gene that causes a failure in initiating cell migration still leads to robust neuronal differentiation. Collectively, these data suggest that transcription programs for neurogenesis and migration are regulated by bHLH factors through partially distinct mechanisms.

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