Stabilization of β-catenin promotes melanocyte specification at the expense of the Schwann cell lineage

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Abstract

The canonical Wnt/β-catenin pathway governs a multitude of developmental processes in various cell lineages, including the melanocyte lineage. Indeed, β-catenin regulates transcription of Mitf-M, the master regulator of this lineage. The first wave of melanocytes to colonize the skin is directly derived from neural crest cells, whereas the second wave of melanocytes is derived from Schwann cell precursors (SCPs). We investigated the influence of β-catenin in the development of melanocytes of the first and second waves by generating mice expressing a constitutively active form of β-catenin in cells expressing tyrosinase. Constitutive activation of β-catenin did not affect the development of truncal melanoblasts but led to marked hyperpigmentation of the paws. By activating β-catenin at various stages of development (E8.5-E11.5), we showed that the activation of β-catenin in bipotent SCPs favored melanoblast specification at the expense of Schwann cells in the limbs within a specific temporal window. Furthermore, in vitro hyperactivation of the Wnt/β-catenin pathway, which is required for melanocyte development, induces activation of Mitf-M, in turn repressing FoxD3 expression. In conclusion, β-catenin overexpression promotes SCP cell fate decisions towards the melanocyte lineage.

Keywords: Cell fate; Determination; FoxD3; Mitf; Mouse; Pigmentation; Proliferation.

Conflict of interest statement

Competing interests S.C. serves a consultant for Q-State Biosciences, Inc. All other authors declare no conflict of interest.

Figures

Fig. 1.

Tyr::Cre/°; βcatex3 $^{flox/+}$ mice present...

Fig. 2.

Overexpression of an active form...

Fig. 3.

GFP- and Pmel-positive cells are...

Fig. 4.

β-Catenin favors the specification of...

Fig. 5.

GFAP-positive cells are defloxed in...

Fig. 6.

The number of paw melanoblasts...

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