Proceedings of German Society for Stem Cell Research (PGSSCR)

Stem cell regulation and lineage commitment in mammalian skin: A role for the Wnt/β-catenin signalling pathway

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Published online on 16 May 2007

Introduction:

Mammalian skin is a highly dynamic tissue and constantly renewed throughout adult life by a population of stem cells capable to produce daughter cells that differentiate along multiple lineages. Stem cells within the epidermis have the ability to regenerate the differentiated cell types of the interfollicular epidermis, hair follicles and sebaceous glands. We are interested in how lineage commitment is regulated in normal skin tissue and during skin tumourigenesis.

Previously, we and others have shown that canonical Wnt/β-catenin signalling plays a crucial role for skin development, stem cell maintenance, and lineage selection. In skin morphogenesis, the level of β-catenin activity determines lineage choice: activation of the pathway stimulates hair-type differentiation, whereas inhibition promotes differentiation of interfollicular epidermis and sebocytes.

Aims of the project:

Important questions are if skin tumour formation originates in epidermal stem cells and if pathways regulating these cells also determine the differentiation process of tumour cells.

Results and Discussion:

Aberrant activation of Wnt signalling occurs frequently in a range of tumours. What we found is that repression of Wnt/β-catenin signalling in mouse epidermis not only changes lineage commitment but also leads to development of sebaceous tumours and that the level of Wnt/β-catenin activity indeed specifies the tumour type. This is confirmed by other mouse models, where activation of the pathway induces skin tumours with hair differentiation. Taken together, the data indicate that similar cellular mechanisms and signalling pathways are applied for normal differentiation of skin progenitor cells and for directing the differentiation program of tumour cells. We present an inducible mouse skin tumour model which allows us to investigate early steps of tumour formation and to analyse potential progenitor cells that give rise to skin tumours.