

Regulating osteoblast and chondrocyte formation from neural crest stem cells

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Over the past decades, stem cells have attracted much attention from the medical and scientific community due to their potential to generate various specialized cell types in the body. Independently of their origin, all stem cells share three common characteristics: they are undifferentiated, they have self-renewal capacity, and if induced they can differentiate into a variety of specialized cell types. Stem cells might, therefore, be particularly suited for the study of disease mechanisms underlying cell degeneration or malignant transformation, for the discovery of potential drugs influencing survival and differentiation of specific cell types, and for therapies aimed at replacing cells and tissue in injured or diseased organs.

In this context, adult stem cells are particularly attractive because patients could act as their own stem cell donors. Recently, our laboratory has described the identification of adult neural crest-derived stem cells (NCSCs) present in the skin [1]. NCSCs exhibit an inherently broad potential to generate a wide variety of cell types, such as neurons, glia, smooth muscle, bone, and cartilage. Nonetheless, adult NCSCs also appear to display significant tissue-dependent differences. Their thorough characterization is thus a prerequisite for determining the adult stem cell source most appropriate for a given application. Moreover, the growth factors and genetic programs promoting specific cell fates need to be elucidated.

One of the key regulatory factors of NCSC development turns out to be transforming growth factor beta (TGF β) [2]. As we have previously shown, conditional ablation of TGF β signaling in NCSCs leads to a phenotype reminiscent of DiGeorge syndrome in human patients that suffer from craniofacial and cardiovascular malformations [3,4]. DiGeorge syndrome represents the most frequent microdeletion syndrome in humans, with an estimated incidence of 1 in 4000 live births.

To better understand the mechanism underlying these malformations we made use of established cell culture systems in combination with genetic approaches in mouse models. This allowed us to identify a novel role of TGF β signaling in the transition of NCSCs to a hitherto undescribed non-neural progenitor cell. This progenitor cell displays alterations in its transcription factor profile, as compared to NCSCs, and exhibits a decreased neural but enhanced non-neural developmental potential. In particular, TGF β promotes the responsiveness to myogenic, chondrocytic and osteogenic cues in these cells. Thus, our data provide the basis to develop a strategy for efficient osteoblast and chondrocyte formation from NCSCs.

REFERENCES: ¹Wong et al., J Cell Biol, 2006, 175(6):1005-15. ²Wurdak et al., BioEssays, 2006, 28(11):1078-86). ³Wurdak et al., Genes Dev., 2005, 19: 530-535. ⁴Ittner et al., J Biol, 2005, 4: 11.1-11.16

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