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Guest Editorial

Highlight: Self-renewal signaling in stem cells

A number of ground-breaking studies recently identified sets of nuclear factors that together have the unique ability to 'reset' an adult differentiated cell type and to 'erase' all previous fate decisions and the transcriptional programs that determine phenotype and function of a differentiated cell (Takahashi et al., 2007; Wernig et al., 2007; Yu et al., 2007). As a result, 'reprogrammed' cells assume a phenotype closely resembling embryonic stem cells and functional studies so far suggest that these cells, termed 'induced pluripotent stem cells (iPS)', also share fundamental functional characteristics with embryonic stem cells, including self-renewal capacity and pluripotency. The iPS concept, reprogramming of somatic cells into stem cells and its obvious potential for regenerative medicine (Hanna et al., 2007), electrified the scientific community since its confirmation in 2007. However, the question of which signaling pathways are required for stem cells to maintain an undifferentiated state and their self-renewal capacity has received relatively little attention.

This issue of *Biological Chemistry* presents a series of articles that all focus on transcriptional regulation and signal transduction pathways that are active in stem cell populations to ensure maintenance of inherent stem cell self-renewal capacity. Reflecting different types of stem cells, self-renewal signaling can occur at multiple levels: articles by Cantz, Edenhofer, Kögler and colleagues highlight roles of the transcription factor OCT4 in pluripotent stem cell populations, while Melchior et al. study the role of the WNT receptor FZD7 in self-renewal signaling of pluripotent embryonic stem cells. However, self-renewal also occurs in bone marrow-derived stem cell populations, including multipotent mesenchymal (Angelov and colleagues) and hematopoietic stem cells (articles by the groups of Dittmar, Giebel and Gratwohl). While central concepts of current stem cell biology are based on classical experiments in the hematopoietic system (Humphries et al., 1981; Spangrude et al., 1988; Osawa et al., 1996), the notion of stem cells in tumors and their requirement for the development of a heterogeneous malignant cell population, as discussed by Dirk Kabelitz, emerged only recently. While the 'cancer stem cell' concept is still controversial to some extent (Kelly et al., 2007), a link between stem cells and cancer is strongly supported by the fact that potent oncogenes, including MYC, OCT4 and RAS (as discussed by Rolf Heumann), have an important role in stem cell self-renewal signaling.

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