Twist1: Complex regulator of cell shape and function

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Transcription factor Twist1 is involved in many processes where cells change shape or function. Thereby, Twist1 is crucial for embryonic development, but has also been implicated in cancer progression. However, the precise contribution of Twist1 to these processes is under much debate. Scientists from the Helmholtz Zentrum München describe a new mode of action: a short-term, transient activation of Twist1 primes cells for stem cell-like properties. By contrast, prolonged, chronic Twist1 activity suppresses stem cell-like traits. These results, published in the journal *Cell Reports*, help to unravel seemingly contradictory observations and illuminate the complexities of transcription factor action in regeneration and tumor progression.

Team leader Christina Scheel summarizes the results: "Twist1 is a developmental master regulator that has also been implicated in cancer progression. We show that transient Twist1 activation primes certain cells for stem-cell-like properties and cellular plasticity. Said differently, induction of these traits depends on Twist1, but they are only displayed by the cells after Twist1 deactivation. By contrast, chronic Twist1 activity suppresses stem-cell-like properties and promotes a phenotype that is characterized by extreme changes in cell shape and function, effectively locking the cells into an invasive, non-proliferative phenotype. Thereby, our results provide an integrative view of seemingly contradictory results concerning the effects of Twist1 in physiological and pathological processes."

Duration of Twist1 activity decisive

Scientists from the Institute of Stem Cell Research and the Institute of Experimental Genetics at the Helmholtz Zentrum München (HMGU) examined the effects of Twist1 activation on breast epithelial cells, paying particular attention to the duration of the Twist1-signal. To their surprise, cells were permanently altered after a short dose of Twist1-activation: they proliferated under very stringent conditions usually permissive only for stem cells and were able to generate complex multicellular structures, suggesting a gain of cellular plasticity.

Twist1 may fuel regeneration

A high level of plasticity implies regenerative potential. However, when activated during tumor development, Twist1 promotes aggressive behaviour in tumor cells. With their investigations, the team was able to reveal a new aspect of how Twist1 regulates cell shape and function and, thereby, impacts regeneration, but also tumor progression.

"Our results offer important insights for further mechanistic studies of regeneration in healthy and tumour cells", explains first author Johanna Schmidt. "The precise delineation of the different modes of action by Twist1 provide the basis for future studies aiming to manipulate its activity either to promote regeneration or target advanced tumors ," adds co-author Elena Panzilius.

More information: Schmidt, J. et al. (2015), Stem-Cell-like Properties and Epithelial Plasticity Arise as Stable Traits after Transient Twist1 Activation, *Cell Reports*, DOI: 10.1016/j.celrep.2014.12.032