

Journal club



THE CHANGING FACES OF CANCER CELLS

The performing arts technique of face-changing is an ancient art form at the heart of Sichuan opera. Its performers change a series of brightly coloured face masks in split seconds to reflect their characters' mood changes. Like this art, cancer has many faces (that is, cell types) that change quickly. There is a rare population of cancer cells, called cancer stem cells (CSCs), that are able to self-renew and regenerate all the cell types that make up the tumour mass.

So, might transcription factors be used to convert differentiated cells into CSCs in the same way that they can be used to produce induced pluripotent stem cells? Mani *et al.* provided an affirmative answer to this question. Forcing the expression of the transcription factors Snail or Twist induced the epithelial-to-

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mesenchymal transition (EMT) in immortalized mammary epithelial cells and, surprisingly, caused cells undergoing EMT to share many of the characteristics of undifferentiated stem cells isolated from either normal or cancer cell populations. This seminal finding established a direct link between EMT and stem cells. Furthermore, gene-profiling studies, carried out by Creighton *et al.*, revealed that EMT markers are highly expressed in human mammary CSCs. This suggests that CSCs might arise from differentiated cells, which has important implications not only in the maintenance of tissue homeostasis during development but also for EMT in carcinomas.

It has been proposed that an enrichment of CSCs might cause disease recurrence. Treatment of cancer patients with standard therapeutics eradicates non-CSC populations and consequently enriches the percentage of CSCs that are intrinsically resistant to cancer therapy. However, it is also possible

that drug treatment might promote EMT to actively increase the number of CSCs. The connection between EMT and stem cell-like properties — which has given us a new ‘behind the scenes’ look at how cancer cells perfect the art of face-changing — will enable us to better understand the formation of metastatic cancer, and the molecular targeting of CSCs that derive from EMT may be a new way to treat this devastating disease.

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ORIGINAL RESEARCH PAPERS Mani, S. A. *et al.* The epithelial-mesenchymal transition generates cells with properties of stem cells. *Cell* **133**, 704–715 (2008) | Creighton, C. J. *et al.* Residual breast cancers after conventional therapy display mesenchymal as well as tumor-initiating features. *Proc. Natl Acad. Sci. USA* **106**, 13820–13825 (2009)