can, on release from senescence, proliferate and show hallmarks of cancer stem cells. The cancer-stem-cell features gained by these post-senescent cells cannot be explained by these cells simply being a cancer-cell subset that failed to enter senescence, because the authors show that entering senescence is a requirement for this process to occur.

The authors found a link between the activation of the Wnt signalling cascade and the senescent state. The observation that this well-studied stem-cell signalling pathway is activated during senescence provides additional confirmation of the surprising link with the induction of stem-cell characteristics. However, it is not clear why this pathway is activated. Nor is it clear whether Wnt ligands are secreted by senescent cells and whether such ligands then act on the same cell that secretes the protein or on neighbouring cells.

Notably, this finding also offers a means of targeting the potentially harmful effects of the cancer stem cells generated. The authors found that treatment of cells with a Wnt-pathway inhibitor could decrease tumour growth on exit from senescence. This discovery should be investigated in the clinic to determine whether it could enhance the effectiveness of chemotherapy.

Although these studies provide strong evidence for a close link between senescence and stemness, most of the work used a genetically engineered model system that allows exit from senescence to be controlled at will by removing a drug. How cancer cells might naturally break through senescence barriers *in vivo*, and whether this might be linked to acquisition of cancer stemness, should be investigated. The authors tried to address this by analysing spontaneous escape from senescence in samples of cancer cells from their mouse model grown *in vitro*, and also detected increased cancer stemness features in this context. Additional confirmation of these findings in non-genetically modified cancer models will, however, be needed. Nevertheless, Milanovic and colleagues' data provide compelling evidence in the systems they studied that, when cancer cells escape from senescence, they have an enhanced capacity to drive tumour growth — a finding that has potential clinical implications. ■

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