

## Feeding back on tumour initiation

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The protein ZEB1 – which is known to promote invasiveness of epithelial tumours– also influences the tumour initiating capacity of pancreatic and colorectal cancer cells, and could possibly promote cancerous cells proliferation once they have reached a new organ. The finding, published online this week in *Nature Cell Biology*, suggests that targeting a feedback loop in which ZEB1 is involved in might represent a promising avenue for the treatment of certain cancers.

The small RNAs of the miR200 family were previously reported to inhibit cell invasion and movement of certain cancerous tissues via direct inhibition of ZEB1. ZEB1 in turn suppresses the expression of miR200. Thomas Brabletz and colleagues now show that miR200 also inhibits various factors required for the maintenance of stem cells characteristics, including factors that promote self-renewal, proliferation and inhibit differentiation. They also demonstrate that loss of ZEB1 in human pancreatic cancer cell lines reduces their tumour initiation potential by suppressing miR200-dependent inhibition of stem cells factors. By examining primary pancreatic cancer tissues of mouse and human origins, they show that less differentiated tumours express high levels of ZEB1 and stem cell factors, while tumours isolated from patients that are long term survivors of pancreatic cancers have low ZEB1.

This study suggests that ZEB1 promotes both tumour spread and initiation by enhancing the stem cells characteristics of the cells that migrate away from the primary tumour to form metastases.

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