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Transcriptional networks governed by E2F factors control a proliferative to invasive switch

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In order to disseminate and seed distant organs, cancer cells become migratory while coordinating invasive, proliferative and genome stability maintenance programs. The ability of epithelial cells to engage into pro-invasive mesenchymal forms is governed by gene expression profiles triggered by several transcription factors. Our group identified cell-cycle regulators E2F1 and E2F2 as key transcription factors necessary for the maintenance of differentiated phenotypes and preservation of genome stability. We now unveil a novel function for these factors whereby E2F1 and E2F2 regulate the proliferative-to-invasive switch in colon cancer cells. E2F1 ^{low}/E2F2^{low} cells display a highly motile and invasive phenotype, while promoting genome instability and attenuating cell growth. Transcriptomic and ChIP analyses revealed that E2F1/2 factors repress the expression of a subset of genes involved in cell adhesion and migration that are linked to invasion, extravasation and metastasis in colorectal cancer. Altogether, our data describes a novel mechanism mediating the shift from a proliferative to an invasive phenotype in colon cancer cells and reveals that while loss of E2F activity limits the growth of cancer cells and promotes genome instability, it concomitantly triggers a transcriptional program that favours invasive traits.