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IN BRIEF

TUMOUR-INITIATING CELLS

The cell that rocks the tumour

Latil *et al.* have shown that the cell of origin of squamous cell carcinomas (SCCs) controls epithelial-to-mesenchymal transition (EMT) and aggressiveness of these tumours. SCCs derived from hair follicles are much more prone to undergo EMT and have more metastatic potential compared with SCCs derived from interfollicular epidermis. Chromatin and transcriptional profiling of these two different epidermal populations during tumorigenesis identified the gene network and different epigenetic states that control tumour initiation and EMT.

ORIGINAL ARTICLE Latil, M. *et al.* Cell-type-specific chromatin states differentially prime squamous cell carcinoma tumor-initiating cells for epithelial to mesenchymal transition. *Cell Stem Cell* http://dx.doi.org/10.1016/j.stem.2016.10.018 (2016)

LEUKAEMIA

Don't let sleeping cells lie

In many patients with acute lymphoblastic leukaemia (ALL), most cells respond to chemotherapy but a minority show resistance and cause relapse with poor outcome. Using patient-derived xenograft models, Ebinger *et al.* identified a subpopulation of resistant and relapse-inducing cells with long-term dormancy and stemness properties similar to those in primary ALL cells from patients at minimal residual disease (MRD). When dissociated from the *in vivo* environment, these cells started proliferating and became sensitive to treatment, which suggests that patients with ALL might benefit from therapeutic strategies that release MRD cells from the niche.

ORIGINAL ARTICLE Ebinger, S. *et al.* Characterization of rare, dormant, and therapy-resistant cells in acute lymphoblastic leukemia. *Cancer Cell* http://dx.doi.org/10.1016/j.ccell.2016.11.002 (2016)

CHEMOTHERAPY

Less is more

In response to maximum tolerated doses of chemotherapy, Chan *et al.* found that cancer-associated fibroblasts are activated through increased activity of signal transducer and activator of transcription 1 (STAT1) and nuclear factor-κB (NF-κB), leading to elevated levels and release of ELR^+ chemokines. These chemokines bind to C-X-C chemokine receptor type 2 (CXCR2) on tumour cell surfaces causing a phenotypic shift to tumour-initiating cells and promoting aggressive tumour behaviours. Metronomic chemotherapy regimens mostly prevented this effect, suggesting that long-term, low-dose chemotherapy might be more effective than high-dose chemotherapy in driving antitumour activity.

ORIGINAL ARTICLE Chan, T-S. *et al.* Metronomic chemotherapy prevents therapy-induced stromal activation and induction of tumor-initiating cells. *J. Exp. Med.* http://dx.doi.org/10.1084/jem.20151665 (2016)

CANCER GENETICS

X-inactivation and cancer incidence

Males have a higher risk than females of developing many cancers but the reasons for this disparity are unclear. Dunford *et al.* analysed exome sequences of 4,126 tumours across 21 cancer types and identified some tumour suppressor genes on the X chromosome that escape X-inactivation in females. Loss-of-function mutations in six of these genes were more common in male than in female tumours; as females would require two deleterious mutations to inactivate these genes, this might explain some of the reduced cancer incidence in females.

ORIGINAL ARTICLE Dunford, A. *et al.* Tumor-suppressor genes that escape from X-inactivation contribute to cancer sex bias. *Nat. Genet.* http://dx.doi.org/10.1038/ng.3726 (2016)