Nature Reviews Clinical Oncology **10**, 428 (2013); published online 2 July 2013;
doi:10.1038/nrclinonc.2013.115;
doi:10.1038/nrclinonc.2013.116;
doi:10.1038/nrclinonc.2013.117;
doi:10.1038/nrclinonc.2013.118

IN BRIEF

GENETICS

Gene-expression profiling reveals subtypes of retinoblastoma

A new study of 21 retinoblastoma samples has identified genetic events that contribute to tumorigenesis. In fact, two groups with distinct expression patterns could be delineated on the basis of the results. The first group expresses genes associated with retinal cell types, and is associated with chromosomal alterations that include 1q and 6p gain and 16q loss. Furthermore, group 1 tumours had aggressive phenotypes. By contrast, group 2 tumours maintained characteristics of cone photoreceptor cells and exploit the metabolic capacity of these cells to promote proliferation.

Original article Kapatai, G. *et al.* Gene expression profiling identifies different sub-types of retinoblastoma. *Br. J. Cancer* doi:10.1038/bjc.2013.283

BASIC RESEARCH

Wnt signalling required for pancreatic carcinogenesis

Although signalling through the Wnt/β-catenin pathway is associated with pancreatic ductal adenocarcinoma, only now has this pathway been shown to be critical for tumorigenesis. This was shown through experiments on β-catenin-null acinar cells, which could not undergo metaplastic transformation to ductal cells—a process central to the development of premalignant lesions. Furthermore, targeting the Wnt pathway with a specific antibody (OMP-18R5) in a transgenic mouse model of pancreatic cancer revealed normal acinar structures and fewer lesions than untreated mice.

Original article Zhang, Y. *et al.* Canonical Wnt signaling is required for pancreatic carcinogenesis. *Cancer Res.* doi:10.1158/0008-5472.CAN-12-4384

IMMUNOTHERAPY

Caution needed when engineering T cells and receptors

In an effort improve the affinity of T-cell receptors (TCRs) for cancer-cell antigens, cells can be engineered to express affinity-enhanced receptors. In a recent study of engineered T cells with TCRs for HLA-A*01-restricted MAGE-A3, two patients (with myeloma and melanoma) died unexpectedly of cardiogenic shock. Autopsy findings revealed considerable myocardial damage; T-cell infiltration was evident on histopathological assessment. Although the heart tissue did not express MAGE-A3, the T-cell killing was thought to be triggered by an unrelated peptide derived from the muscle-specific protein titin.

Original article Linette, G. P. *et al.* Cardiovascular toxicity and titin cross-reactivity of affinity enhanced T cells in myeloma and melanoma. *Blood* doi:10.1182/blood-2013-03-490565

BASIC RESEARCH

Understanding why the naked mole rat is cancer resistant

The naked mole rat's lifespan of 30 years is remarkable, as is its natural resistance to cancer. Researchers have now identified a mechanism responsible for the latter: high levels of high-molecular-mass hyaluronan secreted from fibroblasts, which accumulates because of decreased activity of hyaluronan-degrading enzymes. Suppression of hyaluronan synthesis (or promotion of its degradation) renders the animal susceptible to cancer. Evolutionarily, hyaluronan is thought to increase skin elasticity, which enables the animals to live underground.

Original article Tian, X. *et al.* High-molecular-mass hyaluronan mediates the cancer resistance of the naked mole rat. *Nature* doi:10.1038/nature12234