IN BRIEF

SKIN CANCER

Nicotinamide chemoprevention trial success

Ultraviolet (UV) radiation exposure is known to be the main cause of non-melanoma skin cancers (NMSCs), and preclinical and early clinical studies have shown the protective effects of nicotinamide against UV-induced DNA damage and the development of precancerous lesions. A Phase III double-blind, randomized, controlled trial reports the safety and efficacy of nicotinamide chemoprevention in 386 patients at high risk of NMSC. After 12 months, compared with placebo, treatment with 500 mg nicotinamide twice daily significantly reduced the rate at which new NMSCs and precancerous lesions developed, with no between-group differences in adverse events. This study thus supports the use of nicotinamide — an inexpensive and widely accessible vitamin supplement — for NMSC chemoprevention in high-risk patients.

ORIGINAL RESEARCH PAPER Chen, A. C. *et al.* A phase 3 randomized trial of nicotinamide for skin-cancer chemoprevention. *N. Engl. J. Med.* **373**, 1618–1626 (2015)

TUMOUR IMMUNOLOGY

An epigenetic evasion mechanism

A study in *Nature* identifies an epigenetic mechanism in tumour cells that contributes to immune evasion. In two mouse models of ovarian cancer, combined inhibition of enzymes known to mediate epigenetic silencing in cancer — enhancer of zeste homologue 2 (EZH2) and DNA methyltransferases (DNMTs) — reduced tumour size, slowed tumour progression, and increased tumour T cell infiltration and T helper 1 (T_H1)-type chemokine expression. By contrast, this inhibition did not reduce tumour size in immunodeficient mice, which suggests that epigenetic silencing of T cell-recruiting chemokines in cancer cells promotes tumour growth and progression. Furthermore, inhibition of epigenetic silencing significantly enhanced the *in vivo* efficacy of PD1 ligand 1 (PDL1) blockade and of adoptive T cell therapy. In human ovarian tumour tissue, high expression of EZH2 and DNMT1 significantly correlated with poor prognosis and a reduced number of tumour-infiltrating $CD8^+$ T cells. Together, these data suggest that epigenetic silencing of chemokines in ovarian cancer reduces T cell recruitment to the tumour microenvironment and can thus shape the immune response. As immunotherapies require tumour infiltration of T cells, their efficacy could be augmented by epigenetic reprogramming in cancer patients, as shown here in mouse models.

ORIGINAL RESEARCH PAPER Peng, D. *et al.* Epigenetic silencing of T_H1-type chemokines shapes tumour immunity and immunotherapy. *Nature* http://dx.doi.org/10.1038/nature15520 (2015)

PROSTATE CANCER

Radiosensitization through reduced DNA repair

Radiotherapy is more effective in patients with prostate cancer who receive neoadjuvant chemical castration, but the underlying molecular mechanism has been unclear. A study by Helleday and colleagues reveals that castration enhances the radiosensitivity of prostate cancer cells by reducing non-homologous end joining (NHEJ) repair of DNA double-strand breaks (DSBs). In samples from patients receiving castration treatment prior to radiotherapy, levels of the NHEJ protein KU70 and activity of DNA-PK — a kinase required for NHEJ — were significantly reduced, and there were significantly increased levels of the DSB markers γH2AX and 53BP1. The authors thus implicate defective NHEJ repair in castration-induced radiosensitization.

ORIGINAL RESEARCH PAPER Tarish, F. L. *et al.* Castration radiosensitizes prostate cancer tissue by impairing DNA double-strand break repair. *Sci. Transl Med.* **7**, 312re11 (2015)