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IN BRIEF

GENETICS

Chromatin-remodelling genes affected in neuroblastoma

A recent study has used whole-genome sequencing, exome sequencing, genome-wide rearrangement analyses and massively parallel sequencing techniques to determine the genetic basis of neuroblastoma. On average, 19 somatic alterations per tumour were found. Two new genes not previously associated with neuroblastoma—*ARID1A* and *ARID1B*—were found to be deleted or altered in 11% of the samples studied (71 total). These genes, which are involved in chromatin remodelling and mutations, were associated with early treatment failure and reduced survival. Methods to detect and direct treatment to these targets might provide new avenues for managing patients with neuroblastoma.

Original article Sausen, M. *et al.* Integrated genomic analyses identify ARID1A and ARID1B alterations in the childhood cancer neuroblastoma. *Nat. Genet.* doi:10.1038/ng.2493

CHEMOTHERAPY

Gemcitabine and 5-fluorouracil activate the inflammasome

Two commonly used chemotherapeutic agents, gemcitabine and 5-fluorouracil, have been found to be implicit in their own inefficacy. They both activate the NOD-like receptor family and the pyrine domain containing-3 protein (Nlrp3)-dependent caspase-1 activation complex (the inflammasome) via the release of cathepsin B from lysosomes. Inflammasome activation results in the secretion of IL-1β and, subsequently, IL-17 release by $CD4^+$ T cells. The study, conducted in myeloid-derived suppressor cells, demonstrated that these events limited the activity of the chemotherapy. Furthermore, thymoma-bearing mice without key inflammasome components (*Nlrp3*$^{-/-}$, *Casp1*$^{-/-}$ or those treated with IL-receptor antagonists) responded better to chemotherapy than those with intact inflammasomes. These results suggest that challenge with gemcitabine or 5-fluorouracil could be combined with IL-1 inhibition to improve response.

Original article Bruchard, M. *et al.* Chemotherapy-triggered cathepsin B release in myeloid-derived suppressor cells activated the Nlrp3 inflammasome and promotes tumor growth. *Nat. Med.* doi:10.1038/nm.2999

SCREENING

HPV DNA testing detects more cervical lesions than cytology

A prospective population-based screening study of >200,000 women in Finland has shown that DNA testing for the human papillomavirus (HPV) followed by cytology for positive-testing patients is more effective at detecting precancerous and cancerous cervical lesions than primary cytology alone in a 5-year screening round. In women aged 25–34 years, the cumulative hazard ratio for cervical intraepithelial neoplasia and adenocarcinoma *in situ* was 0.0057 for HPV screening, which compared favourably to that of cytology alone (0.0046). In women aged >35 years, the corresponding data were 0.0022 for HPV DNA analysis and 0.0017 for cytology. Consequently, careful selection of age groups and screening intervals could lead to improved overall detection rates of precancerous cervical lesions using HPV screening. However, similar studies in other countries are needed to determine the extent of the benefit.

Original article Leinonen, M. K. *et al.* Detection rates of precancerous and cancerous cervical lesions within one screening round of primary human papillomavirus DNA testing: prospective randomised trial in Finland. *BMJ* doi:10.1136/bmj.e7789