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IN BRIEF

ADIPOSE TISSUE

Adipocyte exosomes drive melanoma progression

New research has identified a novel mode of communication between adipocytes and cancer cells that regulates tumour aggressiveness. Adipocyte exosomes (ad-exos) purified from conditioned medium of 3T3-F442A mature adipocytes increased melanoma cell migration and invasion *in vitro*. Analysis of the protein cargo of these ad-exos by mass spectrometry revealed the majority of proteins to be involved in lipid metabolism, specifically fatty acid oxidation (FAO). Crucially, inhibition of this pathway blocked the pro-migratory effect of ad-exos on melanoma cells, highlighting the importance of FAO in tumour progression. Shedding of ad-exos and their effect on FAO-dependent melanoma cell migration were also greater in obese mice and humans than in lean controls. The findings could explain why patients with obesity and melanoma have a poor prognosis and lead to new cancer treatments involving FAO inhibitors.

ORIGINAL ARTICLE Lazar, I. *et al.* Adipocyte exosomes promote melanoma aggressiveness through fatty acid oxidation: a novel mechanism linking obesity and cancer. *Cancer Res.* http://dx.doi.org/10.1158/0008-5472.CAN-16-0651 (2016)

REPRODUCTIVE ENDOCRINOLOGY

Acquisition of kisspeptin responsiveness is key to reversal of hypogonadotropic hypogonadism

Although spontaneous activation of the hypothalamic–pituitary–gonadal axis resulting in improved reproductive endocrine function is a hallmark of reversal of idiopathic hypogonadotropic hypogonadism (IHH), clinical features that can confidently predict reversal have yet to be identified. A new study now suggests that dynamic changes in the sensitivity of the gonadotropin-releasing hormone (GnRH) neuronal network to kisspeptin are responsible for this reversal. Six men with IHH and evidence of reversal (testicular volume growth after age 18 years without exogenous gonadotropins or GnRH therapy) at enrolment participated in the study. Upon administration of intravenous boluses of kisspeptin (0.24–2.20 nmol/kg), patients with sustained reversal of IHH ($n = 4$) had robust GnRH-induced pulsatile luteinizing hormone secretion, whereas those who had relapsed back to the hypogonadotropic state ($n = 2$) did not.

ORIGINAL ARTICLE Lippincott, M. F. *et al.* Kisspeptin responsiveness signals emergence of reproductive endocrine activity: implications for human puberty. *J. Clin. Endocrinol. Metab.* http://dx.doi.org/10.1210/jc.2016-1545 (2016)

NEUROENDOCRINOLOGY

Exome sequencing aids targeted treatment of inborn errors of metabolism

Combining whole-exome sequencing with deep clinical phenotyping (that is, clinical and biochemical evaluation) substantially increases the likelihood of obtaining a genetic diagnosis in patients with intellectual developmental disorder and unexplained metabolic abnormalities, according to a new study. Using this combined approach, a genetic diagnosis was obtained in 28 of 41 probands (68%), which included variants in novel genes, candidate genes and those known to cause the disease. Most variants were classified as either pathogenic or probably pathogenic. Importantly, genetic diagnosis altered the clinical treatment of 18 probands (44%), including treatments targeting the cellular or molecular defect. Further use of this approach could improve genetic diagnosis and subsequent management of patients with other neurometabolic disorders.

ORIGINAL ARTICLE Tarailo-Graovac, M. *et al.* Exome sequencing and the management of neurometabolic disorders. *N. Engl. J. Med.* http://dx.doi.org/10.1056/NEJMoa1515792 (2016)