Pituitary hormone receptors and tumorigenesis

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We read with interest the Review 'G-protein-coupled receptors and cancer' by Dorsam and Gutkind published in *Nature Reviews Cancer*[1]. In table 1 the authors state inaccurately that thyrotropin secreting hormone (TSH) and adrenocorticotropin hormone (ACTH) receptors (TSHR and ACTHR, respectively) cause pituitary tumours.

The pituitary gland secretes six polypeptide hormones — ACTH, TSH, growth hormone (GH), gonadotropins (follicle stimulating hormone (FSH) and luteinizing hormone (LH)) and prolactin. These trophic hormones act at their respective target glands (adrenals, thyroid, cartilage, gonads and breast) to regulate peripheral hormone secretion and glandular growth and differentiation[2].

TSH is secreted by the pituitary and signals through the TSHR at the thyroid gland to induce thyroid hormone synthesis. Several naturally occurring mutations are found in the TSHR[3–5]. Activating, somatic TSHR mutations cause toxic thyroid adenomas[6], and activating, germline TSHR mutations can cause hereditary toxic thyroid hyperplasia[7] and familial gestational hyperthyroiditis[8]. Inactivating, germline TSHR mutations can cause partial or complete resistance to TSH[9,10] or isolated central hypothyroidism[11]. No TSHR mutation is yet known to cause pituitary tumours; moreover, TSHR mutations are unlikely do so, as TSH is secreted by the pituitary and acts at the periphery.

ACTH is secreted by the pituitary gland and acts peripherally at the ACTHR (currently known as melanocortin 2 receptor (MC2R[3])) in the adrenal glands to induce adrenal steroid synthesis. An inactivating, germline mutation in MC2R was shown to cause familial glucocorticoid deficiency in 25% of patients with this disease[12]. A deletion of MC2R was found in two very aggressive undifferentiated adrenocortical tumours[13]. Adrenal tumours have not been found to harbour gain-of-function mutations of MC2R[3,14,15]. No MC2R mutation is known to cause pituitary tumours.

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