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Animal models of multiple endocrine neoplasia

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Multiple endocrine neoplasia (MEN) syndromes

Multiple endocrine neoplasia (MEN) syndromes are autosomal dominant diseases with high penetrance characterized by proliferative lesions (usually hyperplasia or adenoma) arising in at least two endocrine tissues (Walls 2014). Four different MEN syndromes have been so far identified: MEN type 1 (MEN1), MEN2A (also referred to as MEN2), MEN2B (or MEN3) and MEN4, which have slightly varying tumor spectra and are caused by mutations in different genes (Thakker 2014). MEN1 associates with loss-of-function mutations in the *MEN1* gene encoding the tumor suppressor menin (Lemos and Thakker 2008). The MEN2A and MEN2B syndromes are due to activating mutations in the proto-oncogene *RET* (Rearranged in Transfection) and are characterized by different phenotypic features of the affected patients (Walls 2014). MEN4 was the most recent addition to the family of the MEN syndromes. It was discovered less than 10 years ago thanks to studies of a rat strain that spontaneously develops multiple endocrine tumors (named MENX). These studies identified an inactivating mutation in the *Cdkn1b* gene, encoding the putative tumor suppressor p27, as the causative mutation of the rat syndrome (Pellegata et al. 2006). Subsequently, germline mutations in the human ortholog *CDKN1B* were also found in a subset of patients with a MEN-like phenotype and this led to the identification of MEN4.

Small animal models have been instrumental in understanding important biochemical, physiological and pathological processes of cancer onset and spread in intact living organisms. Moreover, they have provided us with insight into gene function(s) and molecular