Melatonin exerts direct inhibitory actions on ACTH responses in the human adrenal gland

Campino, C.

Valenzuela, F. J.

Torres-Farfan, C.

Reynolds, H. E.

Abarzua-Catalan, L.

Arteaga, E.

Trucco, C.

Guzmán, S.

Valenzuela, G. J.

Seron-Ferre, M.

In nonhuman primates and rodents, melatonin acting directly on the adrenal gland, inhibits glucocorticoid response to ACTH. In these species, an intrinsic adrenal circadian clock is involved in ACTH-stimulated glucocorticoid production. We investigated whether these findings apply to the human adrenal gland by determining i) expression of clock genes in vivo and ii) direct effects of melatonin in ACTH-stimulated adrenal explants over a) expression of the clock genes PER1 (Period 1) mRNA and BMAL1 [Brain-Muscle (ARNT)-like] protein, ACTH-induced steroidogenic acute regulatory protein (StAR), and 3?-hydroxysteroid dehydrogenase (3?-HSD) and b) over cortisol and progesterone production. Adrenal tissue was obtained from 6 renal cancer patients undergoing unilateral nephrectomy-adrenalectomy. Expression of the clock genes PER1, PER2, CRY2 (Cryptochrome 2), CLOCK (Circadian Locomotor Output Cycles Kaput) and BMAL1, was investigated by RT-PCR in a normal adrenal and in an adenoma. In independ