Diurnal: Developing Circadian Hormone Therapy to Improve Health

Humans have a clock located in the centre of the brain that regulates physiology to synchronise the body to the environmental 24 hour night day cycle and our associated fast feed behaviour. The body clock regulates physiology through the circadian (around the day) release of hormones whose rhythms control metabolism. Jet lag demonstrates the importance of these hormone rhythms as de-synchronisation, when moving through time zones, causes symptoms such as insomnia, sleepiness, loss of appetite, and fatigue. Diseases that result in loss of hormone rhythms are associated with all the symptoms of jet lag, and patients are unable to work and have an increased morbidity and mortality.

Cortisol, the ‘stress hormone’, has a distinct circadian rhythm that is essential to control our metabolism. Cortisol levels build overnight and peak early in the morning, providing us with energy and the ability to manage the stress and challenges of daily life. As a ‘stress hormone’, it has a critical role in combating infections or other sources of physical and mental stress. Cortisol is produced by the adrenal glands and patients with adrenal insufficiency (Addison’s Disease and Congenital Adrenal Hyperplasia among other causes) lose the cortisol rhythm and are at risk of death from an adrenal crisis. In these patients, hormone replacement with cortisol (hydrocortisone) is required. However, the formulations currently available do not mimic the natural circadian rhythm and patients with adrenal Insufficiency suffer from fatigue and a reduced quality of life associated with increased morbidity and mortality.

Prof Richard Ross is Professor of Endocrinology and Head of the Unit of Diabetes, Endocrinology and Metabolism at the University of Sheffield, and CSO of Diurnal Ltd. He saw the potential for generating a cortisol medication that would more closely replicate the natural cortisol circadian rhythm and better help his patients suffering from adrenal insufficiency or congenital adrenal hyperplasia. In 2004, Diurnal Ltd was spun-out from the University of Sheffield to address this major unmet need by optimising the therapeutic performance of approved drugs for hormone-related disorders.

The company now has a number of products in development including Chronocort® (circadian release cortisol with 2 orphan drug designations), Infacort® (a paediatric formulation of hydrocortisone being developed via European Commission funding), Rheumacort®, for the steroid treatment of rheumatoid arthritis, circadian native oral testosterone for the treatment of hypogonadism and Tri4Combi™, which is expected to be the first physiological combination therapy of the thyroid hormones T3 and T4 for patients suffering from hypothyroidism. Phase II trials for Chronocort® started in 2012 and completion is anticipated in 2013.

To date Diurnal Ltd (www.diurnal.co.uk) has successfully raised over £4M for development of its drug product portfolio and the University of Sheffield in collaboration with Diurnal Ltd and partners has been awarded a EU Framework 7 grant worth €5.6 M; TAIN (www.tain-project.org).

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