Since 2004 Diurnal Ltd, a University of Sheffield spin-out company has been developing better therapies for people with hormone-related disorders. Professor Richard Ross, Professor of Endocrinology, Head of the Unit of Diabetes, Endocrinology and Metabolism, and Chief Scientific Officer at Diurnal Ltd, saw the potential for generating a cortisol medication that would more closely replicate the natural cortisol circadian rhythm.

Overview

Our metabolisms synchronise with the night–day cycle using an internal ‘clock’ that releases hormones to a circadian rhythm. When this body clock and the environment become de-synchronised, we feel unwell. Ever had jet lag? Moving through time zones disrupts the release of hormones to a circadian rhythm and can cause insomnia, sleepiness, loss of appetite and fatigue. Diseases that affect hormonal rhythms have all the symptoms of jet lag, reducing patients’ life quality and expectancy.
The challenge

Conditions including Addison’s Disease and Congenital Adrenal Hyperplasia affect the adrenal glands, which produce the ‘stress hormone’ cortisol. Cortisol has a distinct circadian rhythm that builds hormone levels overnight and peaks early in the morning so we can meet the challenges of daily life. It also has a critical role in combating infections or other sources of physical and mental stress.

People with adrenal insufficiency are not only lacking in cortisol but also lose its circadian rhythm. They can be treated with hydrocortisone hormone replacement therapy, but current formulations don’t mimic the body clock’s natural synchronicity with the environment. Diurnal Ltd specifically addresses this major unmet need.

What happened

Drawing on its expertise in circadian-based endocrinology and drug delivery, the company focuses on optimising the therapeutic performance of approved drugs. It finds new ways to use existing drugs that have well-established profiles of safety and efficacy.

Products under development are:
- Chronocort®, circadian release cortisol with 2 orphan drug designations
- Infacort®, a paediatric formulation of hydrocortisone Rheumacort®, for the steroid treatment of rheumatoid arthritis
- circadian native oral testosterone for the treatment of hypogonadism
- Tri4Combi™, which is expected to be the first physiological combination therapy of the thyroid hormones T3 and T4 for people suffering from hypothyroidism

The future

So far, Diurnal Ltd has attracted venture capital of over £4m for the development of its drug product portfolio. Phase II trials for Chronocort® started in 2012, should complete in 2013 and will lead to a submission of market authorisation by the end of 2017. Diurnal Ltd is also a major partner in the TAIN Project, investigating the treatment of adrenal insufficiency in neonates and infants. TAIN has been awarded an EU Framework 7 grant worth €5.6m to develop Infacort®, a new hydrocortisone therapy for babies up to two years old.

Professor Richard Ross said: “Diurnal Ltd is addressing the unmet needs of patients with rare and common hormone deficiencies. By providing physiological hormone replacement therapy we hope to improve the quality of life and health of millions of patients world-wide.”

Find out more at www.diurnal.co.uk and www.tain-project.org.