Potential new treatment for a group of childhood diseases

A new treatment for a currently incurable group of inherited neurological diseases that affect 1 in 10000 children has been revealed, which works by triggering the body's own 'recycling' system. New research by scientists at Orphazyme ApS, published in Science Translational Medicine, reveals a promising method to treat several diseases in the *sphingolipidoses* family of *lysosomal storage diseases*. These debilitating disorders, including Niemann-Pick type C, Fabry, and Sandhoff diseases, involve the accumulation of *sphingolipids* (fat molecules) in the cells and are often fatal during early childhood.

Image from http://stm.sciencemag.org/ on 8 September 2016

Healthy cells have disposal pathways to remove waste products. However, in lysosomal storage diseases, enzymes which should breakdown waste products either don't function or aren't produced at all: leading to a toxic accumulation of waste in the cells. This causes the cells stress, so they stop working properly. Orphazyme researchers together with leading academic experts in the field have shown that a natural stress response protein, called heat shock protein 70 (HSP70) assists cells in breaking down and disposing of accumulating sphingolipids. Using cell and animal models of the three diseases (Niemann-Pick type C, Fabry, and Sandhoff) the team demonstrated that treatment with purified HSP70 reduces the sphingolipid build up and thus the associated symptoms of disease. In a further investigative step, the team showed that a drug called arimoclomol, which stimulates diseased cells to produce their own HSP70, also reduced the accumulated sphingolipids and dramatically improved the disease symptoms. Orphazyme's Chief Scientific Officer Dr Thomas Kirkegaard Jensen said, "This is a great discovery which holds promise for a number of terrible, currently untreated childhood diseases. Our aim is to bring a new class of efficacious drugs to these patients and their families, to make a meaningful difference in their lives."

For patients suffering from sphingolipidoses, waste lipids accumulate in, and damage, all major organs, particularly the brain and nerve cells. Symptoms can include loss of motor function (ataxia), renal failure, seizures, excruciating pain and sight loss. The current treatment options are extremely limited and variable in effect; in many cases the only available approach is to manage pain levels and other symptoms. Based on this exciting discovery, arimoclomol is currently being tested in a clinical trial for treatment of Niemann-Pick type C (see www.AIDNPC.com), as well as for other neurodegenerative diseases such as sporadic inclusion body myositis (sIBM) and amyotrophic lateral sclerosis (ALS/Lou Gehrigs disease). Read the paper at http://stm.sciencemag.org/content/8/355/355ra118

About Orphazyme

Orphazyme ApS is a Danish biopharmaceutical company, which develops paradigm-changing medicines for the treatment of genetic diseases. The lead program is in development as a treatment for lysosomal storage diseases. This family of genetic disorders includes Niemann-Pick disease type C and consists of more than 45 diseases, often affecting children, most of whom are currently untreatable. Orphazyme is backed by leading European VCs. The strong investor syndicate includes Novo A/S, Sunstone Capital, Aescap Venture, Kurma Partners and Idinvest Partners. For more information visit www.orphazyme.com.

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