

Heat shock protein to the rescue for Niemann-Pick type C, Fabry and Sandhoff diseases

A potential treatment for the currently incurable neurological diseases Niemann-Pick type C (NPC), Fabry and Sandhoff has been revealed this week. Research by scientists at Orphazyme ApS, together with leading academic experts, shows a potential method to treat this group of *sphingolipidoses* diseases using heat shock protein-based therapy with a drug called Arimoclomol. These debilitating disorders, which are part of the wider family of lysosomal storage diseases (LSDs), involve the accumulation of *sphingolipids* (fat molecules) in the cells and are often fatal during early childhood. Arimoclomol works by triggering the body's own stress response and could prove a significant medical advance for the 1 in 10,000 children with these diseases. The study was published in Science Translational Medicine and was featured on the front page of the journal.

Healthy cells have disposal pathways to remove waste products, but in lysosomal storage diseases, enzymes which should break down waste products either don't function or aren't produced at all. This leads to a toxic accumulation of waste in the cells and causes the cells stress, so they stop working properly.



Image from <http://www.sciencemag.org/> on 7 September 2016

A natural stress response protein, called heat shock protein 70 (HSP70) helps cells to break down and dispose of accumulating sphingolipids. Using cell and animal models of the three diseases (NPC, Fabry, and Sandhoff), the team demonstrated that treatment with purified HSP70 reduces the sphingolipid build up. Importantly, the team then showed that the drug arimoclomol, which stimulates cells to produce their own HSP70, also reduces the accumulated sphingolipids and dramatically improves 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." Based on this exciting discovery, arimoclomol is currently being tested in a clinical trial for treatment of NPC (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). You can read the paper at: <http://stm.sciencemag.org/content/8/355/355ra118> and hear more about our research at the NPUK 23rd Annual Family Conference, 16th – 18th September 2016.

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, including Niemann-Pick type C, 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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