Therapeutic Management of Menkes Disease and Related Copper Transport Disorders

Summary (1024-character limit)

The Section on Translational Neuroscience of NICHD seeks parties interested in licensing and/or collaborative research to co-develop this therapeutic management of Menkes Disease and related copper transport disorders.

NIH Reference Number

E-062-2015

Product Type

- Therapeutics

Keywords

- occipital horn syndrome

Collaboration Opportunity

This invention is available for licensing.

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Description of Technology

The only currently available treatment for Menkes disease, subcutaneous copper histidinate injections, is successful only in patients with ATP7A gene mutations that do not completely corrupt ATP7A copper transport function (estimated 20-25% of affected patients) and when started at a very early age (first month of life). The combination of viral gene therapy with copper injections provides working copies of the ATP7A copper transporter into the brain, together with a source of the substrate (copper) needed for proper brain growth and clinical neurodevelopment.

Codon-optimized nucleic acids encoding a reduced-size ATP7A protein and compositions of AAV vectors were discovered by NICHD researchers along with methods of administering this therapy. Human P-type ATPase copper-transporting ATPase 1 (ATP7A) transports copper from enterocytes (where it is taken up from dietary copper) into the blood. ATP7A also mediates passage of copper across the blood-cerebrospinal fluid (CSF) barrier and the blood-brain barrier. In Menkes disease and occipital horn syndrome (OHS), copper accumulates in intestinal cells and less copper is absorbed into the blood,

resulting in restricted copper supply to other tissues, particularly the brain. Death in infancy or early childhood is a common consequence. Therapeutic delivery of the copper transport protein via an AAV vector, combined with subcutaneous copper histidinate treatment will relieve the copper deficiency to the brain and permit normal neurological development and function.

Potential Commercial Applications

- Treatment of Menkes Disease, Occipital Horn Syndrome, and of ATP7A-related distal motor neuropathy

Competitive Advantages

Provides working copies of the ATP7A copper transporter into the brain, together with a source of the substrate (copper) needed for proper brain growth and clinical neurodevelopment.

Inventor(s)

Stephen G. Kaler M.D. (NICHD)

Development Stage

- Pre-clinical (in vivo)

Publications

Donsante A, et al.: ATP7A gene addition to the choroid plexus results in long-term rescue of the lethal copper transport defect in a Menkes disease mouse model. Molecular Therapy 19:2114-2123, 2011

Kaler SG: The neurology of ATP7A copper transporter disease: emerging concepts and future trends. Nature Reviews Neurology 7:15-29, 2011

Kaler SG, et al.: Neonatal diagnosis and treatment of Menkes disease. N Engl J Med 358:605-614, 2008.

Patent Status

- **U.S. Patent Filed:** U.S. Patent Application Number 62/244,594, Filed 21 Oct 2015