LYPLA1, a depalmitoylase, identified as Huntington disease target

BY CLAIRE QUANG, STAFF WRITER

APR 29, 2021 | 3:08 PM PDT

DISEASE CATEGORY: Neurology

INDICATION: Huntington disease

Blocking depalmitoylase LYPLA1 could treat Huntington disease by mitigating the BDNF transport impairment that contributes to corticostriatal damage. In cultured cortical neuron precursors generated from patient-derived induced pluripotent stem cells, an LYPLA1 inhibitor tool compound restored trafficking of BDNF-containing vesicles. In a corticostriatal network-on-a-chip disease model, the LYPLA1 inhibitor restored the trafficking of vesicles along the axons, BDNF release at the synapse and numbers of corticostriatal synapses. In mice modelling Huntington disease, the LYPLA1 inhibitor increased synapse numbers, restored motor coordination and reduced anxiety- and depression-related behaviors.

TARGET/MARKER/PATHWAY: Lysophospholipase 1 (LYPLA1; APT1); brain-derived neurotrophic factor (BDNF)

EXPERIMENTAL SYSTEM: Cell culture; mice

LICENSING STATUS: Patent and licensing status unavailable

PUBLICATION DETAILS: Virlogeux, A. et al. *Sci. Adv.*; published online March 31, 2021

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shRNA-based AAV gene therapy for Charcot-Marie-Tooth disease

BY CLAIRE QUANG, STAFF WRITER

APR 29, 2021 | 2:50 PM PDT

DISEASE CATEGORY: Neurology

INDICATION: Neuropathy

A PMP22-targeting gene therapy could treat Charcot-Marie-Tooth disease 1A, a demyelinating neuropathy caused by PMP22 duplication. In a rat model, bilateral sciatic nerve injection of an adeno-associated virus serotype 2/9 (AAV2/9) vector expressing an shRNA against PMP22 increased myelinated fiber density, nerve conduction velocity and large myelinated axon numbers. The AAV gene therapy also reduced disease-associated myelin sheath defects and PMP22 protein levels in sciatic nerve lysates, and prevented motor and sensory defects. Next steps include creating a newco, Nervosave Therapeutics, and seeking partners to develop the therapy, which has been named NVO-101.

UGISense AG has an antisense therapy targeting PMP22 in preclinical development for Charcot-Marie-Tooth disease 1A.

TARGET/MARKER/PATHWAY: Peripheral myelin protein 22 (PMP22)

EXPERIMENTAL SYSTEM: Rats

LICENSING STATUS: Patented; available for partnering

PUBLICATION DETAILS: Gautier, B. et al. *Nat. Commun.*; published online April 21, 2021

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