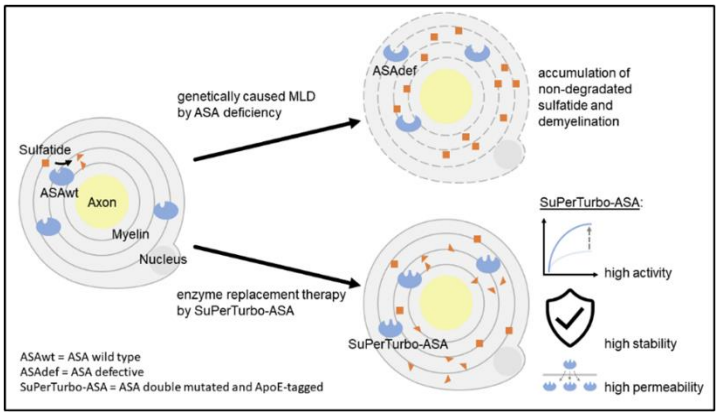
Novel therapy for Metachromatic Leukodystrophy

A SuPerTurbo-ASA – An engineered enzyme for use in gene therapy and enzyme replacement therapy

Invention

Metachromatic leukodystrophy (MLD) is a lysosomal storage disease caused by the deficient activity of arylsulfatase A (ASA). ASA catalyzes the degradation of myelin lipid sulfatides. In patients suffering from MLD, sulfatides are not metabolized, accumulate strongly in cells of the nervous system and cause demyelination. Severe neurological symptoms are the result and lead to death. A treatment option for preserving neuronal integrity would be a gene therapy or an enzyme replacement therapy by a double mutated and ApoE-tagged version of ASA (SuPerTurbo-ASA).



Commercial Opportunities

SuPerTurbo-ASA is the subject-matter of two pending patent applications and can be licensed for the development and commercialisation of a gene therapy or/and an enzyme replacement therapy for MLD patients.

Current Status

	Activity purified enzymes	Half life		Cellular uptake (BBB model)	Therapeutic activity	
		serum (*in vitro*)	intracellular		sulfatide reduction in brain	sulfatide reduction in spinal cord
ASAwt	1	1	1	1	1	1
SuPerTurbo-ASA	x3.3	x7.2	x3.7	x9.5	x7.5	x12.2

SuPerTurbo-ASA has unique features, and a wide range of analyses have already been made. Most importantly SuPerTurbo-ASA is 8- to 12-fold more efficient in removing sulfatide storage from the central nervous system of MLD mice (analyzed in brain and spinal cord) than wildtype ASA.

Altered immunogenicity of SuPerTurbo-ASA has not been detected. This was investigated in a humanised mouse model of MLD with specific immunotolerance to human ASA. Repeated intravenous injections of recombinant human ASAwt or SuPerTurbo-ASA did not induce any side effect in this mouse model whereas murine ASAwt, used as a control, elicited anaphylactic reactions indicated by scratching, decreased cage activity and increased respiratory rate. This points to the fact that the murine immune system cannot differentiate SuPerTurbo-ASA from human ASAwt which may be due to the absence of novel epitopes in SuPerTurbo-ASA.

Relevant Publications

Simonis, H., et al. (2019); *Human Molecular Genetics*, 28(11): 1810-1821.
Böckenhoff, A, et al. (2014) *Journal of Neuroscience*, 34(9): 3122-3129.
Yaghootfam, C. et al. (2023) Engineered arylsulfatase A with increased activity, stability and brain delivery for therapy of metachromatic leukodystrophy, *Molecular Therapy*, 31 (10): 1-13.

An invention of University of Bonn.

Competitive Advantages

- increased transfer across the blood-brain barrier
- increased catalytic rate
- increased half-life and time of operation

Technology Readiness Level

1234**5**6789

Technology validated in lab

Industries

- Pharmaceutical

Ref. No.

4783-5986

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