NOVEL THERAPEUTIC FOR MLD

Ref-Nr: TA-4783

HINTERGRUND

Metachromatic leukodystrophy (MLD) is a genetic lysosomal accumulation disease caused by the deficiency of the enzymatic activity of arylsulfatase A (ASA). This enzyme hydrolyzes 3-O-sulfogalactosyl ceramide (sulfatide) to galactosylceramide and sulfate. Sulfatide is a sphingolipid of the myelin sheath of axons and thus important for nerve cell function. However, impaired lysosomal degradation of sulfatide by a reduction or loss of ASA activity leads to an accumulation of this sphingolipid, which results in progressive demyelination. Consequently, the patients show increasing neurological deficits and eventually die.

LÖSUNG

The inventors have developed an engineering approach for the therapy of MLD: By exchanging three amino acids, the activity of the wildtype human ASA polypeptide could be increased approximately 5-fold. When tested by intravenous enzyme replacement therapy (ERT) of MLD-mice, the triple mutant ASA reduced sulfatide storage in MLD mouse brain 3.4-fold more efficiently than wildtype ASA, resulting in a storage reduction of approximately 50%. Previous clinical studies have demonstrated the feasibility of enzyme compensation therapy for treating MLD. However, it became clear that large amounts of enzyme need to be administered thereby potentially causing significant side-effects. These problems are overcome by the present approach.
VORTEILE

- novel approach for treating MLD
- demonstrated proof of concept: exceeds clearance seen in previous ERT trials by far
- lower amounts of enzyme need to be administered → to expect significantly fewer side effects compared to previous studies

ANWENDUNGSBEREICHE

The mutated enzyme are offered for licensing.

SERVICE

The researcher have generated mouse models for MLD and have validated in vivo efficacy of their therapeutic approach. In case of interest we are pleased to inform you about the patent status.
PUBLIKATIONEN & VERWEISE
