NOVEL THERAPEUTICS FOR MLD – TWO COMPLEMENTARY APPROACHES FOR THE TREATMENT OF METACHROMATIC LEUKODYSTROPHY

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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.

PROBLEMSTELLUNG

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.

LÖSUNG

The inventors have developed two novel and complementary approaches for the treatment of MLD: The first approach is based on the natural products Epicoccolid B and Epipyrone, which are derived from the mold fungus Epicoccum nigrum. These compounds inhibit the cerebroside-sulfotransferase, which is an enzyme that generates sulfatide. Thereby, the sulfatide concentration is lowered. In addition (second approach) the researchers have exchanged certain amino acids of human ASA resulting in a much higher enzymatic activity.
**VORTEILE**

- Novel and complementary approach for treating MLD
- Demonstrated proof of concept

**ANWENDUNGSBEREICHE**

The researcher have generated mouse models for MLD and have validated in vivo efficacy of their therapeutics.

**SERVICE**

In case of interest we are pleased to inform you about the patent status.

**PUBLIKATIONEN & VERWEISE**
