Antibodies to **slow ALS**

BioArctic is conducting two development projects with selective antibodies for the protein TDP-43. The goal is to produce a drug that treats the underlying cause of ALS, thereby slowing the progress of the disease.

People suffering from ALS can expect a rapid degeneration of the motor neurons, the nerve cells in the central nervous system that control the body's muscle activity. The onset age for ALS is normally around 60, but the disease can also affect younger people. Current treatments for ALS may relieve more severe symptoms such as muscle spasms and pain, and to some extent modify the progress of the disease, but there are no cures for ALS, which makes the need for new and efficacious treatments both significant and urgent.

TDP-43 aggregates in the brains of ALS patients

ALS emerges in the motor neurons of the brain, the brain stem, and the spinal cord, which control the body's movements. As with many other degenerative neurological diseases, the impact of ALS on the motor neurons is linked to an inflammation in the nerve cells. Despite many years of intensive research, the process that leads to ALS has not yet been successfully elucidated, but what is known is that aggregates of the TAR DNA-binding protein TDP-43 are a contributing factor in the progress of the disease. Inclusion bodies are found in the brains of individuals with ALS with accumulations of TDP-43 aggregates, and a growing mass of data shows a clear link between TDP-43 aggregates and degeneration of motor neurons. Not only do the protein accumulations hinder the normal function of TDP-43, but they also disrupt various cellular processes, which leads to the nerve cells rapidly dying off. TDP-43 aggregates have also been shown in many patients with other neurological diseases, including contemporaneous dementia and Alzheimer's disease.

Selective antibodies at an early stage

In its ND3014 project, BioArctic is endeavoring to develop selective antibody treatments that target TDP-43. Antibodies make it easier to eliminate the toxic aggregates of misfolded protein, which it is hoped will have a slowing effect on the progress of the disease. Similar to BioArctic's drug candidates for Alzheimer's disease and Parkinson's disease, the antibodies in the ND3014 project target aggregates of misfolded TDP-43 since these forms are regarded as the most harmful to the nerve cells. BioArctic is also pursuing the ND-BT3814 project,

in which an antibody against TDP-43 is being tested in combination with the company's BrainTransporter technology that facilitates the passage of antibodies across the blood-brain barrier. Both projects are currently in the research phase.

Developed as an orphan drug

ALS is classified as a rare disease, which means that drugs against the disease are developed as orphan drugs. However, a certain increase in incidence has been observed in recent years. As a consequence of the increasing average age among the world's population, the number of individuals with ALS is expected to exceed 375,000 globally by 2040, corresponding to an increase of 69 percent compared with 2015. A number of the patients affected are in mid-life and of working age when they fall ill, which means major costs to society. In the US, the cost of ALS is estimated to total over USD 280 million per year. The costs per affected individual are higher for ALS than for other neurological diseases, which underscores the need for medical advances in the field.

ALS in brief

Amyotrophic lateral sclerosis, or ALS, is a neurodegenerative disease that often progresses rapidly. The brain loses the ability to initiate and control the muscles in the body in pace with the motor neurons dying off. When voluntary muscle movement can no longer be controlled, the ability to speak, eat, move, and breathe is affected. The most common cause of death in ALS is respiratory failure. On average, a person dies within three to five years after the initial presentation of symptoms, but certain forms of ALS develop more slowly; in these cases, the patient can live with the disease for over ten years.

150 000

fall ill with ALS every year around the world