CNTF-analogue with improved side-effect profile for weight control

General

Human ciliary neurotrophic factor (CNTF) is a neurotrophic cytokine that exerts a neuroprotective effect in multiple sclerosis and amyotrophic lateral sclerosis. Furthermore, CNTF induces weight loss and improves glucose tolerance in humans. Clinical application of human CNTF and CNTF-analogues, however, has been prevented by a number of adverse side-effects.

State of the art

Human CNTF elicits cellular responses by induction of a receptor complex consisting of the CNTF-receptor (CNTFR), and the alpha-receptors gp130 and leukemia inhibitory factor receptor (LIFR). Furthermore, human CNTF can use both the membrane-bound and the soluble human interleukin-6-receptor (IL-6R) as a substitute for its cognate-receptor. This may be the reason behind some of the observed IL-6-related side-effects of the systemic application of CNTF such as pyrogenic action and acute-phase response in the liver.

A CNTF-analogue, Axokine (Regeneron), was tested as drug against obesity but was not commercialized due to the observed antibody production during clinical trials. CNTF displays a B-cell- and thus immunostimulating action due to the activation of the IL-6R. The observed antibody formation may thus also be caused by the ability of the administered CNTF-analogue to activate the IL-6R.

Engineering a CNTFR-specific human CNTF-variant appears as a prerequisite to avoid IL-6R-related side-effects, thus enabling to improve the safety profile of CNTF and allowing to reinvestigate its clinical benefits.

The invention

A single mutation leads to a novel CNTF-analogue that is unable to interact with the IL-6 receptor. Due to that inability, the CNTFR-specific analogue is a choice candidate to be used in the therapy of a number of neurodegenerative diseases and/or to regulate body weight without IL-6R-related side-effects.

Utilisation concept

Licensing/selling of this invention is sought to a company that will produce, bring to market and distribute the described CNTF-analogue. If desired PVA SH GmbH will further assist by arranging contact with the inventors.

IP DE 10 2011 104 822.0, EP 12727648.3, US 14/127,460 pending.

Contact

PVA SH GmbH
Dr. Alexandra Baumgartner
Wissenschaftszentrum
Fraunhoferstr. 13
24118 Kiel
Germany

Tel.: +49 (0431) 800 99 37
Fax : +49 (0431) 800 99 33
Email: baumgartner@pva-sh.de