Regulation, stimulation, and inhibition of glial cell-derived neurotrophic factor (GDNF) expression

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Tech Ventures Reference: IR 2515, 2518 Glial Cell-Derived Neurotrophic Factor Expression, Delivery and Use Glial cell-derived neurotrophic factor (GDNF) is a target-secreted neuroprotective, neurotrophic, and neuromodulatory factor. GDNF therapy has been shown to yield promising results in treating neurodegenerative diseases. GDNF can affect the mesolimbic dopaminergic pathway, which is associated with drug addiction and hyper-dopaminergic psychiatric conditions such as Schizophrenia. Additionally, GDNF therapy holds promise as a treatment option for antidepressant resistant major depression. However, challenges exist in the therapeutic use of GDNF, including the delivery of GDNF protein into the brain, GDNF expression from viral vectors, and the use of encapsulated GDNF producing cells.

Altering GDNF and CNTF by Manipulation of Sonic Hedgehog Mediated Cell Signaling The development of small molecules that specifically activate the GDNF receptor or induce the expression of GDNF itself in relevant tissues and can be administered systemically would overcome most of the problems mentioned above. This technology demonstrates that the manipulation of sonic hedgehog (Shh) mediated cell signaling causes predictable alterations in GDNF and CNTF (ciliary neurotrophic factor, a potent survival factor for neurons and oligodendrocytes) expression in the adult animal. Existing and to be developed pharmacology targeting the Shh signaling pathway can hence be utilized to either induce or inhibit endogenous expression of GDNF.

Applications: • Neurodegenerative diseases (Parkinson’s Disease, Amyotrophic Lateral Sclerosis, Alzheimer’s, Supra Nuclear Palsy and others) • Dopaminergic hyperactivity like Psychoses (Schizophrenia and others) • Addiction (cocaine, alcohol and others) • Preparations of neuronal extracts and cell suspensions for dopaminergic and cholinergic replacement therapies

Advantages: • Crosses blood brain barrier and overcomes need for direct brain perfusion by cannulae • Overcomes poor diffusion in brain tissue • Has no associated immunogenicity • Modulation of GDNF expression occurs at disease relevant, endogenous sources

Patent Status: Patent Pending

Licensing Status: Available for Licensing and Sponsored Research Support

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