

Super Active Leptin Antagonists with Increased Biological Activity for Treatment of Autoimmune Diseases and CKD associated Cachexia (Yissum)

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Categories	Superactive High Afinity Leptin antagonist, mutein, multiple sclerosis, inflammatory bowel syndrome, rheumatoid arthritis, fibrosis, cardiovascular disease, CKD Cachexia, Osteoarthritis
Development Stage	(1) In vivo tests in animal (mouse) models, (2) Preparation of second generation of antagonists with increased affinity toward leptin receptor and longer in vivo persistence in circulation
Patent Status	Patent number application: WO2011/132189A3
Market Size	\$20B

Highlights

- Advances treatment of many diseases by blocking undesired leptin effects
- Interacts with mammalian leptin receptor with affinity identical to non-mutated leptins
- Can be easily prepared in large quantities as recombinant protein expressed in E. coli
- Effectiveness established in three mice models of human acute and chronic fibrosis

Our Innovation

- Recombinant leptin mutein acts as antagonist
- Isolated DNA molecule encoding super active leptin antagonist
- Strong potential for pharmacologic agent for CKD (Chronic Kidney Disease) associated cachexia, autoimmune and inflammatory diseases, cancers, and cardiovascular disease, among others
- Substitution of two to four amino acid residues of leptin to alanine converts agonist to antagonist without reducing affinity toward leptin receptor

The Opportunity

- Addresses multiple markets for treatment of multiple disease entities, specifically, CKD associated cachexia
- Expands various research fields stressing proteins that inhibit leptin activity

Development Milestones

- Testing super active leptin antagonist activity in additional in vivo models e.g., Cachexia Inflammatory Bowel Disease in mice or others
- Preparation of leptin antagonists with more potent activity in vivo

Additional Information

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- Shpilman M, Niv-Spector L, Katz M, Varol C, Solomon G, Ayalon-Soffer M, Boder E, Halpern Z, Elinav E, Gertler A. [Development and characterization of high affinity leptins and leptin antagonists.](#) J Biol Chem. 286:4429-42 (2011).
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- W.W. Cheung et. al A Pegylated Leptin Antagonist Ameliorates CKD-Associated Cachexia in Mice. J. Am. Soc. Nephrol 25:119-282 (2014).

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