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NRC Institute for Biological Sciences

Novel Peptide(s) for the Treatment of Alzheimer Disease

The Business Opportunity

Alzheimer's disease (AD) is a progressive, neuro-degenerative disease that primarily affects people over 65 years of age, with an incidence rate that doubles for every 5 years after that.

Currently available therapies are symptomatic - there are no effective disease-modifying treatments. Currently marketed Alzheimer's therapeutics have sales exceeding $5B, but the cost of treating and caring for these patients is estimated to be as high as USD $100 billion a year. With the first baby boomers scheduled to turn 65 in 2011, the problem can only get worse, leaving a great need to identify more effective drugs for treatment and prevention of AD.

NRC-IBS discovered novel peptide(s) with strong potential for therapeutic and diagnostic applications in AD.

The Technology

One of the hallmarks of Alzheimer's disease (AD) is the accumulation of ß-amyloid (Aß) in the brain, particularly in senile plaques and cerebral microvessels. A chronic imbalance in the production and clearance of Aß results in its accumulation, which in turn initiates a cascade of events that eventually lead to neuronal dysfunction and cell death. The evidence that the accumulation of Aß initiates AD pathology provides a framework for developing therapeutic strategies based on altering Aß accumulation. Agents that can sequester and/or promote Aß clearance have the potential to be more effective drugs to prevent or treat AD, respectively.

NRC-IBS technology that can be exploited for diagnosis and treatment of AD is based on a novel polypeptide that binds with high affinity physiologically relevant ß-amyloid, $Aß_{1-42}$ and $Aß_{1-40}$. By mapping the Aß-binding domain on this polypeptide, shorter peptides were generated and shown to:

- sequester Aß from solution, serum and plasma;
- reduce Aß aggregation;
- inhibit Aß binding to cellular proteins from normal and AD brains;
- inhibit cellular uptake of Aß in primary cortical neurons;
- reduce brain Aß burden in transgenic animal models of AD
- reduce behavioral deficits in transgenic animal models of AD
- transmigrate the blood-brain barrier (BBB) when conjugated (as fusion proteins) with the BBB-permeable single domain antibodies
- be non-toxic after escalating doses *in vivo*

Therefore, these peptides can potentially be used as AD diagnostic or AD disease-modifying therapeutics acting as:

- a "sink" to sequester and facilitate the clearance of soluble Aß in circulation to reduce Aß burden.
- "decoy" peptides to disrupt the pathological interaction of Aß with intra- or extra-cellular proteins.

Furthermore, Aβ-binding peptides (ABPs) can be engineered to cross biological membranes and access intracellular Aß. This is particularly important since intracellular Aß is believed to play a major role in synaptic dysfunction and neurodegeneration well before the accumulation of insoluble Aß in senile plaques.

Patent Position

Patents Pending – PCT. NRC IBS Case 11630

The Market

AD is the predominant cause of progressive intellectual and cognitive failure in the aging population and claims over 100,000 lives a year, making it the 4th leading cause of death in adults. In the US, Alzheimer's disease (AD) affects about 15% of the population over 65 years of age, and over 40% of people over 80 years of age. The projected maket for AD is over $7.8B in 2010, with a bigger potential market for a prophylactic treatment regimen once early-detection biomarkers are developed.

Technology Transfer Possibilities

- Development of this technology through a joint collaboration.

Contacts

Stacey Nunes
Tel.: (613) 993-9212
Business Relations
E-mail: stacey.nunes@nrc.gc.ca

Dr. Yves Geoffrion
Tel.: (613) 991-6377
Business Relations
E-mail: yves.geoffrion@nrc.gc.ca