**KUIC Technology Profile**

**Therapeutics for Alzheimer's Disease**

**Summary:**
Novel Cyclophilin D inhibitors to treat Alzheimer's and other neurodegenerative diseases.

**Overview:**
Alzheimer's Disease is a neurodegenerative disease, a hallmark of which is the accumulation of amyloid-beta (Alpha, Beta) oligomers in the synapses of mitochondria. This accumulation of amyloid-beta (Alpha, Beta) oligomers impairs various mitochondrial functions such as cellular respiration, energy metabolism and calcium homeostasis. In addition, amyloid-beta accumulation affects the permeability of the Mitochondrial Permeability Transition pore (mPTP). Amyloid-beta-induced dysfunction of the mitochondria is believed to be one of the mechanisms through which Amyloid-beta accumulation causes toxicity in Alzheimer's Disease. Cyclophilin D (CypD) is an isomerase associated with the mitochondrial membrane that is overexpressed in Alzheimer's Disease. CypD is known to play a central role in opening the mPTP, which can cause cell death. Together, this suggests that CypD may be a mediator of Amyloid-beta-induced toxicity in Alzheimer's Disease. Thus, a treatment that inhibits CypD may confer a therapeutic benefit on patients with Alzheimer's Disease by reducing or eliminating the toxic effects caused by Amyloid-beta oligomers accumulation.

**Application:**
These CypD inhibitors can be used in the treatment Alzheimer's Disease.

**How It Works:**
Studies have shown that treatment with CypD inhibitors reverse both impaired mitochondrial respiratory function and cell degeneration; both of which are caused by amyloid-beta peptide accumulation in mitochondrial synapses. The CypD inhibitors are effective in carrying out these functions because (1) they are soluble, (2) they are capable of passing the blood brain barrier, and (3) they are not toxic.

**Benefits:**
These inhibitors are capable of increasing mitochondrial respiratory function and cell viability, thus reducing the toxic effects caused by amyloid-beta peptide accumulation. Because these inhibitors carry out these functions, they could be used as a treatment to prevent the onset of Alzheimer's Disease or as a therapy to treat individuals with Alzheimer's Disease.

**Why It Is Better:**
Currently the only available therapies for Alzheimer's Disease is to treat symptoms that result from the disease. The current invention treats the underlying causes of the onset and progression of Alzheimer's Disease.

**Other Applications:**
Because CypD also plays a role in diabetes, these CypD inhibitors could be developed into a therapy that treats diabetes and complications that result from diabetes.

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