Neuroprotective Agents and Therapeutic Targets for Parkinson’s Disease

APPLICATION AREAS
Pharmaceutical Development

ABSTRACT
Parkinson’s disease (PD) is a neurodegenerative disorder that affects over six million people worldwide. Its most prominent symptoms, which result from the death of dopamine-producing cells, are related to movement, and include tremors, difficulty with walking, rigidity, and slow movement. Current treatments tend to merely control symptoms of Parkinson’s disease, while future therapeutic goals include the development of neuroprotective agents that slow disease progression or may even result in curing it.

ISU researchers have developed a portfolio of technologies with potential as neuroprotective agents for the treatment of PD and as targets for the development of novel therapies. This technology suite includes ISURF #’s 3172, 3411, 3655, and 3728. ISURF #3172 is an irreversible and competitive peptide inhibitor of the protein kinase C δ (PKCδ) cleavage site that demonstrates potent anti-apoptotic effects. This cell permeable inhibitor is more potent than the commonly used inhibitor Z-DEVD-fmk and has been shown to block caspase-3-dependent activation of PKCδ and DNA fragmentation in neuronal cell culture; neuronal protection has been demonstrated using Parkinson’s disease models. ISURF #3411 describes effects of a PKCδ inhibitor which increases dopamine synthesis and confers neuroprotective effects in PD animal models, while ISURF #3655 describes inhibition of neurotoxic cytokine release and production in microglial cells by this inhibitor. ISURF #3728 includes the design and synthesis of analogs of the inhibitor with simpler structures and increased activity that have been demonstrated to confer neuroprotection in cell culture models of PD.

REFERENCE(S)


| ISURF: 3172, 3411, 3728 |
INTELLECTUAL PROPERTY STATUS
A number of patents have issued or are pending for this portfolio of technologies, including:

- **US Patent No. 7,632,819**: Methods and compositions for inhibiting PKC delta cleavage for treatment and prevention of neurodegeneration and apoptosis
- **US Patent No. 8,653,023**: Dual beneficial effect of dopamine enhancing and neuroprotective actions of PKC delta inhibitors for treatment of Parkinson’s disease
- **US Patent No. 8,586,768**: Design, synthesis and functional characterization of rotterlin analogs
- **US 2011/0059174 A1**: PKC delta regulates neuroinflammatory events

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