Final Progress Report

SC SCIRF-11-002: Estrogen receptor agonist for treatment of spinal cord injury
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We recently finished our research on the above grant award. We successfully conducted all the experiments in cell culture and animal models as proposed in the Specific Aims of this spinal cord injury (SCI) grant. WE explored the therapeutic efficacy of estrogen (EST) receptor agonists in SCI. Therapeutic actions of EST are mediated via the EST receptor alpha (ERα) and the EST receptor beta (ERβ). Our study involved the use of propyl pyrazole triol (PPT, an agonist for ERα), diarylpropionitriile (DPN, an agonist for ERβ), and EST (an agonist for both ERα and ERβ) to determine the most suitable ER agonist for attenuating the inflammatory response and cell death in ventral spinal cord 4.1 (VSC4.1) motoneurons in culture (Specific Aim 1) and also in acute SCI in rats (Specific Aim 2). Our hypothesis for Specific Aim 1 was that post-treatment with an ER agonist would increase ER expression for mediation of neuroprotective effects in VSC4.1 motoneurons exposed to the pro-inflammatory cytokine tumor necrosis-alpha (TNF-α). Our results from the Specific Aim 1 demonstrated that post-treatment with PPT, DPN, and EST increased expression of ERα and ERβ in varying degrees leading to prevention of neurodegeneration in VSC4.1 motoneurons exposed to TNF-α. For Specific Aim 2, our hypothesis was that primary injury to spinal cord would lead to secondary injury causing gliosis, inflammation, and neurodegeneration but treatment of SCI in rats with the optimal dose of an ER agonist could inhibit inflammation, Ca²⁺ influx, Ca²⁺-dependent pathways, and mitochondrial damage to provide neuroprotection. Our results from the work on this Specific Aim 2 showed that activation of inflammatory and proteolytic pathways caused neurodegeneration in acute SCI in rats and treatment with PPT, DPN, and EST provided neuroprotective effects. We established that EST was the most effective EST receptor agonist for best neuroprotection in acute SCI in rats. Since this award in 2011, we published 8 peer-reviewed papers using the results generated from our studies in cell culture and animal models of SCI. In course of this funding period, we also presented 8 abstracts on our SCI related research in national and international scientific meetings. Moreover, this grant helped us generate interesting preliminary results for submission of a VA Merit grant on SCI. Our VA Merit grant did score and we planned its further submission to get it funded. Finally, we would like to sincerely acknowledge the funding from the SC SCIRF for our research accomplishments in the field of SCI.

Papers (our peer-reviewed publications on research in SCI since 2011):


Abstracts (our presentations on research in SCI since 2011):


