

STATE BOARD OF EQUALIZATION



Appeal Name: STATE-OF-THE-ART TECHNOLOGIES, INC.

Case ID: 521969 ITEM #: B9

Date: JUNE 21, 2011 Exhibit No: _____

TP FTB DEPT _____

pain^{7[5]}. Separately, constant C-fiber nerve stimulation to transmission pathways in the spinal cord results in even more release of inflammatory mediators but this time within the spinal cord.

Inflammation causes increased production of the enzyme cyclooxygenase-2 (Cox-2) and 5-lipoxygenase (5-LOX), leading to the release of chemical mediators both in the area of injury and in the spinal cord. Lipoxygenases (LOX) and cyclooxygenase (COX) enzymes can insert oxygen into the molecule of arachidonic acid and thereby synthesize inflammatory mediators leukotrienes [due to 5-lipoxygenase (5-LOX) activity] and prostaglandins (via COX activity)⁸. Widespread induction of Cox-2 expression in spinal cord neurons and in other regions of the central nervous system elevates inflammatory mediator prostaglandin E₂ (PGE₂) levels in the cerebrospinal fluid. The major inducer of central Cox-2 upregulation is inflammatory mediator interleukin-1^β in the CNS^{9[6]}. Basal levels of

^{7[5]} : Clin J Pain 1991;7 Suppl 1:S8-15

Pathophysiological mechanisms of fibromyalgia.

Zimmermann M.

⁸ FASEB J 2000 Jul;14(10):1464-9

Putative role of neuronal 5-lipoxygenase in an aging brain.

Manev H, Uz T, Sugaya K, Qu T.

^{9[6]}

Nature 410, 471 - 475 (2001) © Macmillan Publishers Ltd.
Interleukin-1-mediated induction of Cox-2 in the CNS

the enzyme phospholipase A₂ activity in the CNS do not change with peripheral inflammation. Abnormal development of sensory-sympathetic connections follows nerve injury, and contributes to the hyperalgesia (abnormally severe pain) and allodynia (pain due to normally innocuous stimuli). These abnormal connections between sympathetic and sensory neurons arise in part due to sprouting of sympathetic axons. Studies have shown that sympathetic axons invade spinal cord dorsal root ganglia (DRG) following nerve injury, and activity in the resulting pericellular axonal 'baskets' may underlie painful sympathetic-sensory coupling¹⁰. Sympathetic sprouting into the DRG may be stimulated by neurotrophins such as nerve growth factor (NGF), brain derived neurotrophic factor (BDNF), neurotrophin-3 (NT-3) and neurotrophin 4/5 (NT-4/5). The central nervous system response to pain can keep increasing even though the painful stimulus from the injured tissue remains steady. This "wind-up" phenomenon in deep dorsal neurons can dramatically increase the injured person's sensitivity to the pain. Local tissue inflammation can

contributes to inflammatory pain hypersensitivity
Tarek A. Samad, Kimberly A. Moore, Adam Sapirstein,
Sara Billet, Andrew Allehorne, Stephen Poole,
Joseph V. Bonventre & Clifford J. Woolf

¹⁰ Eur J Neurosci 1999 Mar;11(3):837-46

Adrenergic innervation of rat sensory ganglia following proximal or distal painful sciatic neuropathy: distinct mechanisms revealed by anti-NGF treatment.

Ramer MS, Bisby MA.

TAXPAYER EXHIBIT

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June 21, 2011