

How Does Provant Treat Pain?

Regulation of cytokine and edema-related genes

April 2014 Newsletter

We have been reviewing how Provant treats pain two ways: anti-nociceptive analgesia and anti-inflammatory. Last month we provided an overview how Provant changes membrane potential, activating second messengers. This newsletter focuses on cytokine and edema-related genes, which second messenger activity regulates.

This table summarizes the effect:

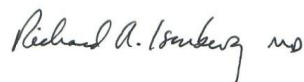
Interleukins	Interleukins are proteins involved in cell-to-cell communication, regulation of cell growth, differentiation, and motility. Interleukins may be pro-inflammatory or anti-inflammatory. Some interleukins are involved in a autocrine feedback loop that amplifies the effect of Provant.	↓ IL-1 β ↑ IL-10
Tumor Necrosis Factors (TNF)	TNF is an essential mediator in a broad range of biological processes, and has pro-inflammatory effects.	↓ TNF- α
Aquaporins	Aquaporins are proteins that form pores in the cellular membrane. Aquaporins selectively conduct water molecules in and out of the cell and help regulate edema.	↑ Aquaporins
Cyclo-oxygenase (COX), Lipo-oxygenase (LOX)	Provant effects COX and LOX, which are responsible for the production of Resolvins. Resolvins are involved in ending inflammation in the CNS and peripheral tissue.	↑ COX ↑ LOX

The May newsletter will focus on endogenous opioid production, Provant's anti-nociceptive analgesia effect. To learn more about Provant's mechanism of action, please contact your local Regenesys representative, or visit <http://bit.ly/1nvVhSr>

And remember: FDA has cleared the use of Provant for patients with metallic implants in the area of treatment. This includes metal joints, rods, plates, screws, and pins.



Sincerely,



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 Vice President, Clinical and Regulatory Affairs