

## How Does Provant Treat Pain?

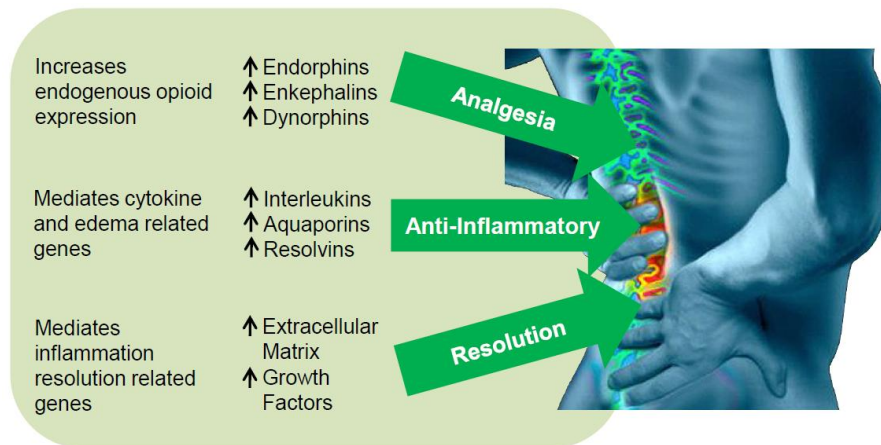
### *By Mediating Agents Involved in the Inflammatory Process and Nociception*

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Provant Therapy uses pulsed electromagnetic energy to facilitate reduction of the pain and edema in post-operative superficial soft tissues. *In vitro* evidence indicates that Provant alters ion gradients, leading to changes in membrane potential and activation of intra-cellular secondary messengers. This results in a cascade of gene expression and associated protein activity. These agents are involved in the inflammatory process and nociception.

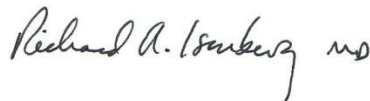
Our *in vitro* understanding of the mechanism of action is that Provant treats pain two ways:

1. **Anti-nociceptive ANALGESIA:** by inducing production of endogenous opioids (endorphins, enkephalins, dynorphins) by keratinocytes, which turn off pain signals at the nerve ending.
2. **ANTI-INFLAMMATORY:** by up-regulating anti-inflammatory mediators, and down-regulating pro-inflammatory mediators, including cytokine and edema related genes.



To learn more about Provant's mechanism of action, please contact your local RegenesiS representative, or visit <http://bit.ly/1nvVhSr>

Sincerely,



Richard Isenberg, MD  
Vice President, Clinical and Regulatory Affairs