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Pain transcriptomics and therapeutics

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Dysfunctions of pain neural systems can lead to chronic pain conditions that are frequently resistant to treatment and can severely degrade quality of life. The ability to effectively treat pain is critically dependent on a detailed, quantitative, and comprehensive analysis of the molecular properties of nociceptive sensory neurons. These neurons occupy the beginning of the pain pathway and their cell bodies in dorsal root (DRG) or trigeminal ganglia connect the body to the central nervous system. Upon injury or pathophysiological insults such as diabetic neuropathy, they become "peripheral generators" which drive sensitization processes at higher level of the neuraxis. Important peripheral generators are DRG neurons that express the TRPV1 vanilloid-ligand-gated ion channel. These neurons transduce sensations of painful heat and inflammation, and play a fundamental role in clinical pain from cancer and arthritis. We have used the ultrapotent TRPV1 agonist resiniferatoxin (RTX) in animal and human clinical trials to produce a highly selective chemoaxotomy of pain-sensing neurons. Loss of the TRPV1-dependent peripheral generators produced a potent pain reduction in both cancer and arthritis in canine clinical pain and we are evaluating this in human cancer pain. These results prompted us to elucidate the complete transcriptome of TRPV1-expressing DRG neurons using next-generation RNA-Seq. We also performed transcriptome analysis of the non-TRPV1 neuro-glial ganglionic and selective genetic and chemical ablation. The transcriptomic data define distinct molecular signatures within a clinically important neuronal population and provide an overall framework for understanding the pain processes at the molecular level.

Biography

Michael J Iadarola completed his PhD in Pharmacology from Georgetown University Medical School in 1980. He has been involved in research on epilepsy, antipsychotics, and for the past 25 years, the neurobiology of pain and pain control systems with an emphasis on molecular, translational and clinical studies. His current research focuses interventional approaches to analgesic treatment and understanding the complete gene expression repertoire of primary sensory neurons using next-generation RNA sequencing. In 2014, he received the Fredrick W.L. Kerr award in basic science from the American Pain Society in recognition of "Total career achievements that have made outstanding contributions to the field of pain research."

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