

***STOP* THE PAIN**



It's time to find a cure!

The Facial Pain Research Foundation





It's Time To Find a Cure

The Facial Pain Research Foundation

Accelerating the world of pain research.

MISSION:

Research committed to cure Trigeminal Neuralgia and other neuropathic pain.



“The Facial Pain Research Foundation is fostering incredibly creative research that is introducing cutting edge technology to address questions concerning the origin of Trigeminal Neuralgia and other neuropathic pain.”



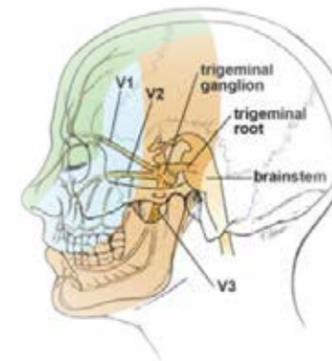
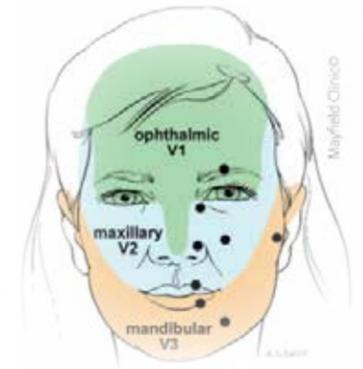
*Allan Basbaum, PhD, Professor and Chair
Dept. of Anatomy UCSF School of Medicine*

What is Trigeminal Neuralgia?

Trigeminal Neuralgia (TN) is considered one of the most painful conditions found in medicine today. It is sometimes referred to as the suicide disease. TN is in the neuropathic pain class and is a disorder of the fifth cranial (trigeminal) nerve, one of 12 pairs of nerves that are attached to the brain. The most common form of TN (called TN1) causes extreme, sporadic, sudden burning or shock-like facial pain in the areas of the face where the branches of the nerve are distributed.

Affected areas include the lips, eyes, nose, scalp, forehead, upper jaw, and lower jaw. TN leads to pain that can occur in quick succession lasting a couple of minutes or in volleys lasting as long as two hours.

A second form of TN, called TN2 (which can occur simultaneously with TN1), is characterized by constant aching, burning, stabbing pain of lower intensity than TN1.



With TN, intense terrifying pain can be ignited by even the slightest of triggers, such as a light breeze or applying makeup. The condition often results in social isolation due to fear of an attack, which can lead to depression and even suicide.

Scientists have been uncertain about the source of TN. It may be caused by a blood vessel pressing on the trigeminal nerve as it exits the brain stem. It may also be caused by damage to the protective coating around the nerve (the myelin sheath) or as a result of genetic mutations. **Because it is an intense chronic pain condition with no known cure to date, TN patients are often prescribed opioids to deal with the pain.**



“If not for the vision of the Foundation, most of the scientists would not have the opportunity to work together. A better understanding of Trigeminal Neuralgia will inexorably lead to new discoveries in pain disorders.



*Kim Burchiel, MD, Professor and Chair
Emeritus Dept. of Neurological Surgery OHSU*

About The Facial Pain Research Foundation

In 2004 Albert Rhoton Jr. (pictured right) past president of the American Association of Neural Surgeons and Michael Pasternak, president of the Trigeminal Neuralgia Association (TNA) asked Doug Anderson, director of the McKnight Brain Institute at the University of Florida the question, "What research is necessary to cure Trigeminal Neuralgia and related neuropathic pain?"



Shortly after, at the TNA National Conference, Doug presented his theory that the use of stem cells, differential gene expression and gene therapy approaches may help to find a cure. It is this theory that prompted the development of a research initiative.

It became apparent that TN occurs in a narrow population, clear of many variables. The trigeminal nerve is easy to access and the severe pain can be recreated in the laboratory. Consequently, researchers began using the pain caused by a damaged trigeminal nerve as a prototype to assist in solving other conditions such as Multiple Sclerosis, migraines, spinal nerve damage, and Epilepsy.

In 2011 The Facial Pain Research Foundation (FPRF) was established. The Foundation's purpose is to help support this research and cure many types of neuropathic pain beginning with Trigeminal Neuralgia.



Goals for Research Funding

- 1. Provide seed money.** Initial capital will help jumpstart researchers in institutions to develop new discoveries to cure pain.
- 2. Encourage further monetary investment.** Funding may be through the NIH or other sources.
- 3. Provide continued support.** Support is given through additional funds and collaboration of resources from other scientists.

"Our target is to prove that we can reduce or even block the pain signaling in the trigeminal nerve with gene therapy. We envision a rapid route to the clinic, making a significant difference for people with Trigeminal Neuralgia and other debilitating pain conditions."

Todd Golde, MD, PhD, Director McKnight Brain Institute, University of Florida



A Message From the President



The Foundation has raised over \$4-million to fund six distinct research programs. It has helped create two venture capitalized research corporations. The \$4-million served in a multiplier capacity resulting in \$30 million in venture capital, NIH, or other Foundation fundings for research.

Scientists know that facial and head pain are biologically the worst that humans can experience. I know this pain. Those who are presently pain free know that the disorder typically comes "roaring back." There are no "guarantees" and it is a constant worry for TN sufferers.

Our researchers say that TN cures will hopefully lead to treatments for other neuropathic pain conditions like phantom and back pain, and nerves damaged by chemotherapy. The Foundation is moving "lightning fast" in the world of chronic pain research to find the cures. We are special. No other research foundation in the world is attempting to do what we are doing.

I am in awe of our Foundation scientists, trustees, donors and fund-raising volunteers. We have decided to imagine something as fantastic as "walking on the moon!" **We truly believe we are going to end TN and related neuropathic pain.**

Just imagine no more damaged nerves.

I ask you to join us on this amazing medical and scientific journey. Hold on, it's going to be a thrilling ride.

Michael Pasternak, PhD
Member NIH IPRCC

"NIH funding for neuropathy research is predicted to decrease. Therefore, more than ever we rely on the support of the Facial Pain Research Foundation in order that our work to better understand the causes of neuropathic pain can go forward."

Lucia Notterpek, PhD, Professor and Chair, Dept. of Neuroscience, McKnight Brain Institute, University of Florida



"The FPRF pushes the conversation about pain forward. The results are innovative research projects that are advancing cures for TN and neuropathic pain."

*Ze'ev Seltzer, BMS, DMD
University of Toronto*

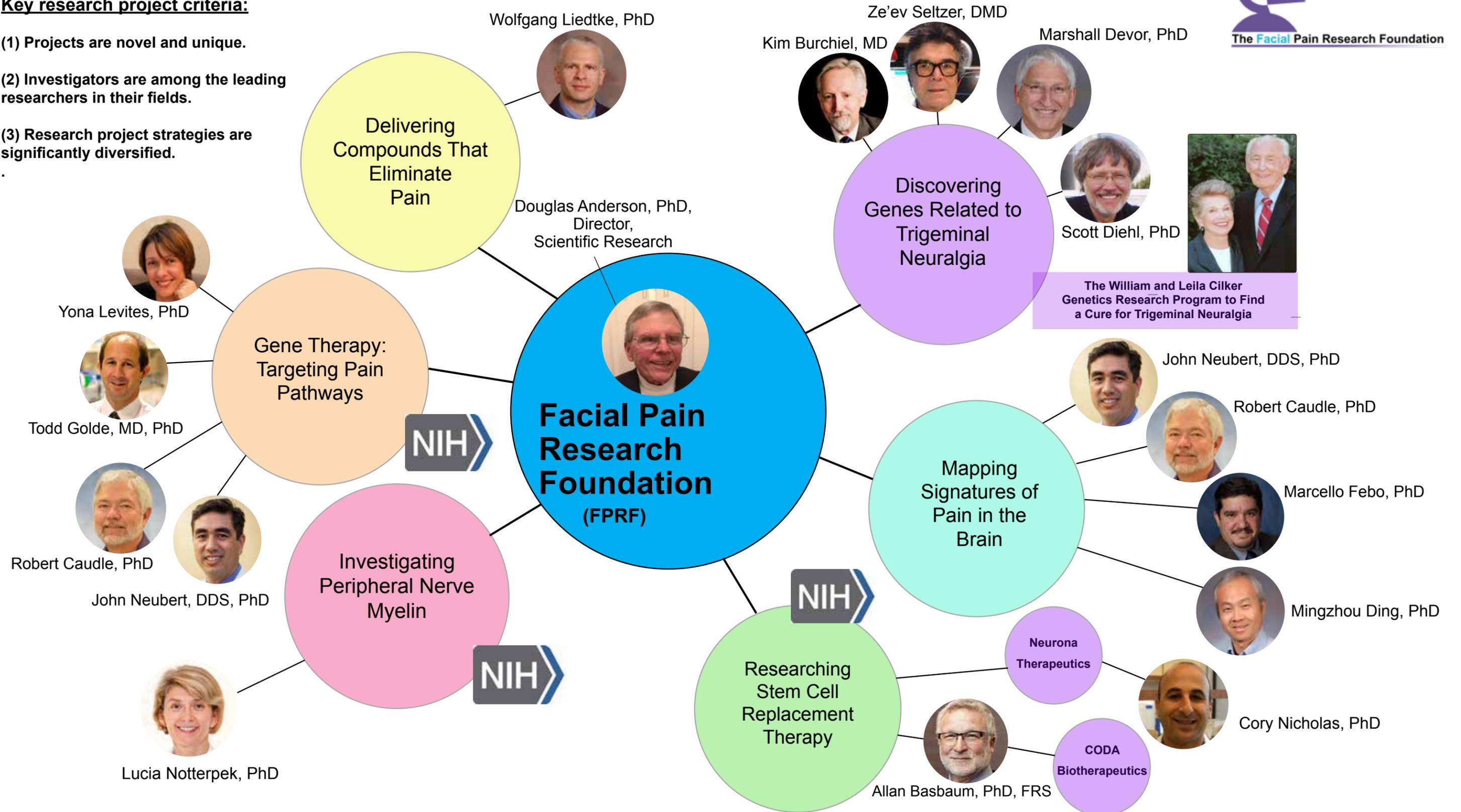


International Research Consortium and Research Projects



Key research project criteria:

- (1) Projects are novel and unique.
- (2) Investigators are among the leading researchers in their fields.
- (3) Research project strategies are significantly diversified.



Signature Research Projects



Investigating Protein-Lipid Interactions in Peripheral Nerve Myelin

Lucia Notterpek, PhD (Principal Investigator)

For years, it has been proposed that the primary cause of TN pain has been loss or damage to the insulating myelin sheath of the trigeminal nerve (demyelination) by the pulsations of an overlying blood vessel. Myelin is a multi-layered membrane made up of specific lipids and proteins. Due to its molecular composition, myelin functions as an insulating material in the nervous system (NS). Myelin wraps around many axons in both the peripheral (PNS) and central nervous systems (CNS) forming the myelin sheath which is instrumental in maintaining the normal conduction velocity in nerves.

Consequently, an intact myelin sheath is necessary for the proper functioning of the NS. Peripheral myelin is derived from and maintained by Schwann cells. The overall goal of this project is to define specific protein-lipid interactions, with a focus on PMP22, and cholesterol in the establishment and maintenance of lipid membrane domains in peripheral myelin. In the absence of PMP22, myelin is prone to compression-induced damage leading to localized myelin injury. For completing the aims of the project we are using cultured cells and nerves from normal and PMP22-deficient mice and engineered molecular constructs.



Mapping Towards a Cure: Identification of Neurophysiologic Signatures of Trigeminal Neuralgia Pain

John K. Neubert, DDS, PhD, (Project Coordinator), Mingzhou Ding, PhD, Marcelo Febo, PhD, Robert M. Caudle, PhD

This complex project is designed to investigate the cause of TN in both animals (rats) and humans. Thus, the initial focus of this translational study is to use state of the art magnetic resonance (MR) scanners to determine if the neurobiology of TN in rats replicates or is very similar to the neurobiology of TN in humans. If similar imaging/activation patterns are seen in both rats and humans, then large numbers of compounds and perhaps other promising or

novel therapeutic approaches can be screened in rats with the best of the best selected for inclusion in clinical trials. In addition, discovery of the relevant trigeminal nerve targets provides regions for treatments that can specifically block the pain of TN and eliminate or limit unwanted side effects because the treatment can be delivered locally and not systemically.

Signature Research Projects



Cell Replacement Therapy as a Treatment for Injury-Induced Neuropathic Pain

Allan Basbaum, PhD, FRS (Principal Investigator)

One of the primary research tactics targeted and supported by the FPRF since its inception has been the development of a unique therapeutic approach which involves transplanting cells that produce a pain inhibitory neurotransmitter(s) that can suppress the devastating pain of TN pain. The preclinical laboratory studies have been focused on demonstrating how cell replacement therapy (specifically, transplanting immature precursor cells that produce a neurotransmitter known to inhibit pain) might be used not only to suppress some common types of persistent and difficult-to-treat pain, but also to identify and cure the conditions that give rise to them. The

studies have developed to the extent that they contributed to the formation of a new company. This company is starting to extend the concept of transplantation of cells that produce inhibitory neurotransmitters in animals to humans for the management of different neurological conditions that appear to arise from loss of inhibition.



Finding the Genes that Predispose to Trigeminal Neuralgia: The William H. and Leila A. Cilker Genetics Research Program

Marshall Devor, PhD (Project Coordinator), Scott R. Diehl, PhD, Kim J. Burchiel, MD, Ze'ev Seltzer, DMD

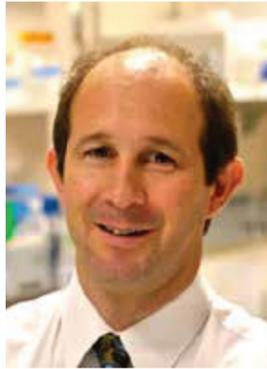
This project was conceived with the assumption that the risk for getting classical TN has a genetic basis. It has as its primary objective identifying genetic mutation(s). These can be expressed as sequence variant(s) or polymorphism(s) associated with the development of TN pain. DNA is collected from TN patients identified by rigorous genotyping. Analysis of the whole genome is achieved by using the latest in genome-wide association studies (GWAS) technology and compared to matched reference controls to determine if there are candidate sequence variant(s) or polymorphism(s)

present in the genome of the TN patients that are not found in the controls. Such sequence variants might cause TN pain by directly affecting the function of the proteins that these genes encode, or by altering other aspects of gene expression. Either way, assuming that genetics is indeed the basis for developing TN, there are high probabilities that this project will reveal the genes and ultimately the pathophysiological mechanisms that cause the lesions to be painful. With this knowledge, molecular targets for treatments that will cure the pain can be identified not only for TN but perhaps also for a variety of other facial and segmental neuropathic pain conditions.

DNA Collection Centers

- John YK Lee, MD, Dept. of Neurosurgery, Univ. of Pennsylvania, PA
- Edward F Chang, MD, UCSF Dept of Neurological Surgery, San Francisco, CA
- Douglas Kondziolka, MD, Dept. of Neurosurgery, NYU, New York, NY
- Kim Burchiel, MD, Neurosurgery, Oregon Health & Science Univ., Portland OR
- William Friedman, MD, Neurosurgery, Univ. of Florida, Gainesville FL
- Joanna Zakrzewska MD, Eastman Hospital, London, UK
- Konstantin Slavin, MD, Neurosurgery, Univ. of Illinois-Chicago, Chicago, Ill
- Mojgan Hodaie, MD, Neurosurgery, Univ. of Toronto, Toronto, Canada
- John Alksne, MD, UCSD, San Diego, CA

Signature Research Projects



Evaluation of Adeno-Associated Virus (AAV) Constructs Directed at Pain Pathway Targets – a rapid approach for identification of effective therapies for Trigeminal Neuralgia

Todd E. Golde, MD, PhD, (Principal Investigator), John K. Neubert, DDS, PhD, Yona Levites, PhD, Robert M. Caudle, PhD

The purpose of this project is to investigate novel viral-based delivery therapeutics that will be aimed at specific targets within the pain processing network. This group of investigators posits that advances in specific gene-targeting vectors will allow for the rapid identification of potential therapies for the treatment of trigeminal neuralgia (TN). Importantly, our team has significant expertise in the design,

synthesis and testing the safety and efficacy of Adeno Associated Virus (AAV) viral constructs with genes known to be involved with pain inhibition. Once safety and efficacy has been established, we expect that animal testing with this viral-based delivery system can be used as a way to rapidly reduce the time to discover novel new therapies. These therapies will have singular effectiveness in preventing TN pain.



Novel Ways to Deliver Compounds that can Eliminate the Pain of Trigeminal Neuralgia

Wolfgang Liedtke, MD, PhD, (Principal Investigator)

The focus of our project is to develop novel techniques for direct anatomic targeting of specific components of the trigeminal system. The primary advantage of this approach is with the delivery of the drug directly to the lesioned area. Only a small fraction of the normal systemic dose of the drug will be needed. It should eliminate or at least minimize the unwanted side effects associated with systemic or whole body delivery of the drug. This method will utilize the combination of material science with cell engineering. The objective is to

construct a delivery system made of either immunologically inert biocompatible polymers designed to hold human fibroblast-like cells or specially created few-walled carbon nanotubes. Both are designed to allow a concentrated application of pain inhibiting substances directly to the lesion site.

Facial Pain Research Foundation Board Members

The Board of the Facial Pain Research Foundation consists of leaders from the business, legal, entertainment and medical community whose personal and family lives have been dramatically altered by the traumatic pain caused by Trigeminal Neuralgia. Some are pain-free today. Some are not. Some have family members who suffer with TN. All tirelessly serve with compassion and empathy to help support and fund the Foundation's goal to find a cure for the painful debilitating effects of living with Trigeminal Neuralgia.



Michael Pasternak, PhD is President of The FPRF and Founding Trustee. He is focused full-time on the Foundation's research, fund-raising, and organizational activities. He is pain-free from TN today.



Douglas K. Anderson, PhD. is professor and chairman emeritus of neuroscience at the University of Florida, College of Medicine and McKnight Brain Institute. He is FPRF's Director of Research.



Myron A. Hirsch, PhB., Secretary of The FPRF and Founding Trustee. He is an author, editor and book publisher. His wife, Harriet, experienced a return of TN in August 2010. Today Harriet is again pain-free.



Jay Winer PhB., Treasurer of The FPRF formerly served as executive director of public relations and community affairs for The Grove Park Inn Resort and Spa in Asheville, N.C. He has been with The FPRF for 12 years.



Roger L. Levy, Esq., LLM, AIFA, Founding Trustee Emeritus is a former attorney now serving as CEO of Cambridge Fiduciary Services LLC. He has been pain-free from TN since 1997.



Suzanne Grenell, MBA is a writer, motivational speaker and author. She is a two-time breast cancer survivor and is pain free after suffering with TN for 12 years.



Elizabeth Cilker Smith, MA is former vice president of Cilker Orchards in California and West Coast Coordinator for The FPRF. She suffered from TN for six years and is currently pain free.



Pat Tomasulo is the Sports Anchor on the WGN Morning News in Chicago. His wife Amy has suffered from TN for years and the couple has raised over \$700k for research.



Richard Baron, Esq., is managing principal of the Law Firm of Richard Baron & Associates. He has experienced the pain of TN and is an avid supporter of The FPRF.



Daniel P. DiCaro is a business leader with a strong background in corporate finance, mergers and acquisitions, private equity and venture capital financing. He has suffered from TN and is committed to finding a cure.

Why Should I Contribute?



Help us double our investment in research!

Show your generosity to The Facial Pain Research Foundation and together we will find a cure for thousands of people in pain. Your contribution will help lead to scientific answers for other related disorders including Multiple Sclerosis, Epilepsy, neuropathy and back pain.

95% of each donation funds research projects to accelerate a cure for Trigeminal Neuralgia and through that end other neuropathic pain. **Every dollar is needed!**

Many volunteers live moment-to-moment in agonizing pain. Their confidence in our Foundation helps create grassroots fundraising efforts to raise money. Join us and help find a cure.

• Donate Now *It's Time to Find a Cure*

On the Web:
FacingFacialPain.org

By Mail:
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Gainesville, FL 32608-9313

The Facial Pain Research Foundation, Inc.
is a 501(c)(3) Non-Profit Organization



“The Facial Pain Research Foundation’s ambitious goal to find cure for neuropathic pain is certainly attainable.”

*Joanna Zakrzewska, MD, DDS
FRPF International Science Coordinator
Eastman Dental Hospital,
University College London Hospitals*

Worldwide Research Locations

