Common Fund Concept Clearance: Stimulating Peripheral Activity to Relieve Conditions (SPARC) Stage 2

Council of Councils
January 29, 2021

Gene Civillico, PhD

National Institutes of Health
Office of Strategic Coordination - The Common Fund

OSC (Common Fund)

The Common Fund

Concept Clearance: SPARC Stage 2

SPARC-VOX

Objective: Leverage SPARC Stage 1 capabilities to accelerate bioelectronic medicines

SPARC-V: Map the human vagus nerve

SPARC O: Open-source modular neuromodulation platform

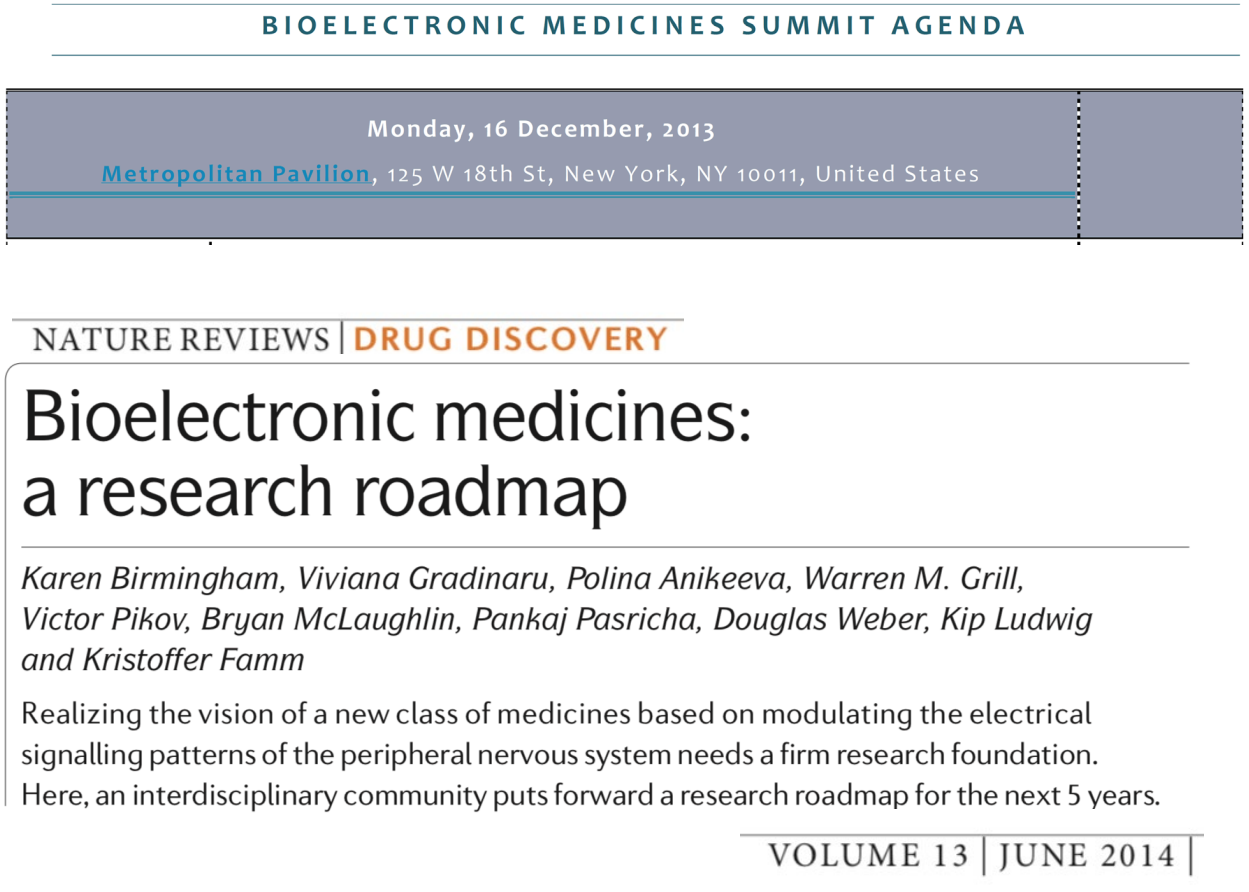
SPARC X: Prize challenges for demonstration of next-generation capabilities

Funds Available $33M/year

Program Duration: 3 years

Council Action: Vote on support of Program

Program origins



BIOELECTRONIC MEDICINES SUMMIT AGENDA

Monday, 16 December, 2013

Metropolitan Pavilion, 125 W 18th St, New York, NY 10011, United States

NATURE REVIEWS | DRUG DISCOVERY

Bioelectronic medicines: a research roadmap

Karen Birmingham, Viviana Gradinaru, Polina Anikeeva, Warren M. Grill, Victor Pikov, Bryan McLaughlin, Pankaj Pasricha, Douglas Weber, Kip Ludwig and Kristoffer Famm

Realizing the vision of a new class of medicines based on modulating the electrical signalling patterns of the peripheral nervous system needs a firm research foundation. Here, an interdisciplinary community puts forward a research roadmap for the next 5 years.

VOLUME 13 | JUNE 2014 |

<u>Identified critical priority areas:</u>

Biological maps of structure and function

Advancement of interface technology

Early establishment of therapeutic feasibility

Collaborative data mining and standards

...all enabled by "an emerging community of 'bioelectricians' "

Stimulating Peripheral Activity to Relieve Conditions (SPARC)

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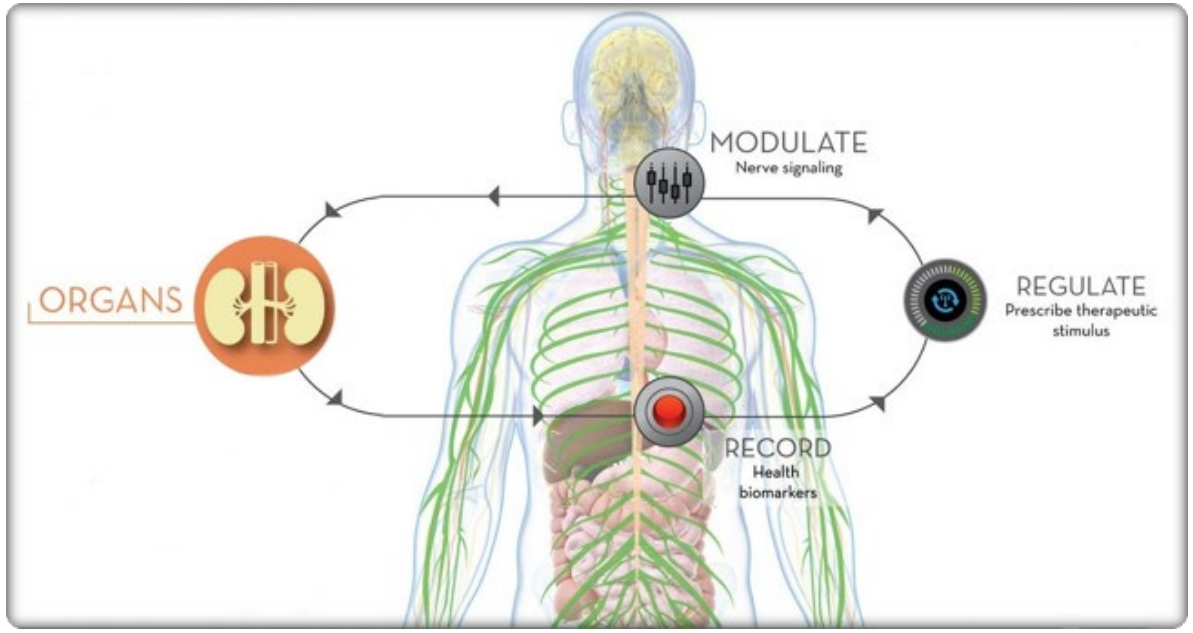

Opportunity: Neuromodulation of end-organ function holds promise in treating many diseases/conditions.

Challenge: The mechanisms of action for neuromodulation therapies remain poorly understood.

SPARC program goals:

- Capitalize on recent advances in technology to deliver detailed, integrated functional and anatomical neural circuit maps for organs.
- Provide the scientific foundation necessary to pilot new and improved neuromodulation devices and stimulation protocols that are more advanced and effective.

Catalyze the development of next-generation bioelectronic medicines by providing access to high-value datasets, maps, and predictive simulations.

Mapping innervation across organs

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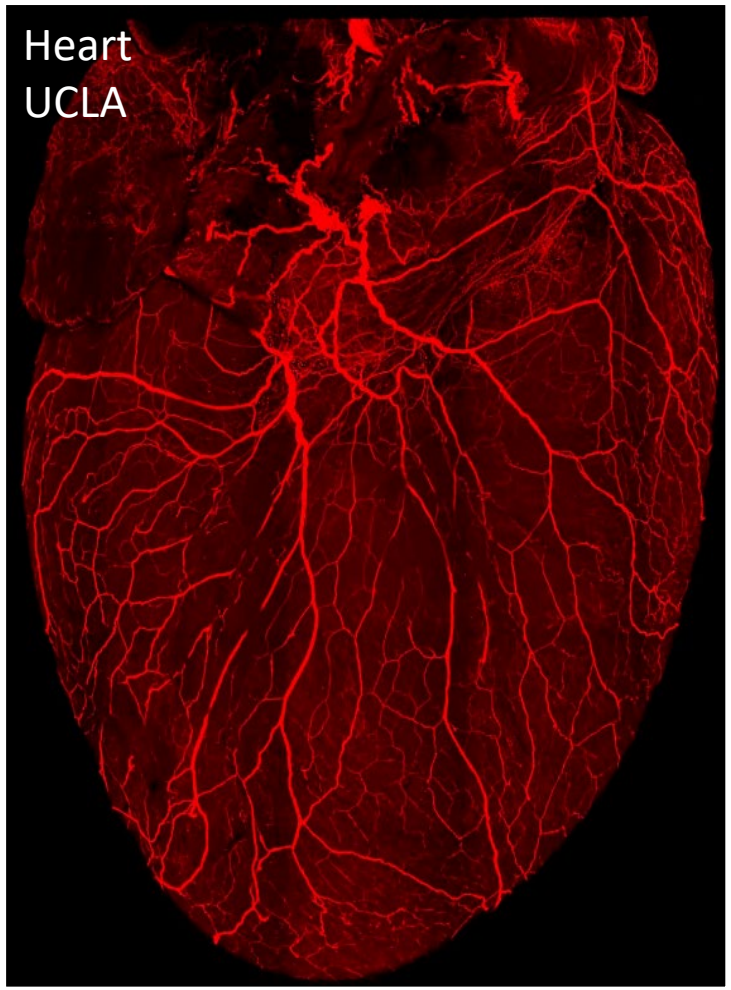

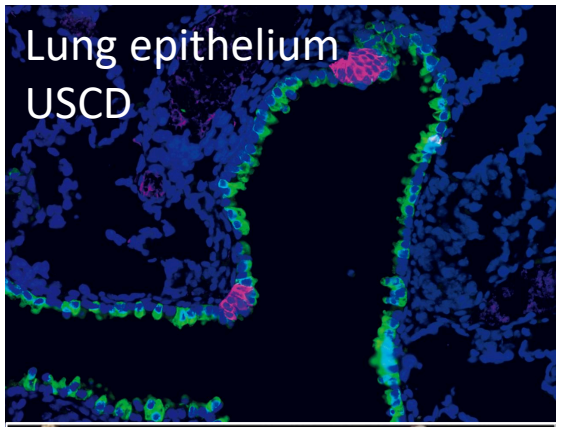

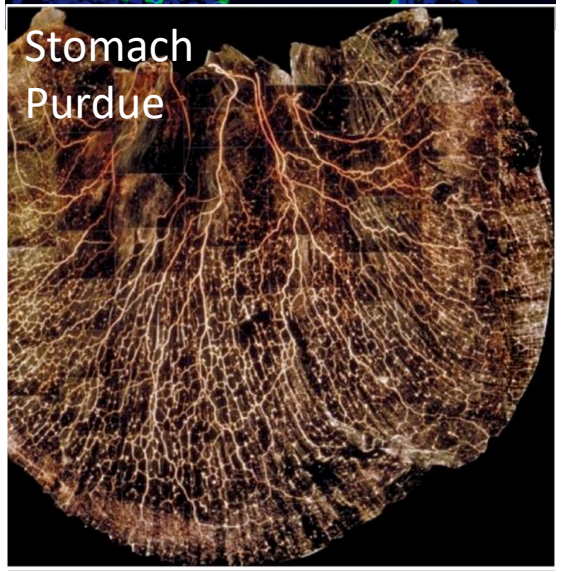

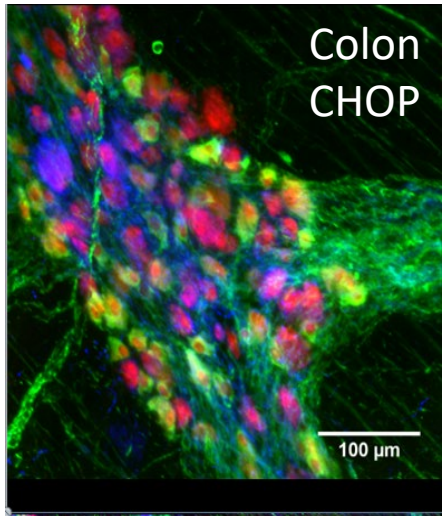

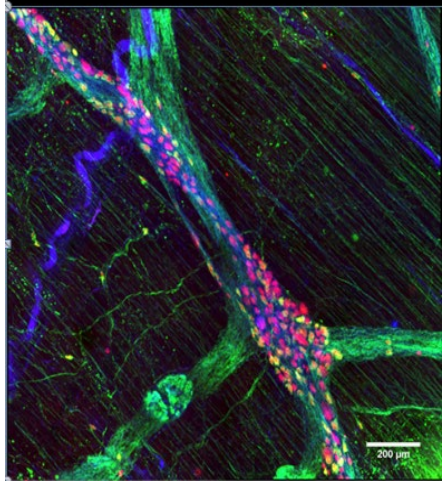

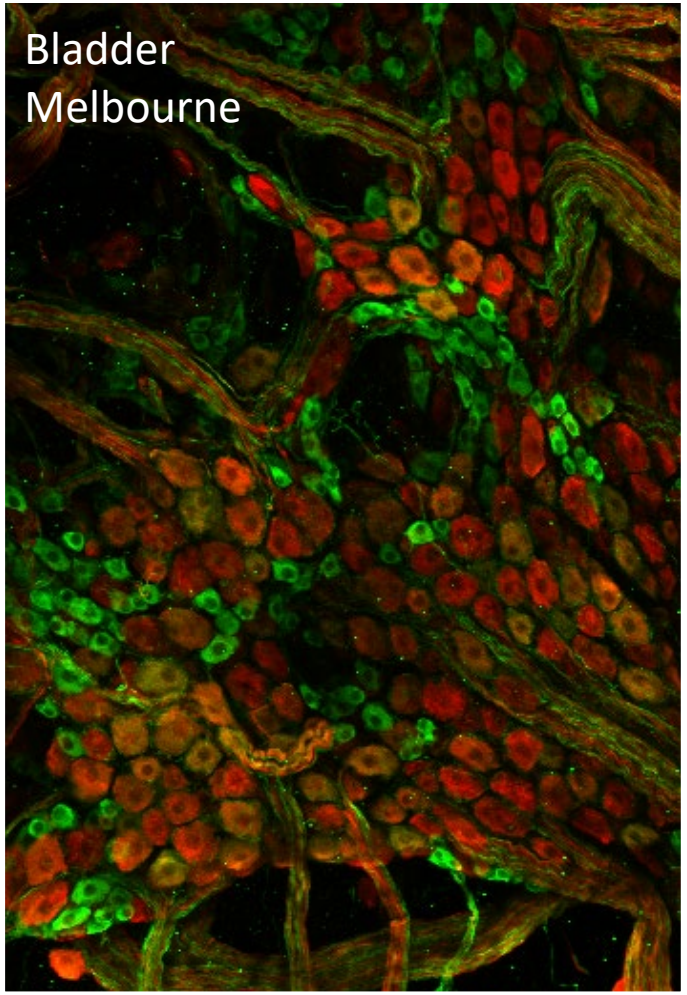

Stimulating Peripheral Activity to Relieve Conditions (SPARC)

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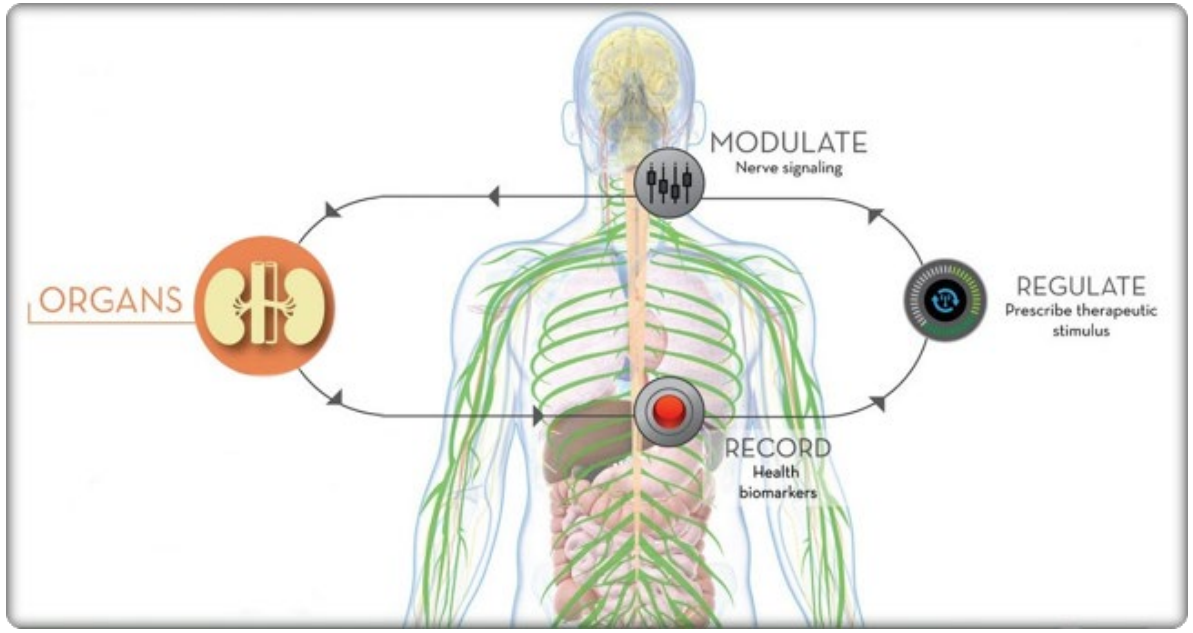


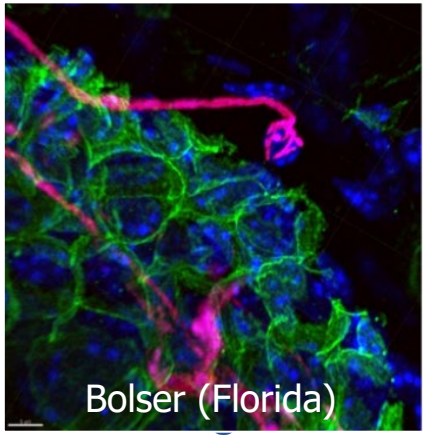
MAPS: High-resolution anatomical tracing, *in vivo* electrophysiology, live cell imaging, and transcriptomics for mapping peripheral neural networks

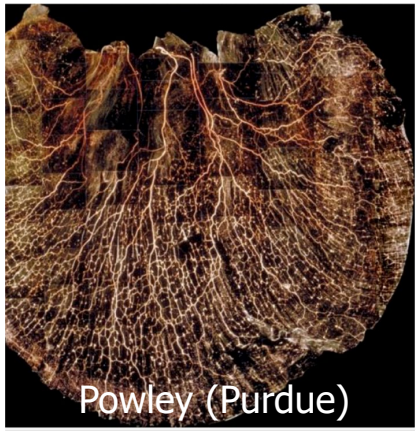
TOOLS: New probe and sensor technologies for mapping

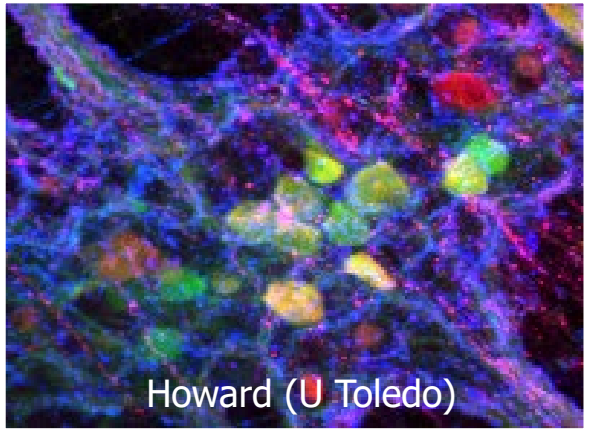
TRANSLATION: Partnerships to drive studies in humans

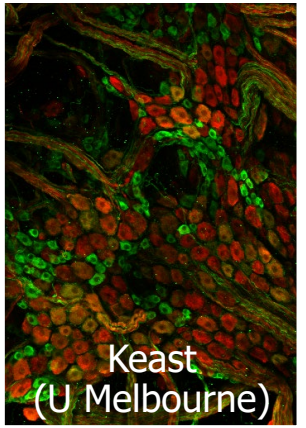
DATA RESOURCES: Integrative online hubs to synthesize and share map data and build predictive multiscale simulations


Shivkumar (UCLA)


Bolser (Florida)


Powley (Purdue)


Howard (U Toledo)


Keast (U Melbourne)

Selected publications

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Journal of Neural Engineering

PAPER

Flexible microelectrode array for interfacing with the surface of neural ganglia

Zachariah J Sperry[1,2], Kyounghwan Na[3], Saman S Parizi[3], Hillel J Chiel[4,5,6], John Seymour[1,3], Euisik Yoon[1,3] and Tim M Bruns[1,2,7]

The influence of respiration on brainstem and cardiovagal response to auricular vagus nerve stimulation: A multimodal ultrahigh-field (7T) fMRI study

Roberta Sclocco [a, b, *], Ronald G. Garcia [a, c], Norman W. Kettner [b], Kylie Isenburg [a], Harrison P. Fisher [a], Catherine S. Hubbard [a], Ilknur Ay [a], Jonathan R. Polimeni [a], Jill Goldstein [a, c, d], Nikos Makris [a, c], Nicola Toschi [a, e], Riccardo Barbieri [f, g], Vitaly Napadow [a, b]

Science Contents News Careers Journals

SHARE

RESEARCH ARTICLE

A gut-brain neural circuit for nutrient sensory transduction

Melanie Maya Kaelberer[1], Kelly L. Buchanan[2], Marguerita E. Klein[1], Bradley B. Barth[3], Marcia M. Montoya[3], Xiling Shen[3], Di…

+ See all authors and affiliations

nature International journal of science

Letter | Published: 02 January 2019

A wireless closed-loop system for optogenetic peripheral neuromodulation

Aaron D. Mickle, Sang Min Won, Kyung Nim Noh, Jangyeol Yoon, Kathleen W. Meacham, Yeguang Xue, Lisa A. McIlvried, Bryan A. Copits, Vijay K. Samineni, Kaitlyn E. Crawford, Do Hoon Kim, Paulome Srivastava, Bong Hoon Kim, Seunghwan Min, Young Shiuan, Yeojeong Yun, Maria A. Payne, Jianpeng Zhang, Hokyung Jang, Yuhang Li, H. Henry Lai, Yonggang Huang, Sung-Il Park, Robert W. Gereau IV & John A. Rogers

nature COMMUNICATIONS

ARTICLE

https://doi.org/10.1038/s41467-019-09770-1 OPEN

Identification of peripheral neural circuits that regulate heart rate using optogenetic and viral vector strategies

Pradeep S. Rajendran[1], Rosemary C. Challis[2], Charless C. Fowlkes[3], Peter Hanna[1], John D. Tompkins[1], Maria C. Jordan[1], Sarah Hiyari[1], Beth A. Gabris-Weber[4], Alon Greenbaum[2], Ken Y. Chan[2,6], Benjamin E. Deverman[2,6], Heike Münzberg[5], Jeffrey L. Ardell[1], Guy Salama[4], Viviana Gradinaru[2] & Kalyanam Shivkumar[1]

BBC Sign in

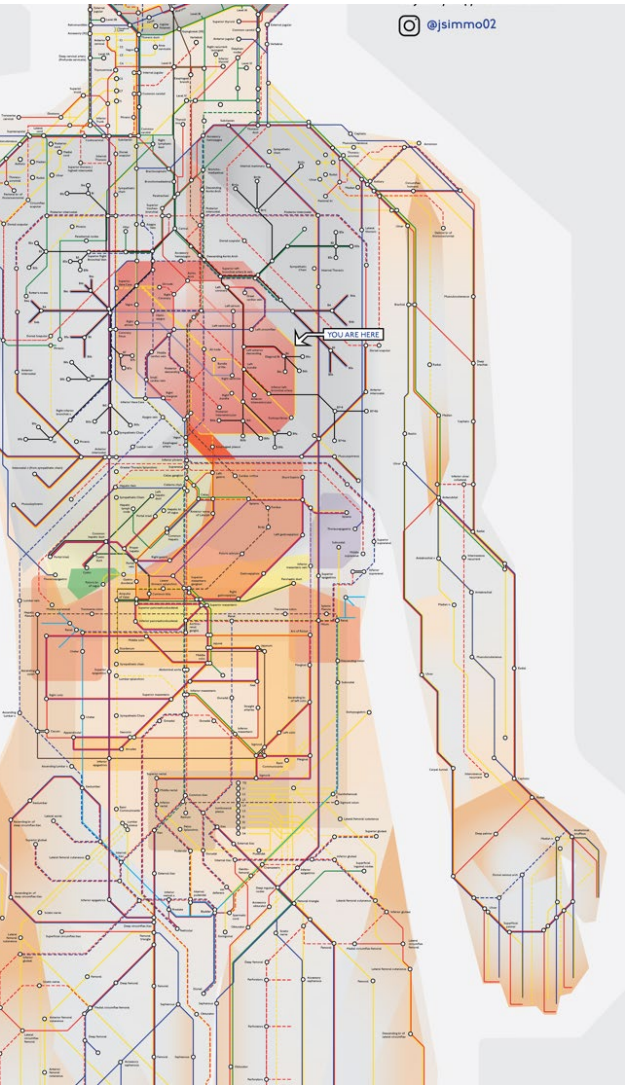
Machine Minds

By Gemma Church
16th December 2019

A new generation of "smart" implantable devices could replace traditional medication to treat a range of chronic conditions, including cardiac disease.

SPARC-V: Map the human vagus nerve

The Common Fund



Sub-initiative 1: Construct high-res connectivity profiles for at least 100 human vagal nerves, at standardized points of interest
Budget: $8M/year x 3 years

Sub-initiative 2: Recruit at least 500 patients with implanted VNS hardware for parameter sweep studies with standardized multisystem endpoints
Budget: $7M/year x 3 years

Sub-initiative 3: Continue development of the Portal (sparc.science) and associated tools to host and work with these data products
Budget: $6M/year x 3 years

Image credit: Jonathan Simmons, MD @jsimmo02

Why focus on the vagus nerve?

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Vagal nerve stimulation (VNS) is established as a treatment modality, but still has breakthrough potential due to the rudimentary mechanistic basis of current treatments.

Via its connections to multiple organ systems, the vagus spans NIH IC missions by impacting function across cardiac, gastric, immune domains, and others yet unknown.

SPARC stage 1 projects focusing on vagal anatomy and physiology have produced some of the most exciting work. We should build on this.

SPARC-O: Open-source neuromodulation

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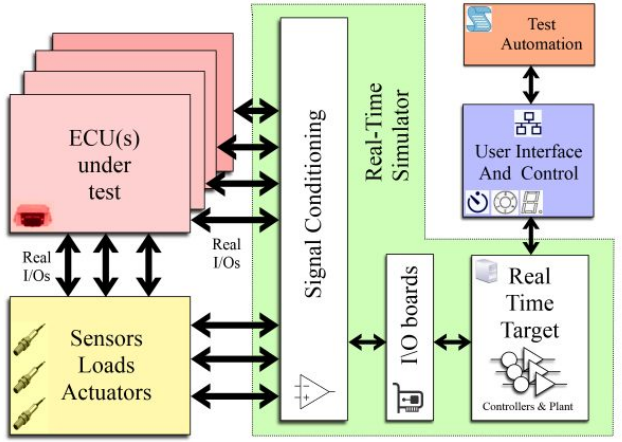
Neuromodulation researchers need a clinical grade neurostimulation and recording platform with strategic independence from existing major players

Applicants will propose to create interoperability specifications and compatible modules that can be combined into custom hardware profiles and supported sustainably.

Initiative to be co-designed and co-led by NIH BRAIN and SPARC teams

Funding to phase over to BRAIN over three years, depending on strategic alignment and progress

Budget: $10M/year x 3 years



SPARC-X: Prize challenges for demonstration of next-generation VNS capabilities

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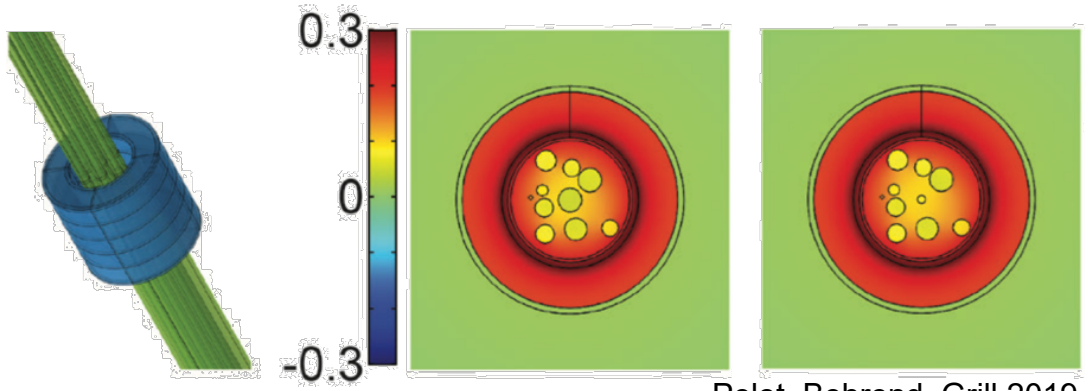
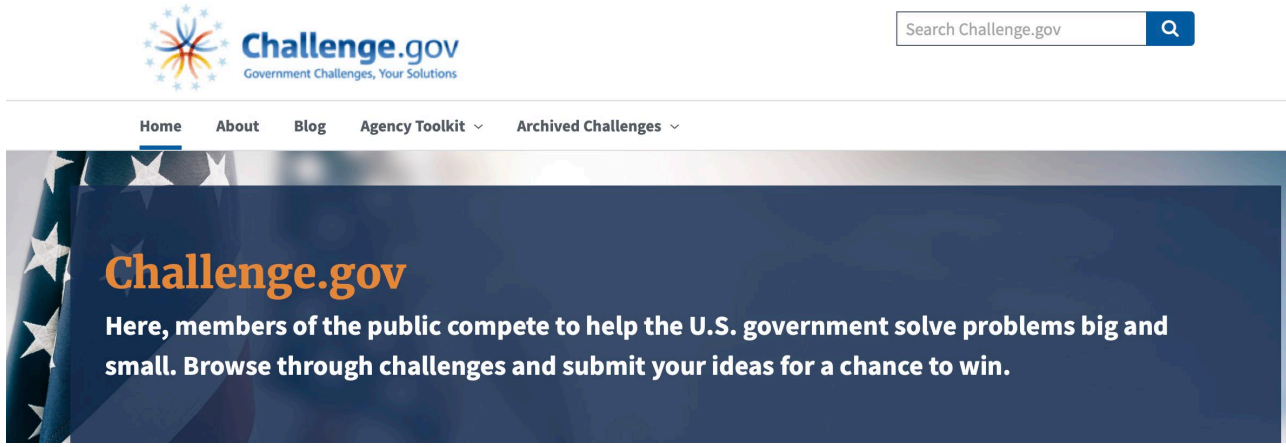
Challenge goal: Demonstrate independent vagal modulation of multiple endpoints in a large animal model



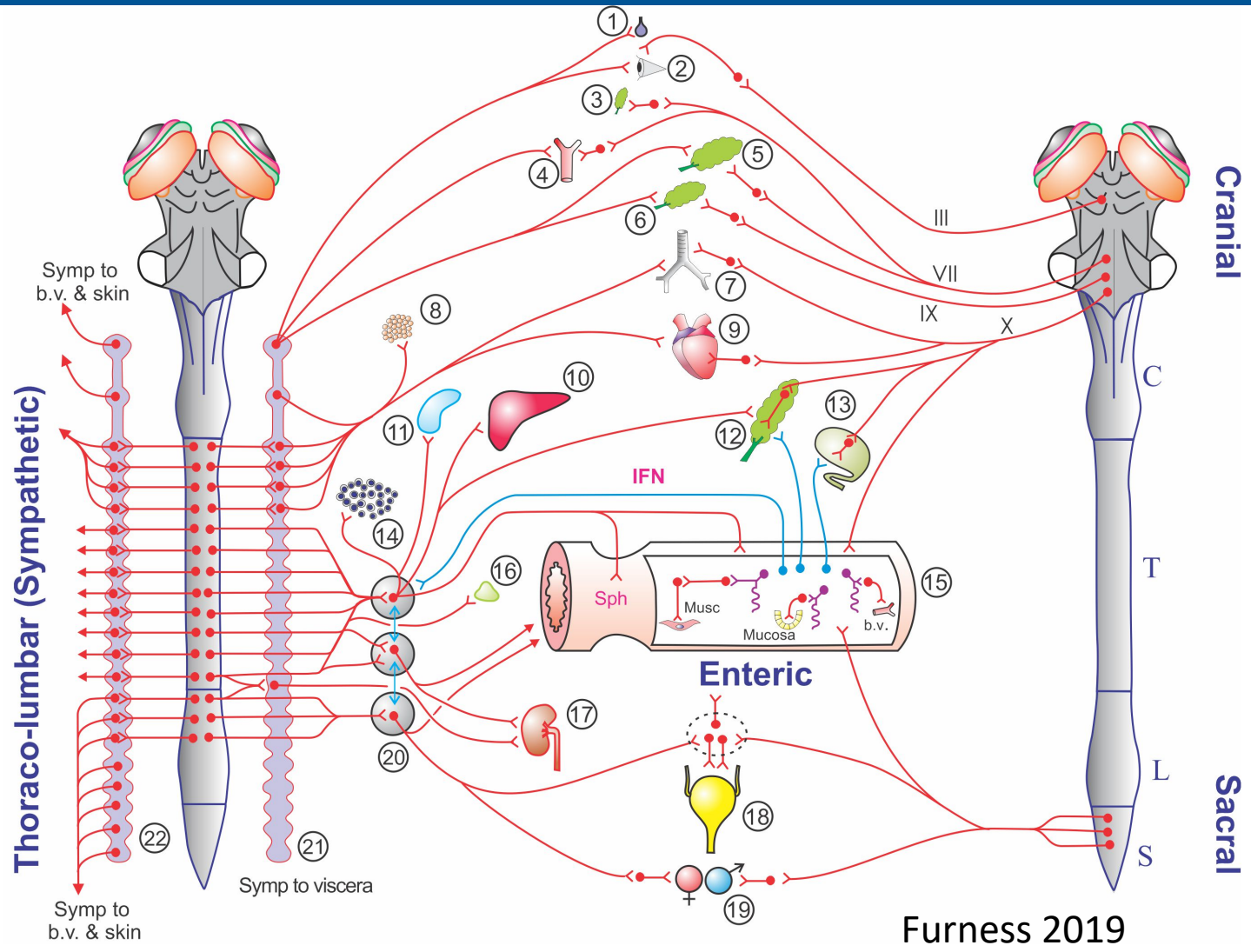
Pelot, Behrend, Grill 2019



Increasingly difficult stages, with increasing prize awards:

Stage 1 prize: $100K, for plans
Stage 2 prize: $1M, for proof of concept demonstration
Stage 3 prize: $5M, for demonstration of repeatability
Prizes only awarded for work meeting benchmarks

Discussion



Furness 2019

Background Slides

Additional Detail on SPARC Structure and Accomplishments

National Institutes of Health

Office of Strategic Coordination - The Common Fund

SPARC Program Challenge

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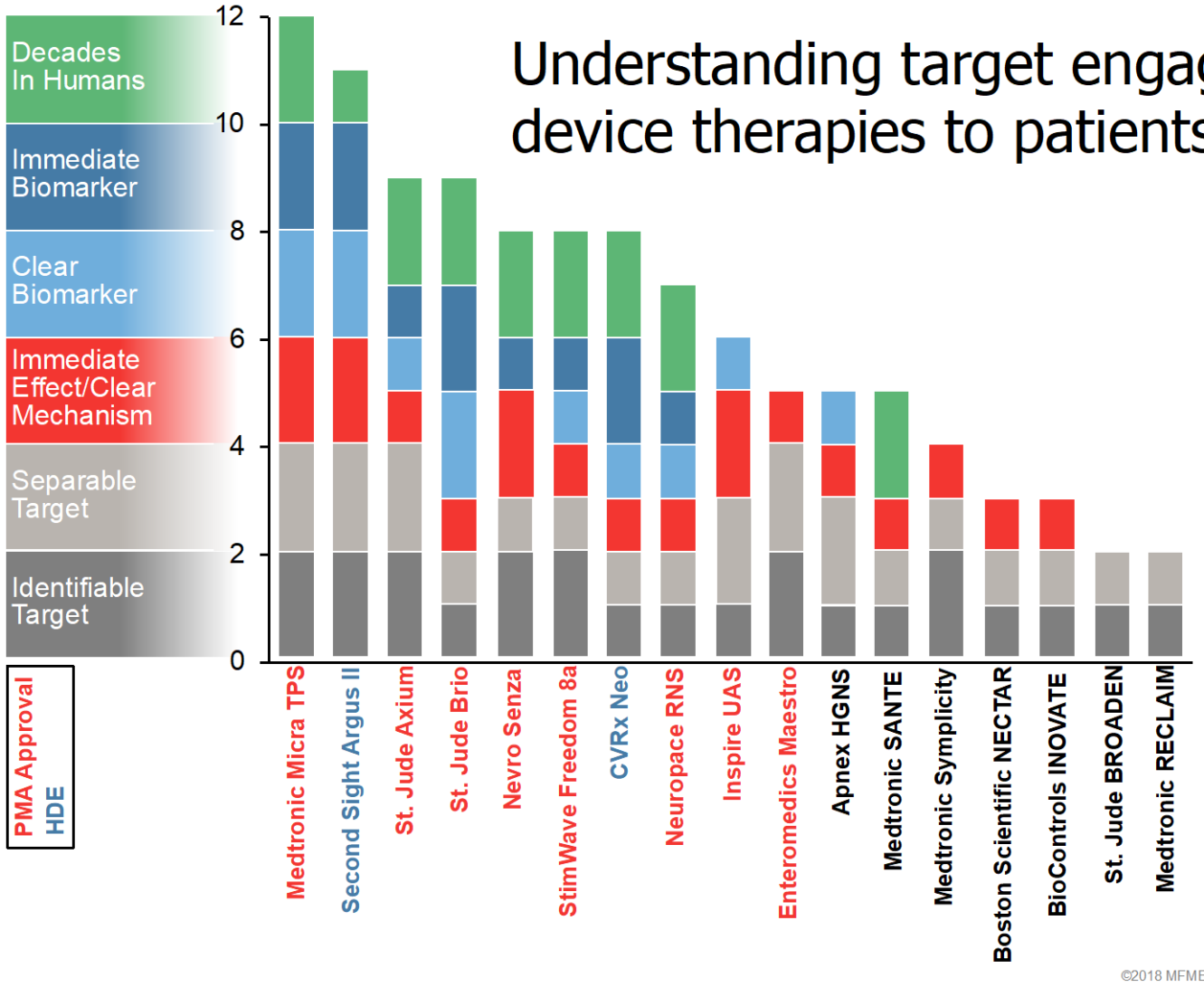


A semi-quantitative framework for predicting neuromodulation device success in gaining market approval (*in preparation*)
Ross EK,* Hachmann JT,* Harris JP, Asp A, Settell ML, Batton A, Hara S, Nicolai EN, Kurani S, Ludwig KA.

SPARC

an NIH Common Fund program

FRIDAY JULY 26, 2019

09:00 – 17:00
SPARC Data Resource Center Hands on Experience
Odyssey & Pathways, Level 1

09:20 – 11:40
SPARC Data Resource Center Portal Roll Out
Centennial Ballroom A&B, Level 1

17:15 – 18:00
SPARC Plenary Talk
Neuromodulation & Robustness to Perturbation of a Rhythmic Circuit
Centennial Ballroom A&B, Level 1

HANDS-ON DEMONSTRATIONS

SPARC DATA PORTAL | JULY 26 - 27
Odyssey, Pathways & Innovation Rooms, Level 1

SPARC TECHNOLOGY SHOWCASE | JULY 27
Artistry, Imagination & Entrepreneur Rooms, Level 2

SATURDAY JULY 27, 2019

08:15 – 10:15
SPARC-ISAN Career Launcher Symposia
Centennial Ballroom A&B, Level 1

10:15 – 17:00
SPARC Technology Showcase
Artistry, Imagination, Entrepreneur Rooms, Level 2

10:15 – 17:00
SPARC Data Resource Center Hands on Experience
Innovation, Level 1

10:40 – 11:40
SPARC: Tools to Study & Modulate Autonomic Function – Session I
Centennial Ballroom A&B, Level 1

13:00 – 15:10
SPARC: Tools to Study & Modulate Autonomic Function – Session II & III
Laureate, Level 1

EXPLORE THE AUTONOMIC NERVOUS SYSTEM

Open Access

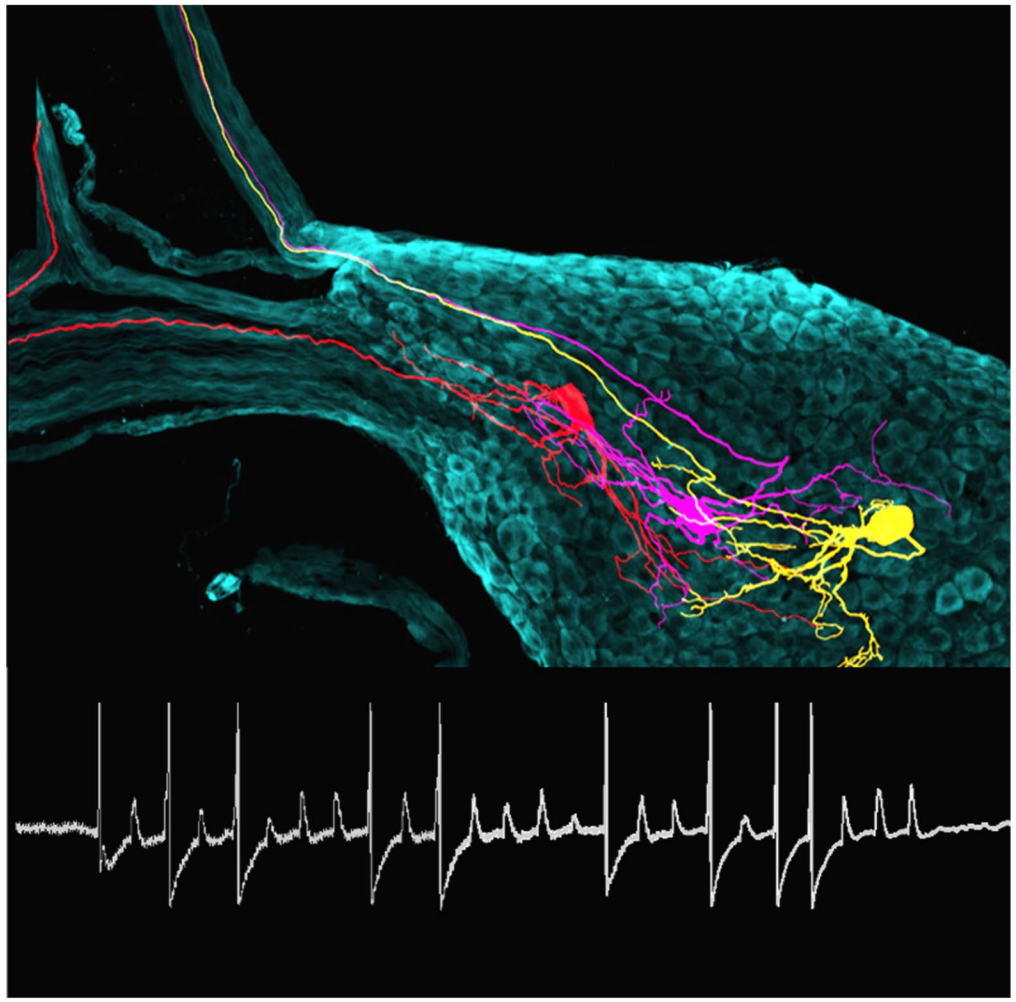
SPARC

an NIH Common Fund Program

PORTAL

www.data.sparc.science

#openscience @NIH_CommonFund



SPARC Initiatives Overview

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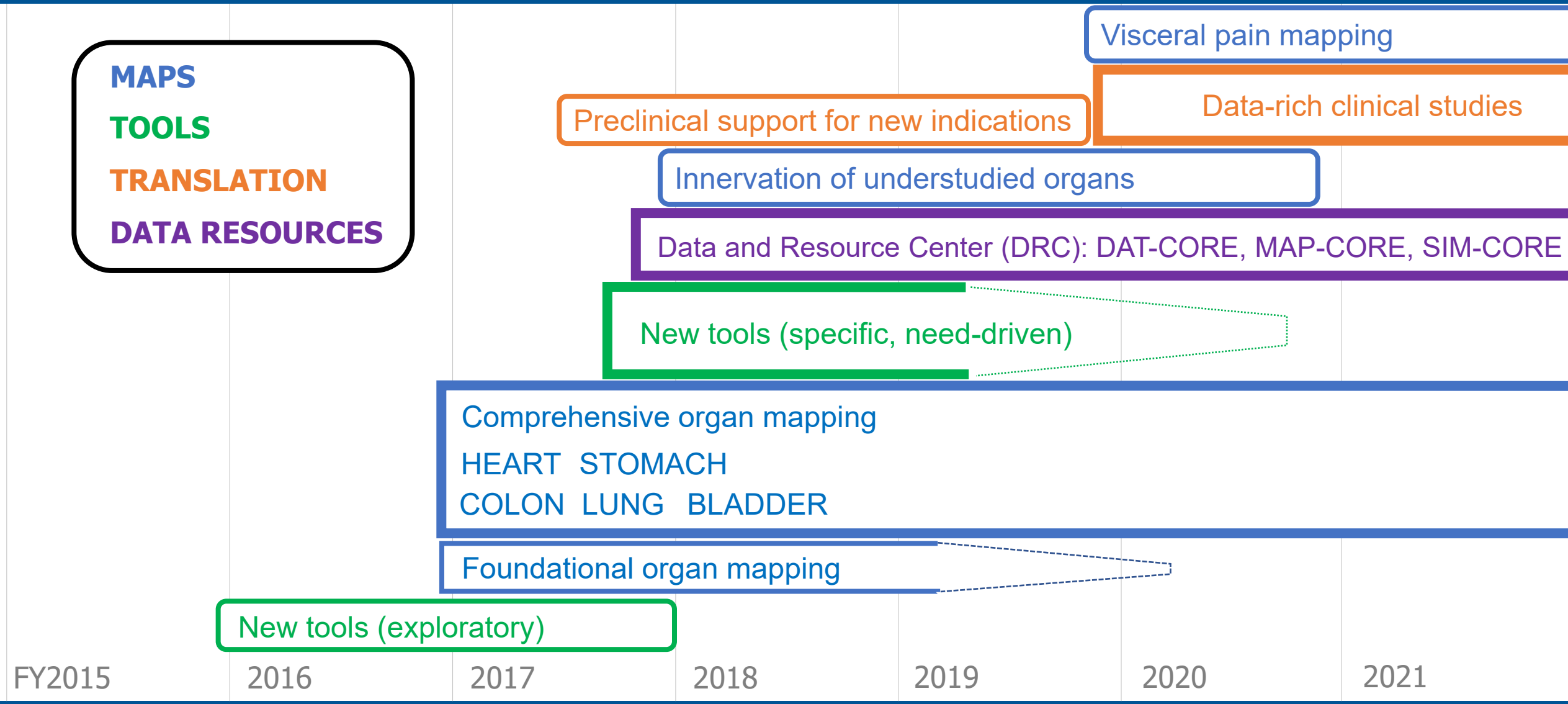
MAPS

TOOLS

TRANSLATION

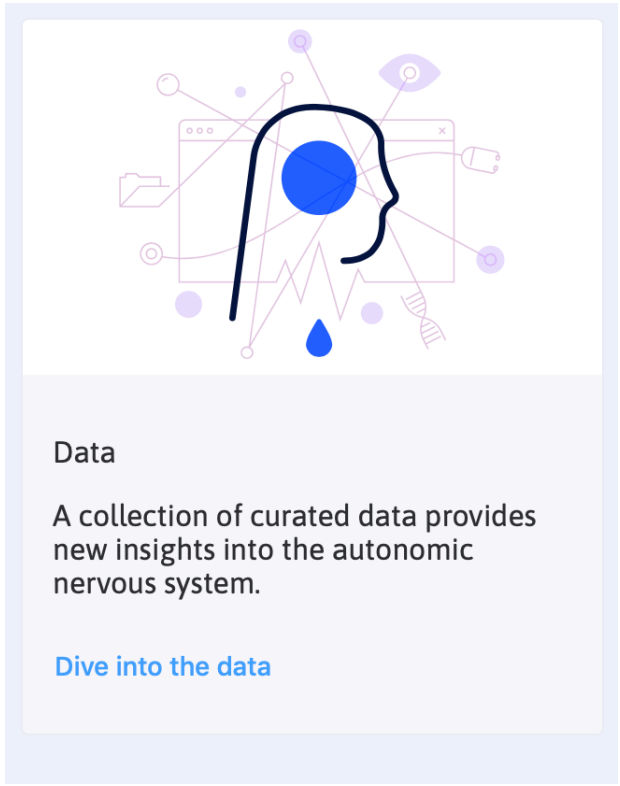
DATA RESOURCES

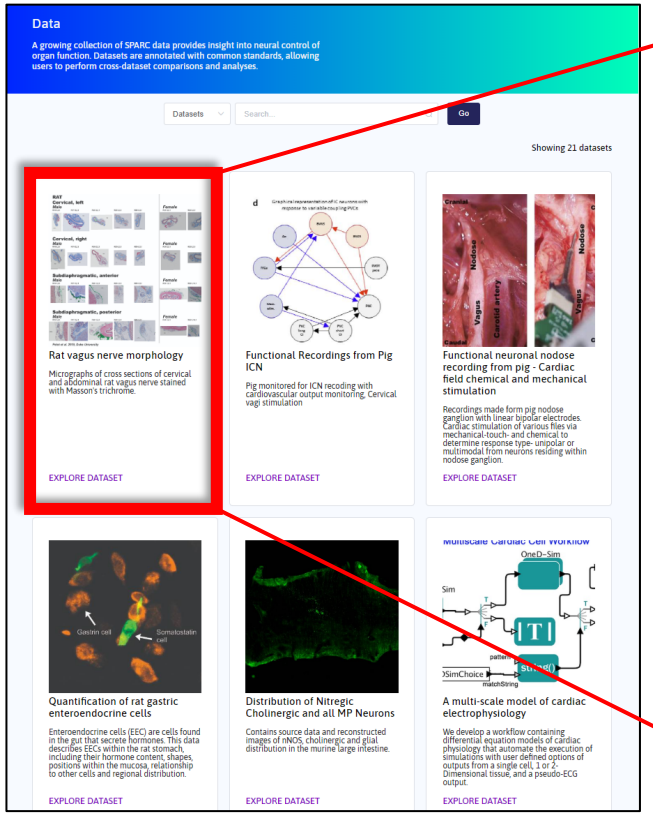


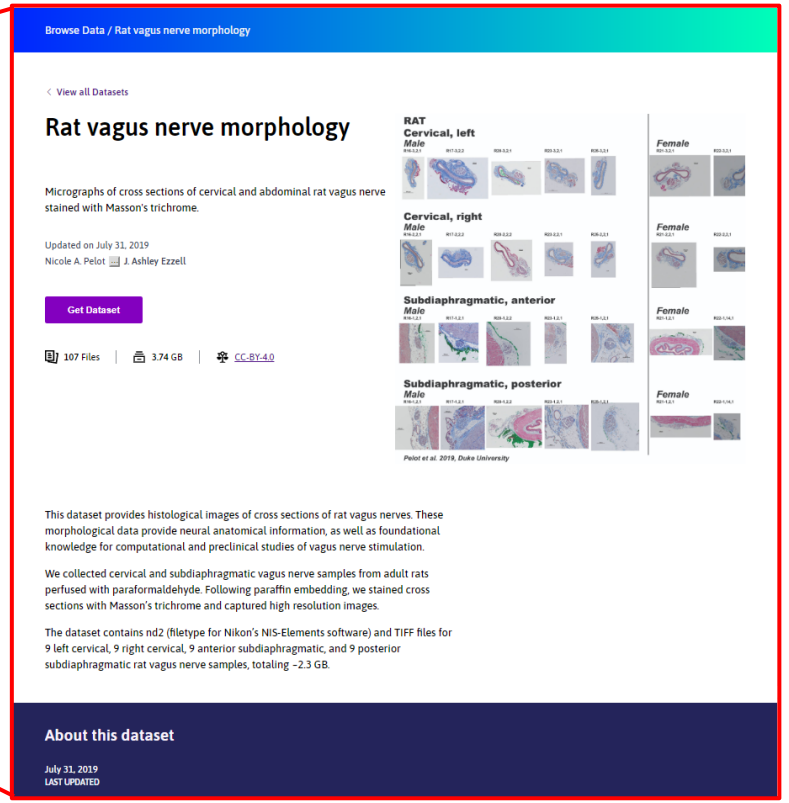
The SPARC Portal

The Common Fund

http://sparc.science







- CC-BY 4.0 license
- Data citation instructions
- 58 datasets now, more continually curated
- Protocols publicly available at protocols.io

SPARC Discovery Highlights

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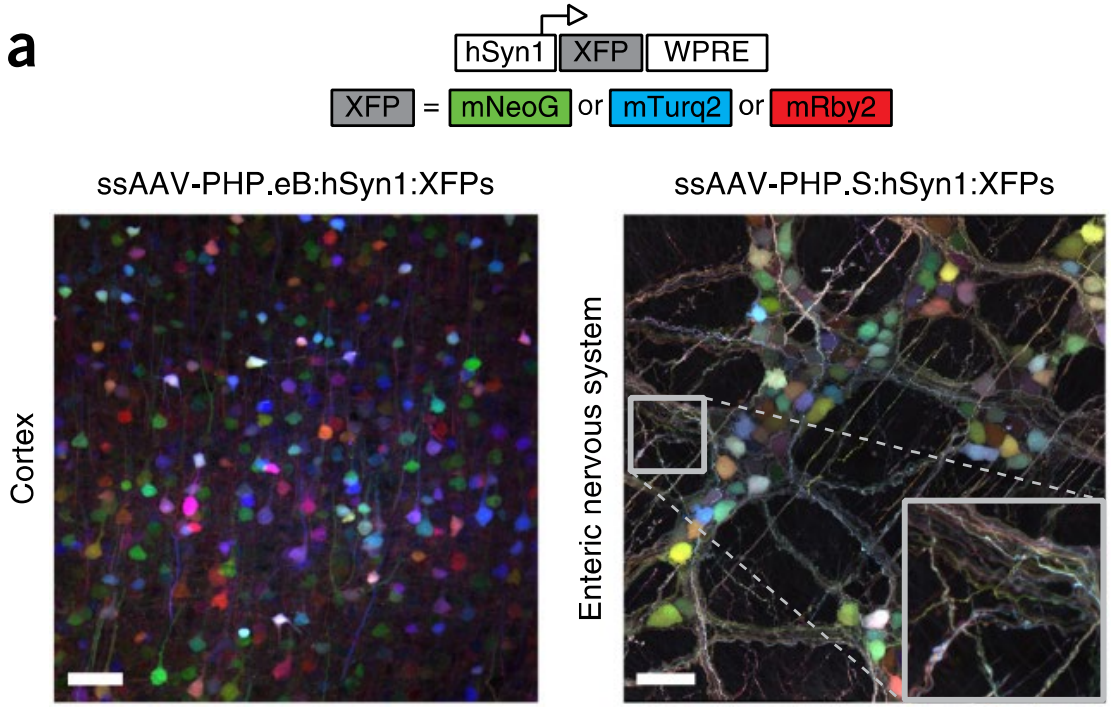
ADVANCE ONLINE PUBLICATION NATURE NEUROSCIENCE

Engineered AAVs for efficient noninvasive gene delivery to the central and peripheral nervous systems

Ken Y Chan, Min J Jang, Bryan B Yoo, Alon Greenbaum, Namita Ravi, Wei-Li Wu, Luis Sánchez-Guardado, Carlos Lois, Sarkis K Mazmanian, Benjamin E Deverman & Viviana Gradinaru



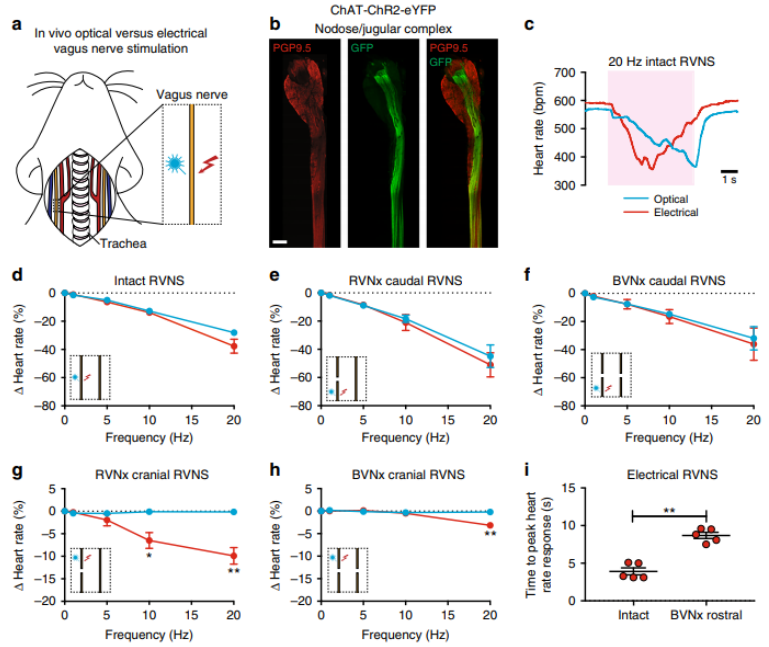
nature COMMUNICATIONS

ARTICLE

https://doi.org/10.1038/s41467-019-09770-1 OPEN

Identification of peripheral neural circuits that regulate heart rate using optogenetic and viral vector strategies

Pradeep S. Rajendran[1], Rosemary C. Challis[2], Charless C. Fowlkes[3], Peter Hanna[1], John D. Tompkins[1], Maria C. Jordan[1], Sarah Hiyari[1], Beth A. Gabris-Weber[4], Alon Greenbaum[2], Ken Y. Chan[2,6], Benjamin E. Deverman[2,6], Heike Münzberg[5], Jeffrey L. Ardell[1], Guy Salama[4], Viviana Gradinaru[2] & Kalyanam Shivkumar[1]



SPARC Discovery Highlights

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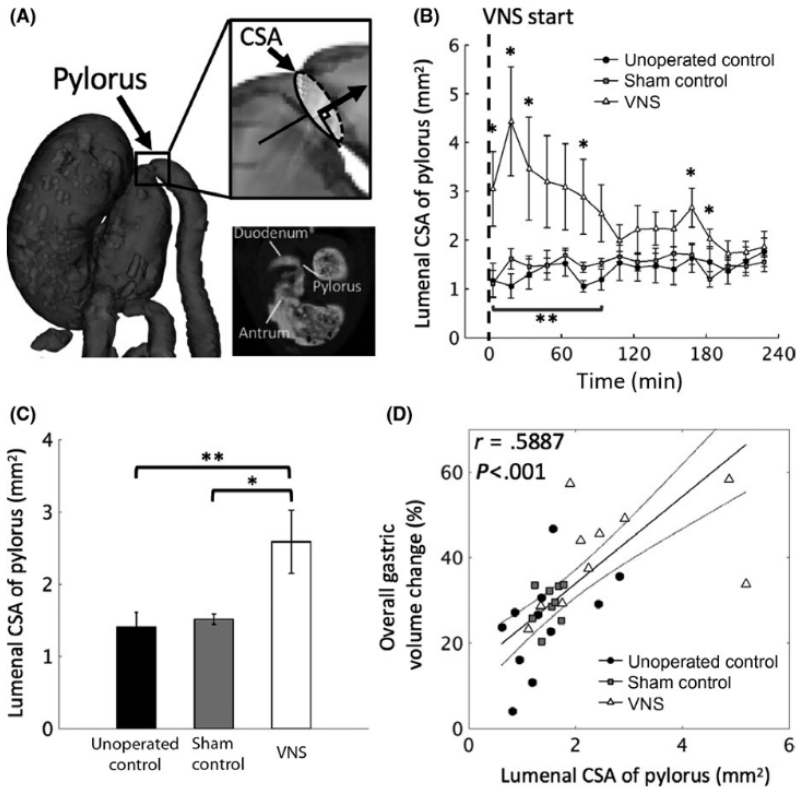
ORIGINAL ARTICLE

WILEY Neurogastroenterology & Motility NGM

Vagus nerve stimulation promotes gastric emptying by increasing pyloric opening measured with magnetic resonance imaging

K.-H. Lu[1,2] | J. Cao[2,3] | S. Oleson[3] | M. P. Ward[3,4] | R. J. Phillips[5] | T. L. Powley[2,5] | Z. Liu[1,2,3]



Contents lists available at ScienceDirect

Brain Stimulation

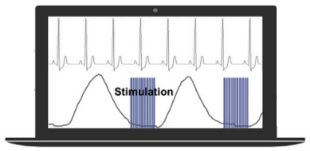
journal homepage: http://www.journals.elsevier.com/brain-stimulation

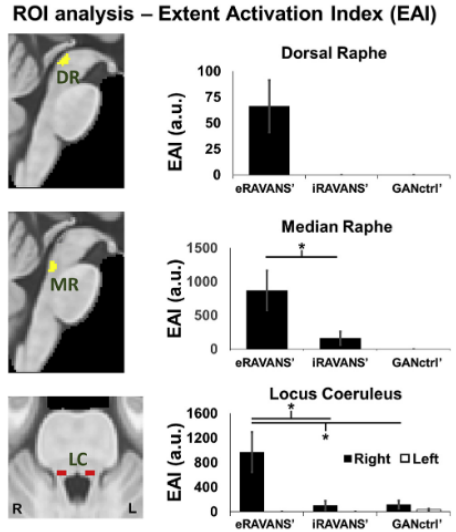
ELSEVIER

The influence of respiration on brainstem and cardiovagal response to auricular vagus nerve stimulation: A multimodal ultrahigh-field (7T) fMRI study

Roberta Sclocco [a, b, *], Ronald G. Garcia [a, c], Norman W. Kettner [b], Kylie Isenburg [a], Harrison P. Fisher [a], Catherine S. Hubbard [a], Ilknur Ay [a], Jonathan R. Polimeni [a], Jill Goldstein [a, c, d], Nikos Makris [a, c], Nicola Toschi [a, e], Riccardo Barbieri [f, g], Vitaly Napadow [a, b]

Stimulation phase locked to respiration phase





SPARC Discovery Highlights

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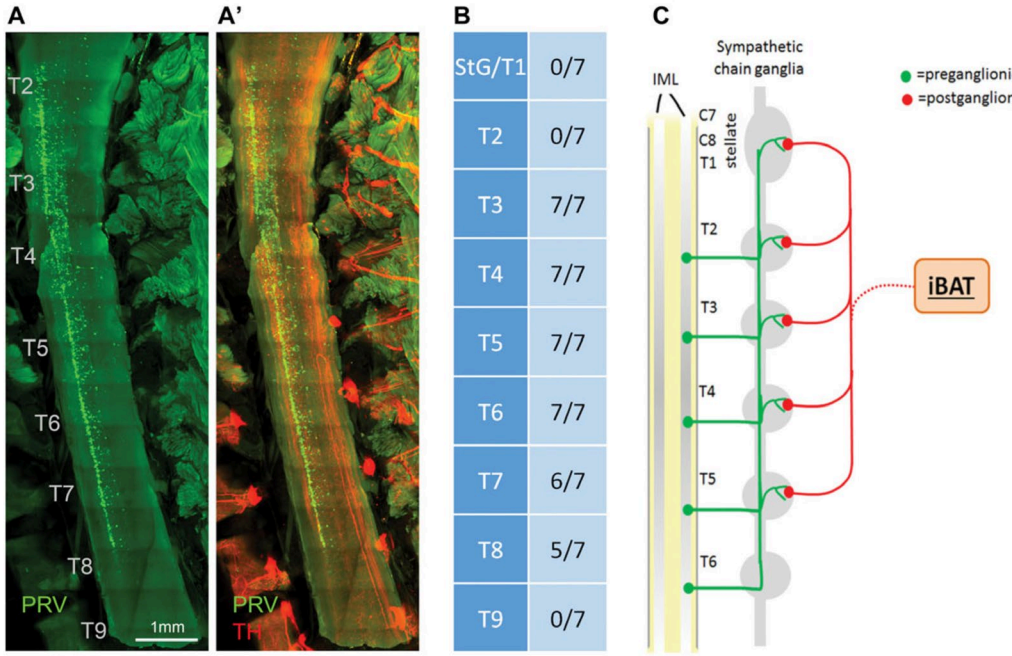
ANNALS OF THE NEW YORK ACADEMY OF SCIENCES
Special Issue: *Autonomic Nervous System Regulation and Metabolic Diseases*
ORIGINAL ARTICLE

Sympathetic innervation of the interscapular brown adipose tissue in mouse

Marie François,[a] Hayden Torres,[a] Clara Huesing,[a] Rui Zhang, Carson Saurage, Nathan Lee, Emily Qualls-Creekmore, Sangho Yu, Christopher D. Morrison, David Burk, Hans Rudolf Berthoud, and Heike Münzberg

Neurobiology of Nutrition and Metabolism Department, Pennington Biomedical Research Center, Louisiana State University System, Baton Rouge, Louisiana

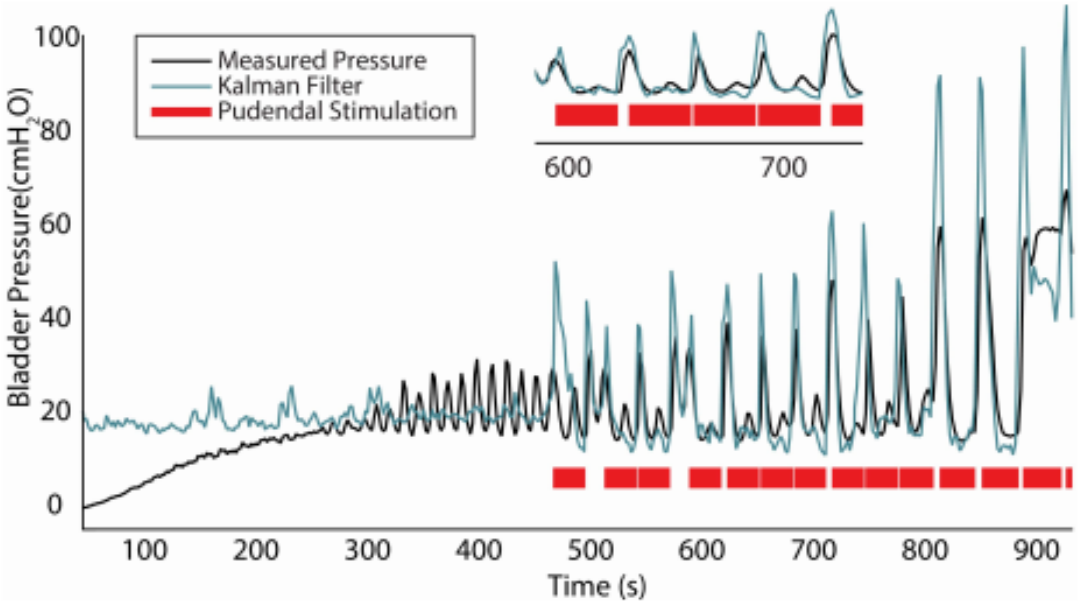


B	
StG/T1	0/7
T2	0/7
T3	7/7
T4	7/7
T5	7/7
T6	7/7
T7	6/7
T8	5/7
T9	0/7

EMB IEEE TRANSACTIONS ON NEURAL SYSTEMS AND REHABILITATION ENGINEERING, VOL. 27, NO. 6, JUNE 2019 1209

Real-Time Bladder Pressure Estimation for Closed-Loop Control in a Detrusor Overactivity Model

Zhonghua Ouyang, Zachariah J. Sperry, Nikolas D. Barrera, and Tim M. Bruns, *Member, IEEE*



Industry partnerships, three types

NIH The Common Fund

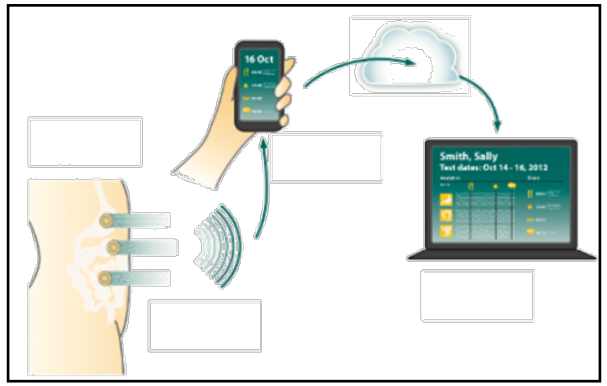
Type I: SPARC-supported teams with industry partners

- Michigan with Cortec (Bruns, LUT nerve interface)
- IU with Medtronic (Chen, subcutaneous sympathetic activation for AF)
- Purdue with Axion Biosystems (Ward, gastric vagal signals interpreted at neck)
- Louisville with Medtronic (Harkema, spinal stim for bowel and bladder in SCI)

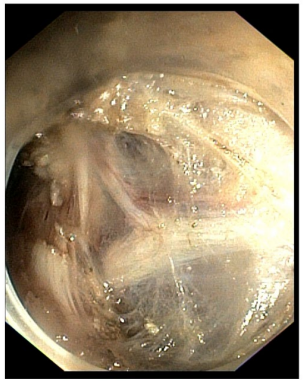
Type II: SPARC-supported teams with commercial activities/ambitions

Micro-Leads
(McLaughlin)

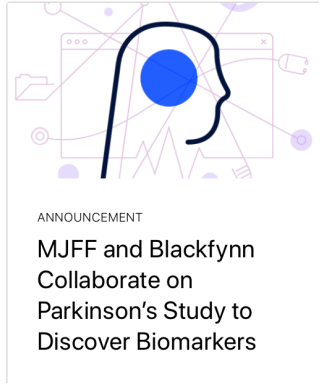
CALMI^2
(Gregersen)



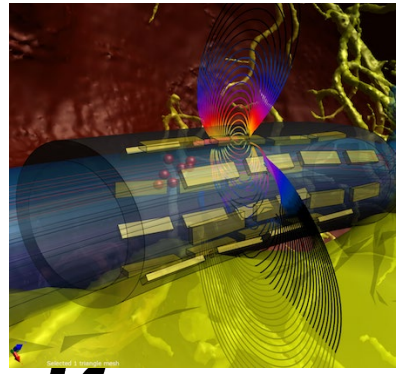
G-Tech
(Axelrod)



Feinstein
(Miller)



Blackfynn
(Wagenaar)



IT'IS FOUNDATION
(Kuster)

Industry partnerships, three types

The Common Fund

Type III: Licensing of IP from SPARC-supported teams

Case study: SPARC-funded Vitaly Napadow working with bioelectronic medicine company Cala Health

Cala Health Licenses Innovative Technology from Partners Healthcare to Develop and Deliver Novel Therapies for Patients with Chronic Disease

Collaboration Created to Advance Non-invasive Neuromodulation Therapy

March 12, 2019 10:30 AM Eastern Daylight Time

BURLINGAME, Calif.--(BUSINESS WIRE)--Cala Health, Inc., a bioelectronic medicine company developing wearable therapies for chronic disease, today announced that they have licensed technology from Partners Healthcare Innovation and its affiliate, Massachusetts General Hospital (MGH) to enhance the company's non-invasive neuromodulation platform for investigating and treating chronic diseases.

The technology licensed by Cala Health was developed from research on transcutaneous vagus nerve stimulation (tVNS) and Respiratory-Gated Vagal Afferent Nerve Stimulation (RAVANS) in the MGH research lab of Vitaly Napadow, PhD, LicAc. As part of this agreement, the MGH researchers who originally created the technology will work with Cala Health as scientific advisors in development to further accelerate the investigation of non-invasive therapies.

"This collaboration with MGH's cutting-edge research team provides a clear opportunity to accelerate development of wearable neuromodulation therapies for many chronic diseases," said Kate Rosenbluth, PhD, Founder and CEO, Cala Health. "By working together, our combined team can discover, develop and deliver breakthrough therapies for patients living with these conditions."

"This collaboration is the result of years of research and development on the links between brain and cardiac function, and our team is excited to be working with an established company that has experience taking new devices through clinical studies and regulatory clearance," said Jill Goldstein, PhD, Executive Director of the Women, Heart and Brain Global Initiative (a collaboration between MGH and the Harvard T.H. Chan School of Public Health) and Professor of Psychiatry and Medicine, Harvard Medical School, and the Helen T. Moerschner Endowed MGH Research Institute Chair in Women's Health.

"There is a great need to offer effective therapies that are not based on drugs or invasive implants. Non-invasive neuromodulation may help address that need," said Vitaly Napadow, Associate Professor at the Martinos Center for Biomedical Imaging at Massachusetts General Hospital and Harvard Medical School in Boston.

CALA HEALTH, INC.

More News

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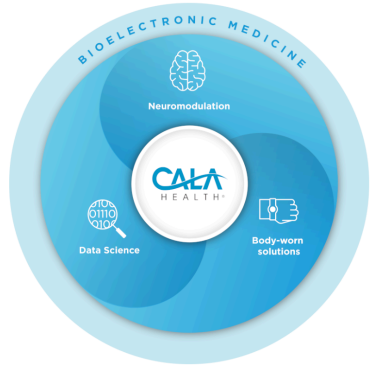
ABOUT CALA HEALTH®

Cala Health is a bioelectronic medicine company transforming the standard of care for chronic disease. The company's wearable neuromodulation therapies merge innovations in neuroscience and technology to deliver individualized peripheral nerve stimulation. The first indication for Cala Health's wearable therapy is essential tremor, a disease experienced by more than seven million people and characterized by severe hand tremors. New therapies are under development in neurology, cardiology and psychiatry. The company is headquartered in the San Francisco Bay Area and backed by leading investors in both healthcare and technology.

COMPANY STORY



Making translational connections

The Common Fund

Partnerships

Medtronic
Louisville - spinal stim for bowel and bladder in SCI

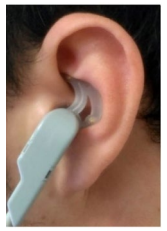
Indiana University – cardiac and skin sympathetic neuromodulation

Medtronic BIOCIRCUIT TECHNOLOGIES
Purdue - cutaneous cervical vagal signals

Takeda Purdue - gastric MRI

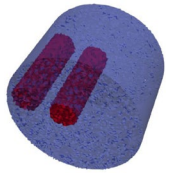
Michigan - LUT nerve interface
CorTec

Licensing of IP



CALA HEALTH
licensed auricular vagus stim tech from SPARC awardee MGH

GALVANI BIOELECTRONICS



Has joint IP with UCL for EIT technology supported by SPARC and GSK

Potential Commercial Products

California Medical Innovations Institute

Transiting colonic pressure sensor

Micro-Leads, Inc.

HD microelectrode Spinal stimulating array

G-Tech Medical

Electrogastrogram