



# Bioelectronic Medicines

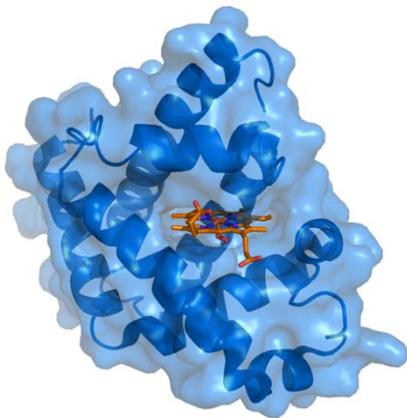
Using the Peripheral Nervous System to Treat Chronic Disease

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VP, Bioelectronics R&D, GSK  
Nov 14, 2014

# A treatment modality that leverage the nervous system

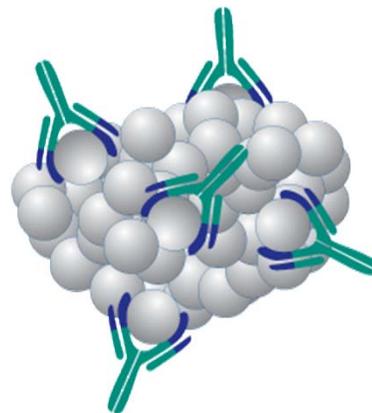


## Signalling control



**Small molecules** leverage intra- and extra-cellular signalling cascades

## Immune control



**Vaccines and antibody drugs** leverage the immune system

## Neural control

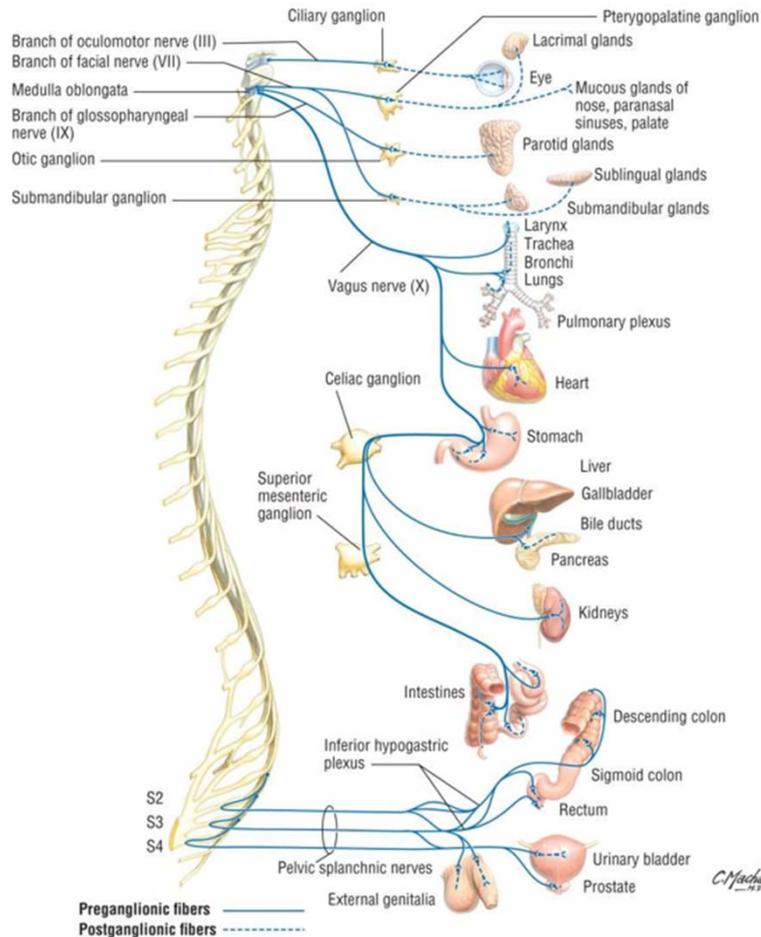


**Bioelectronic medicines** will leverage the nervous system

Image source: [http://en.wikipedia.org/wiki/Ligand\\_\(biochemistry\)](http://en.wikipedia.org/wiki/Ligand_(biochemistry)); <http://www.rndsystems.com/resources/images/6295.gif>; <http://www.empowher.com/media/reference/x-linked-adrenoleukodystrophy>

# Nerves exert control over virtually all our organs

## Parasympathetic nervous system



## Sympathetic nervous system

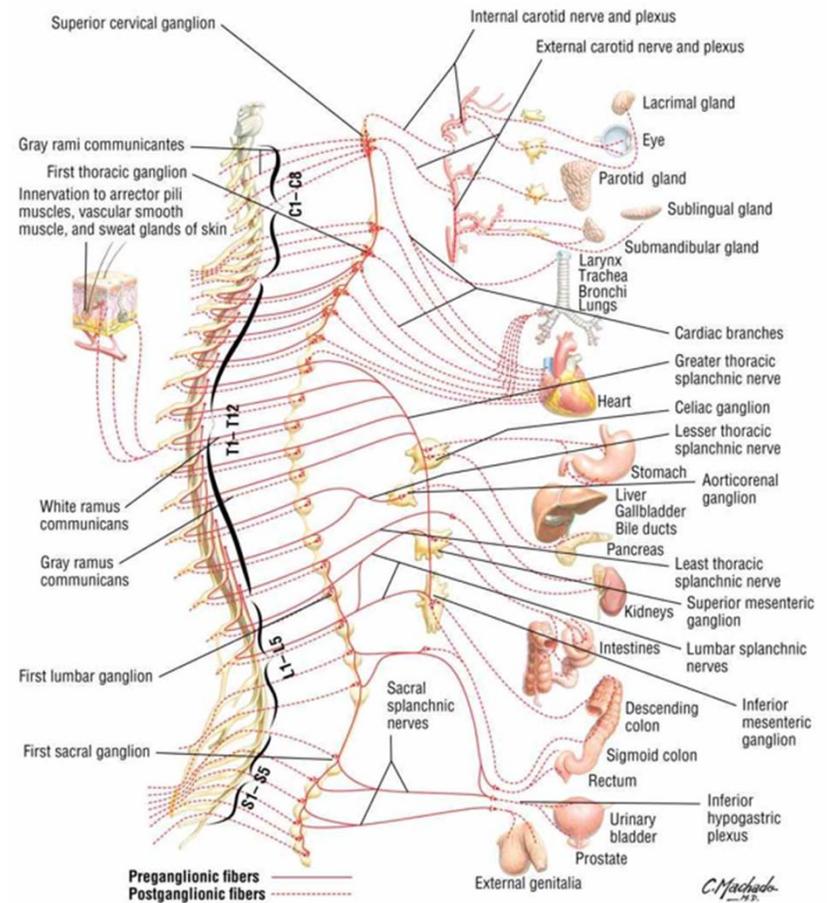


Image source: Atlas of Human Anatomy, 5th edition, Frank H Netter

## While brain research is...

- Arguably the biggest scientific challenge of our time
- Critical for understanding most neural circuits
- A centre stage for innovative technology development

## Therapeutic precision tuning will start in the periphery

- Chronic diseases affecting billions
- Near-organ nerves with lower level of complexity
- More reliable animal models of disease
- Objective clinical endpoints
- Accessible intention points; low-risk surgery

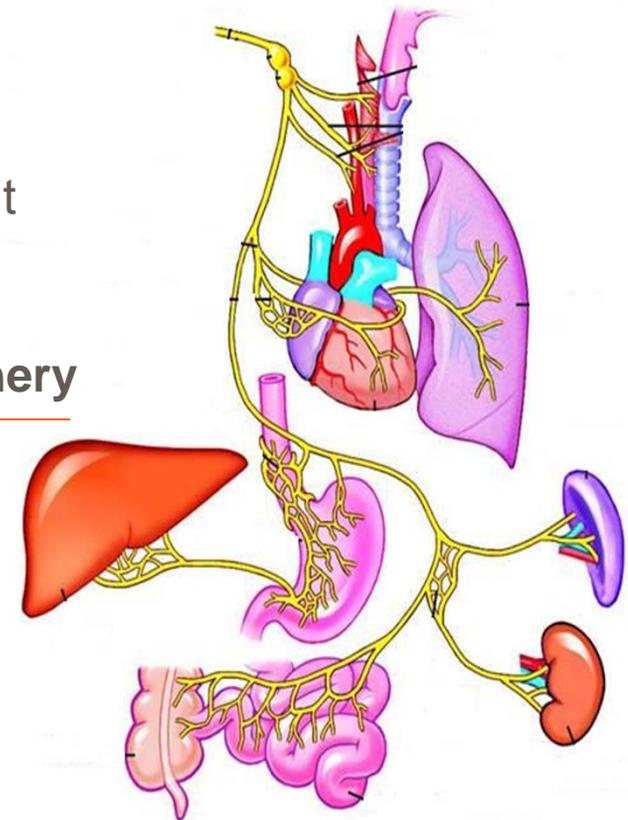
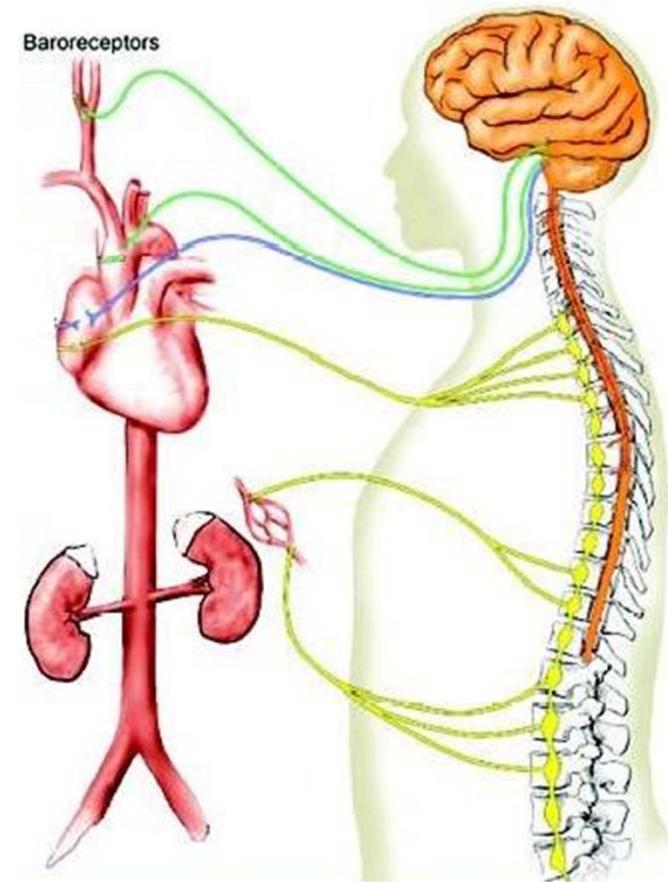
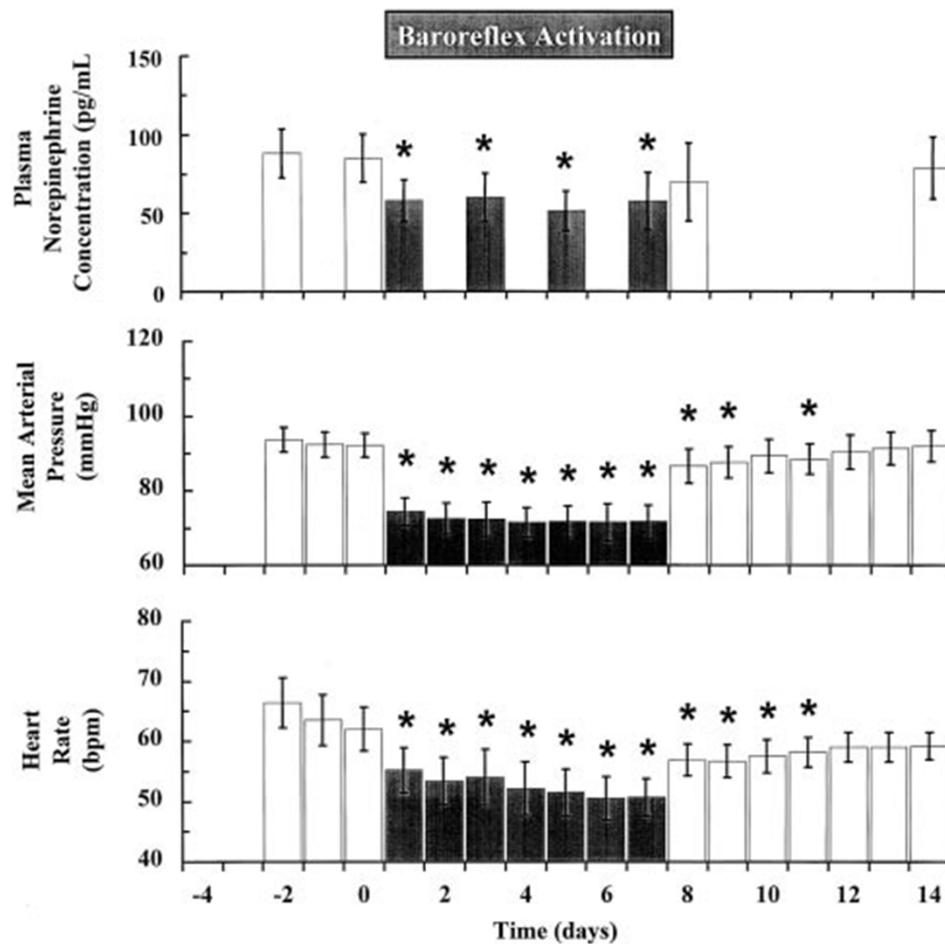


Image source: Mosby's Medical Dictionary, 8th edition

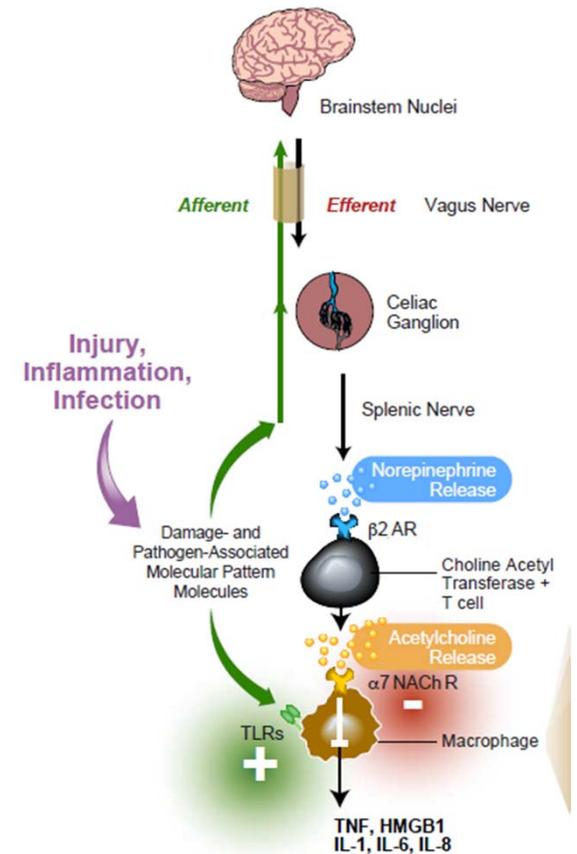
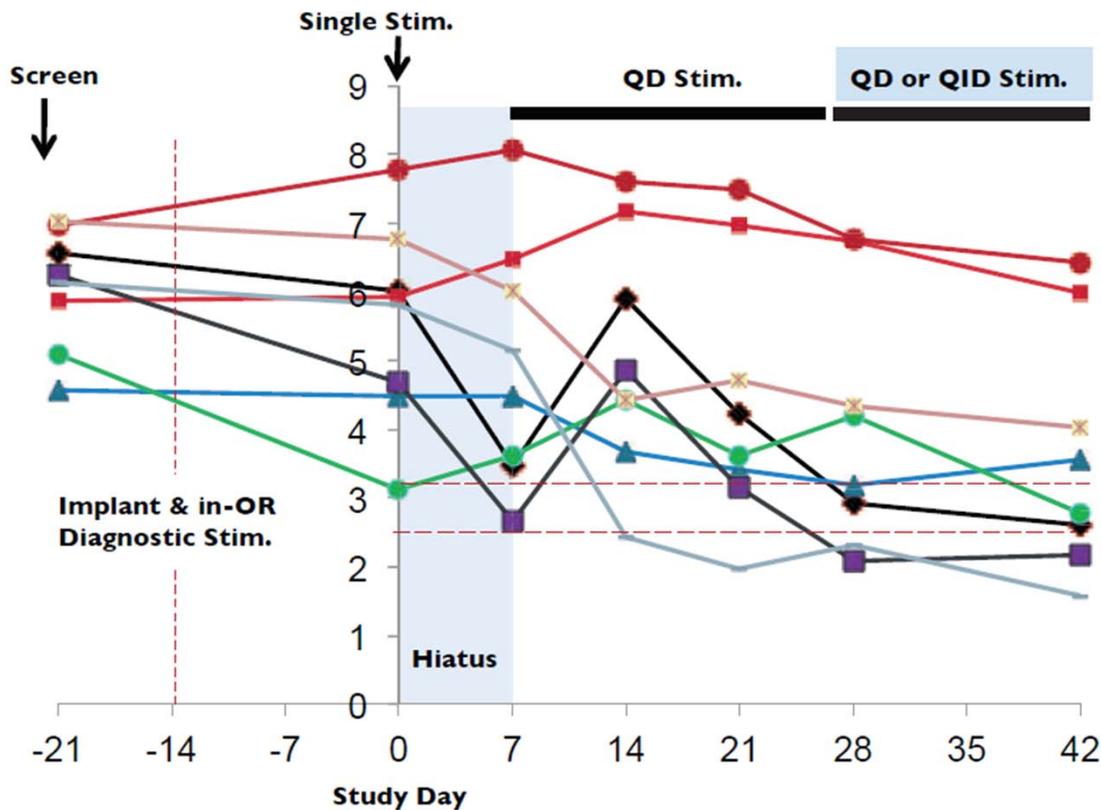
# In hypertension baroreceptor stimulation reduces sympathetic outflow, heart rate and blood pressure



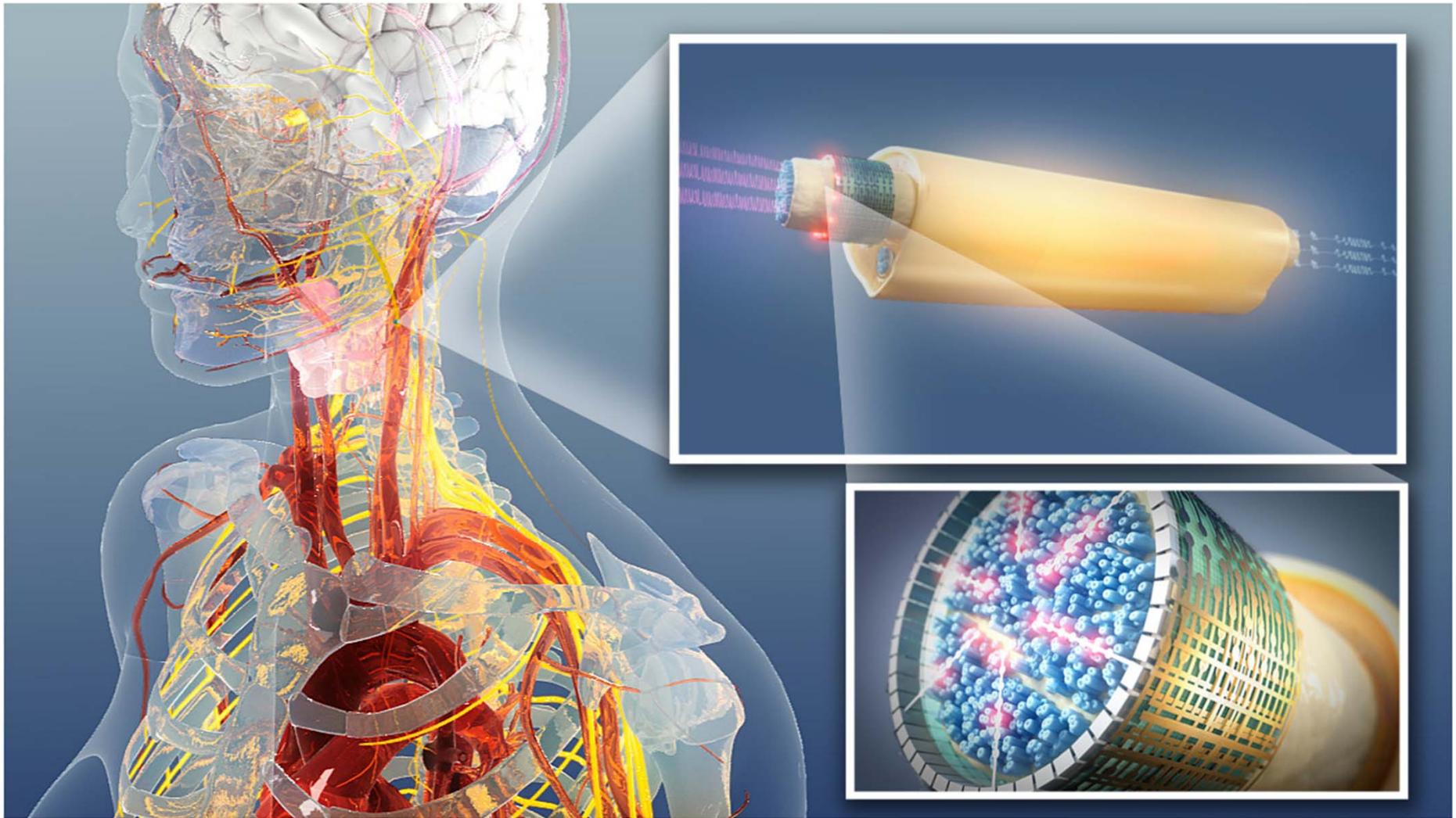
# In rheumatoid arthritis, vagus nerve stimulation suppresses cytokine production



DAS28 in 8 RA patients that had failed on methotrexate after vagus nerve stimulation



# A leap towards precision treatments



# Exploratory research network for proof of principle for diseases and interfaces



## Philosophy

- **Integrate** experts and technologies
- Test **hypotheses** central to future medicines
- Work as a **network**, helping to accelerate

**33 projects**

**4 continents**

**16 diseases**

**40 PIs (at 26  
institutions)**

**9 countries**

**(24 nerves)**

**13 interfaces**

# Venture fund to nurture early manifestations of bioelectronic medicines and key platforms



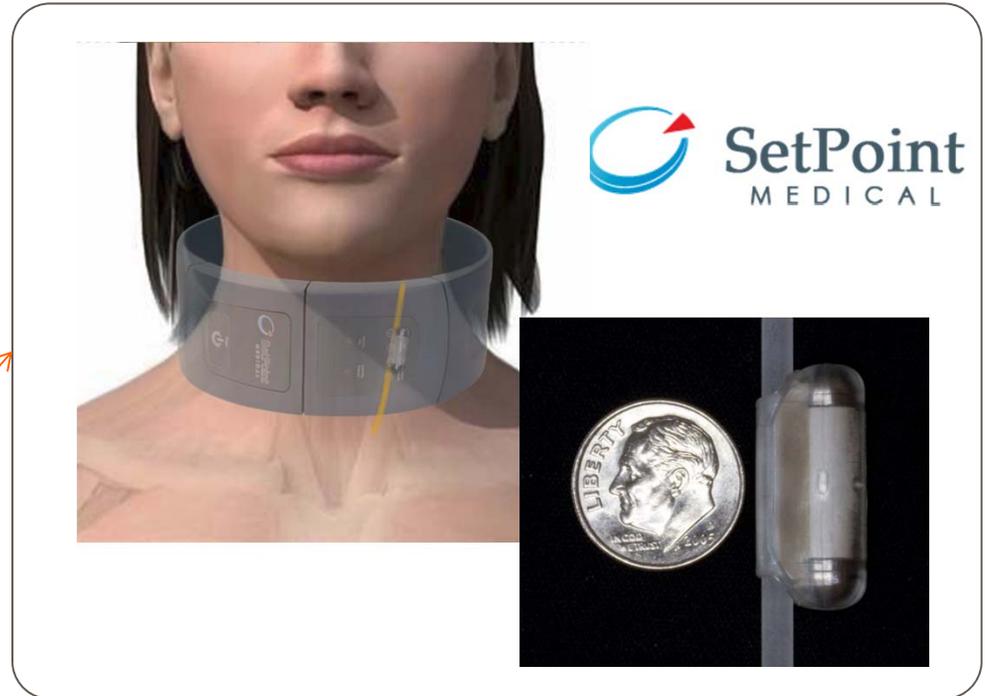
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*Investment focus for \$50m fund*

- Companies developing **bioelectronic medicines**
  - New start-ups
  - First-generation devices pioneering aspects of bioelectronic medicines

- Companies advancing **technology platforms** that will be critical components of bioelectronic medicines



- Energy
- Material
- Surgical

Image source: SetPoint Medical

# Road-mapping and coordination with the broader research community



**COMMENT**

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## A jump-start for electroceuticals

Kristoffer Famm and colleagues unveil a multidisciplinary initiative medicines that use electrical impulses to modulate the body's neu...

Imagine a day when electrical impulses are a matter of medical treatment. Your doctor will administer electroceuticals that target individual nerve fibres or specific brain circuits to treat an array of conditions. These treatments will modulate the neural impulses controlling the body, repair lost functions and restore health. They could, for example, ease tension from cells to treat diabetes, regulate food intake to treat obesity and correct balance in smooth-muscle tone to treat hypertension and pulmonary diseases.

All this is within reach if researchers from disparate disciplines in academia and industry work together. Here, we outline what needs to be done to bring about electroceuticals and unveil a public-private research initiative and a research network that will catalyse the field.

Electrical impulses — are the language system. Variably are regulated this common coding. Two features make targets for therapy: they comprise a distributed network of nerve bundles —

14 APRIL 2012 | 9

**COMMENT**

## Bioelectronic medicines: a research roadmap

Karen Bremington, Vikrama Chandrasekhar, Palina Anshakov, Warren M. Grill, Victor Pliskov, Brian McLaughlin, Pankaj Pasricha, Douglas Weber, Alp Ludvig 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.

With the rapid rise in technology for the precision detection and modulation of electrical signalling patterns in the nervous system, a new class of treatments known as bioelectronic medicines seems within reach. Specifically, the peripheral nervous system will be at the centre of these advances, as the functions it controls in chronic disease are extensive and its small number of fibres per nerve renders them more tractable to targeted modulation.

The vision for bioelectronic medicines is one of miniature, implantable devices that can be attached to individual peripheral nerve segments in the vicinity, extending beyond early clinical examples to hypertension and lung cancer. Such devices will also detect and modulate neural signalling patterns, achieving therapeutic effects that are targeted to single neurons or specific organs. This precision could be further enhanced through closed-loop systems that use devices that can record neural electrical activity and physiological parameters, analyse the data in real time and modulate neural signalling accordingly. For this vision to be realized, a solid research foundation for bioelectronic medicines is needed. This article provides a research roadmap for the next 5 years towards generating that base.

An emerging community of 'bioelectronicists' This roadmap has its origins in a meeting of research leaders from academia, industry and government in December 2011, for which neurophysiologists, neural engineers, disease biologists, neurosurgeons, as well as data and material scientists came together to define the research path towards bioelectronic medicines. These principal research areas crystallized in the meeting: the creation of a record of nerve data; the advancement of neural interfacing technology; and the early establishment of therapeutic feasibility. The direction in these areas has been further professionalized and refined by the authors of the roadmap, with the intention of engaging and expanding an emerging research community interested in bioelectronic medicines. Key elements of the plan in these three areas are summarized here, with detailed points and references provided in Supplementary Information S1 (http://dx.doi.org/10.1038/nrn3584).

Creation of a visceral nerve atlas As with the large-scale genomics and brain projects (see the NIH literature report for further information), a biological map of structure and function — underpinned by data recording standards and optimal practices that enable collaborative data mining — will be crucial. This roadmap focuses on the measurement of visceral organs, such as the lungs, heart, liver, pancreas, kidney, bladder, gastrointestinal tract and lymphoid and reproductive organs. Their specific innervation, including sympathetic, parasympathetic, sensory and enteric systems, needs to be mapped, with the goal of achieving resolution at the level of nerve fibres and action potentials.

Strategic knowledge of the detailed peripheral nerve wiring will guide the reduction of organ-specific points of investigation. The key research steps towards establishing such a structural map are to expand the toolbox for high-resolution tracing and mapping of visceral nerve fibres, establish the terms and inter-specific variations of organ innervation, and then build detailed maps in the most appropriate animal model for each organ. Another important early priority is to advance techniques for imaging the anatomical course and targets of visceral nerves in humans, paving the way for precision implantation of bioelectronic medicines in the clinic.

Ultimately, the focus should be on decoding the neural signalling patterns that control individual organs. This approach will begin with simultaneous recordings of both neural signalling and biomarkers of organ function

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## Stimulating Peripheral Activity to Relieve Conditions (SPARC)

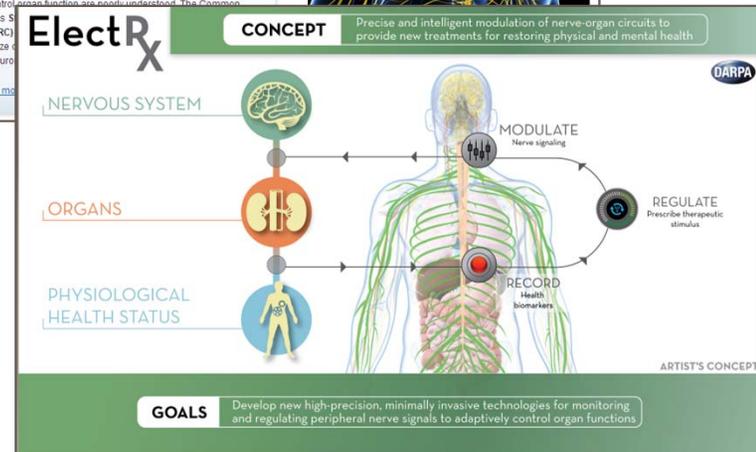
OVERVIEW WORKING GROUP MEMBERS RESEARCH FUNDING PUBLICATION NEWS

Common Fund Home > Programs > Stimulating Peripheral Activity to Relieve Conditions (SPARC)

Fund's S (SPARC) catalyze neuro

Program Snapshot

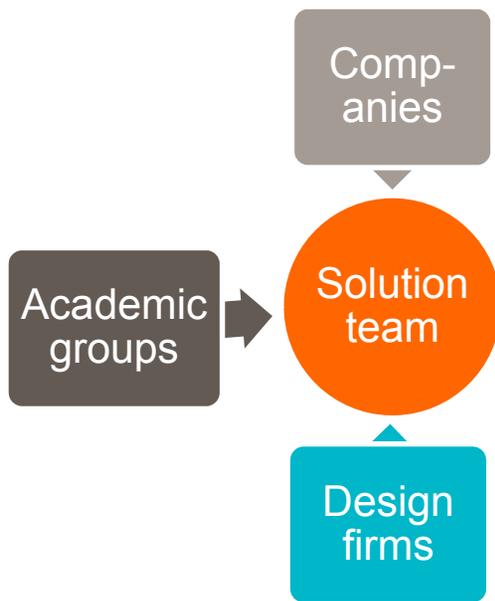
All organs in the body are stimulated by nerves, which send signals that affect the organ's function. Modulation of nerve signals to control end-organ function has recently been recognized as a potentially powerful way to treat many diseases and conditions, such as hypertension, heart failure, gastrointestinal disorders, type II diabetes, inflammatory disorders, and more. However, the mechanisms of action for therapies in which nerves are stimulated to control organ function are poorly understood. The Common



# Innovation challenge to remove a key research barrier



A miniaturised, implantable, wireless device that can chronically record, stimulate and block functionally-specific neural signals to and from a single visceral organ



**1x + rat + 60d = \$1m**

organ-specific function

Implant, wireless, normal

stable, reproducible

First validated solution

<http://www.bioelectronicmedicinesresearch.com>

**\$5m Fund** with up to \$1.2m for teams trying to solve the challenge

# BRAIN Initiative and PNS therapies linked by circuit mapping and innovative technologies

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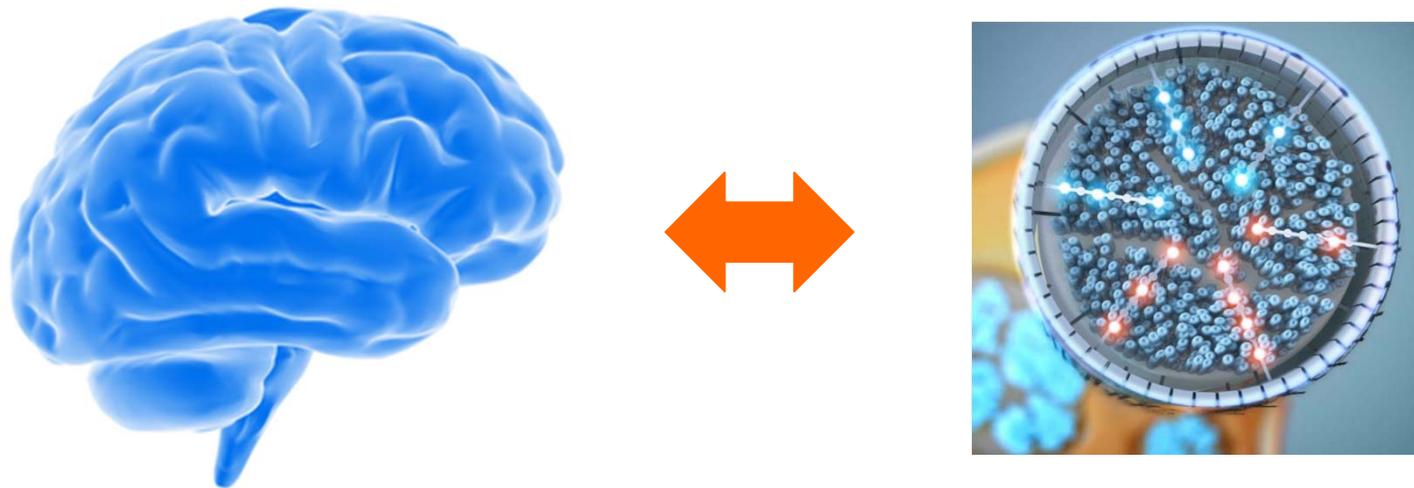


Image source: [http://www.huffingtonpost.com/daniel-burrus/why-the-human-brain-initi\\_b\\_3103869.html](http://www.huffingtonpost.com/daniel-burrus/why-the-human-brain-initi_b_3103869.html)



*Thank You*