

Title of proposed program: S.P.A.R.C. - Stimulating Peripheral Activity to Relieve Conditions

What is the major obstacle/challenge/opportunity that the Common Fund should address?

In the medical device industry, an area of heavy development is neuromodulation to control end-organ system function in health and disease. Despite the substantial increase in industry activity - and some remarkable demonstrations of efficacy - the mechanisms of action for each of the therapies remain poorly understood. Points of implantation along the neural axis are selected primarily by trial and error; for example, neuromodulation devices for heart failure and hypertension have been clinically tested along the cardio-renal axis at the carotid baroreceptors, the carotid sinus nerve, the vagus nerve, the spinal cord, the renal nerves, and even in deep brain structures. Without understanding the functional neural anatomy as it pertains to the intended therapeutic effect, unwanted side effects at each of these points of intervention, and the variability of functional cell-types and their distributions at each of these points across a population, it is problematic to develop novel minimally-invasive electrode designs, stimulation protocols, and therapy targets. This lack of mechanistic understanding contributes to unpredictability of clinical trial outcomes, variability in responsiveness of treatment, and also hampers the development of more efficacious devices.

What would the goals of the program be?

The long term goal of a program on Stimulating Peripheral Activity to Relieve Conditions (SPARC) would be to provide the scientific foundation to catalyze development of new or more efficacious therapies utilizing closed-loop neuromodulation of end-organ system function. Building this foundation would primarily entail creating detailed functional maps of end-organ system control in appropriate animal models, and validation of these maps for human translation. The SPARC program would capitalize on recent advances in technology - and anticipated new technology developments facilitated by the SPARC program - to deliver detailed, integrated functional and anatomical neural circuit maps in five organ systems. These maps would be leveraged directly to develop and pilot five novel electrode designs, with corresponding stimulation protocols and minimally invasive surgical procedures, to improve existing neuromodulation therapies or pursue new indications.

Why is a trans-NIH strategy needed to achieve these goals?

The fundamental biological understanding of the functional neuroanatomy of each end-organ systems requires techniques and technology that are organ-specific, as well as overlapping between organs. Catalyzing neuromodulation to control end-organ system function would require physiologists with expertise relevant to each end-organ system, neuroscientists, engineers that specialize in the development of technologies for academic research, translational engineers, and the surgical community for each end-organ system. The SPARC

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Program would need to leverage and coordinate a diverse set of expertise located across ICs at the NIH to be successful, and therefore is very appropriate for a Common Fund program.

What initiatives might form the strategic plan for this topic?

Initiative 1. Biology: Anatomic and Functional Mapping

Initiative 2. Next Generation Tools

Initiative 3. Off-label Use of Existing Market-Approved Technology for Small Market Indications

Initiative 4. Data Coordination

Together, the first two initiatives would deliver a detailed, integrated functional and anatomical neural circuit map in five organ systems. They would develop and pilot novel electrode designs, minimally invasive surgical procedures, and stimulation protocols leveraging insights from the functional maps to improve existing neuromodulation therapies or pursue new indications. The third initiative would support partnerships between industry, FDA/CDRH and NIH-supported investigators to explore the utility of existing devices approved for clinical use to address new, small-market indications. These markets are too small to motivate industry investment in isolation, so we propose to support proof-of-concept demonstrations in humans to attract industry interest in pursuing FDA approval as a labeled indication. The goal for the Data Coordination Center (Initiative 4) would be to assemble data from all SPARC biology and technology projects into a coordinated data resource, develop user-friendly computational tools, and incorporate next generation computational modeling methods as they become available. The Data Coordination Center would focus both on the project-driven needs within the Common Fund program and on establishing a resource for data generated by the Program for the wider research community.

If a Common Fund program on this topic achieved its objectives, what would be the impact?

A successful SPARC Common Fund program would catalyze development of new and more efficacious therapies utilizing closed-loop neuromodulation of end-organ system function. It would improve our ability to stratify patients by identifying likely responders to neuromodulation, and it would expand the number of organ systems amenable to neuromodulation.