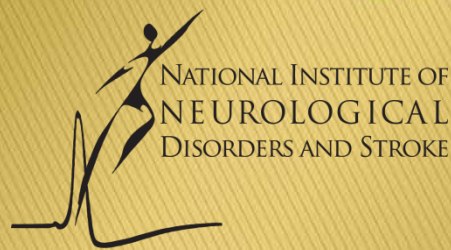


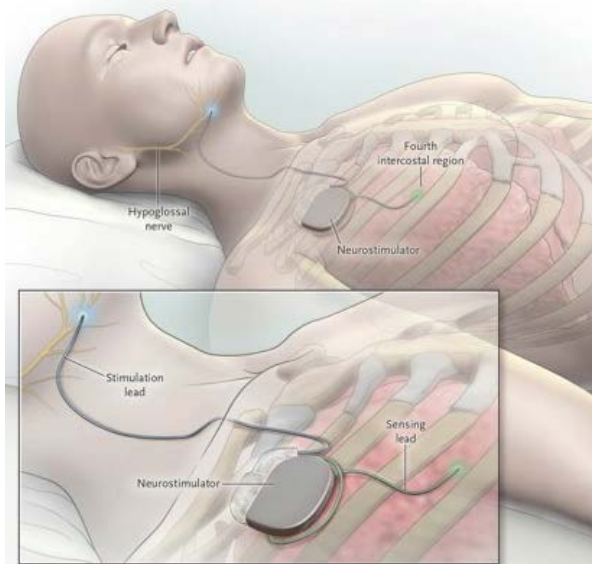
Opportunities for Neurotechnology at NINDS/NIH

Dr. Kip Ludwig

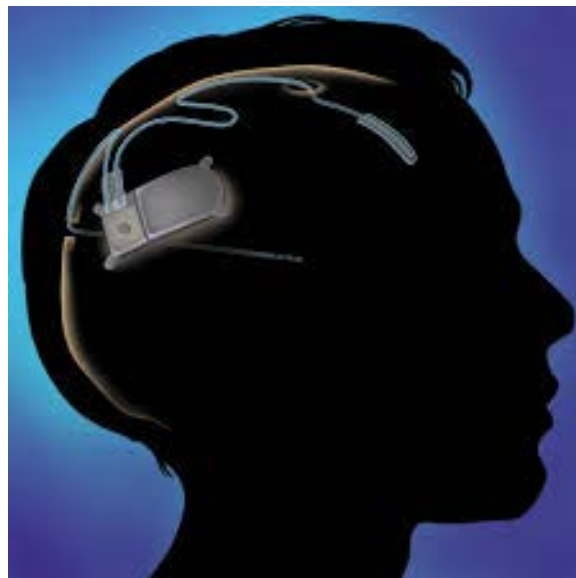
Program Director for Neural Engineering, NINDS/NIH



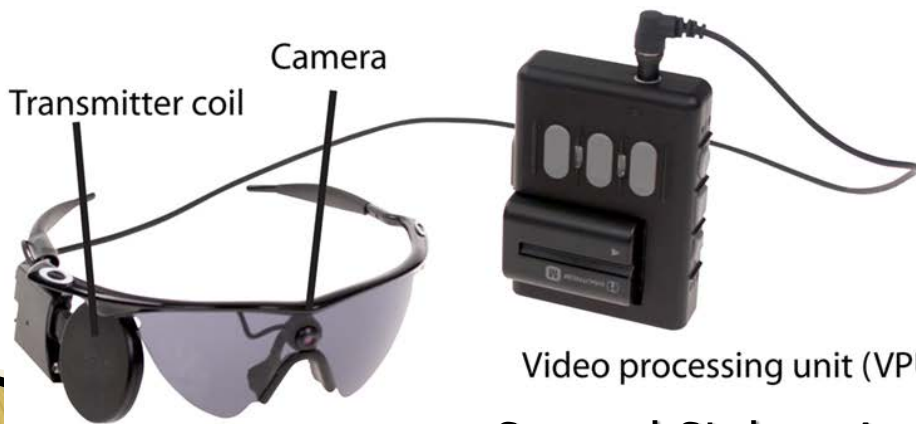
Recent U.S. Neuromodulation Approvals: RCT Pivotal Trials



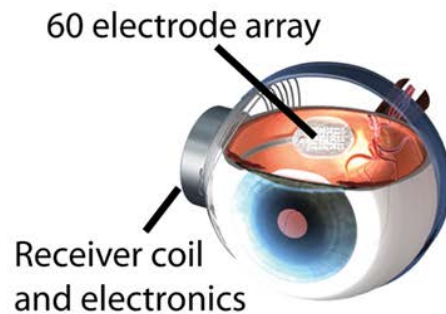
Inspire



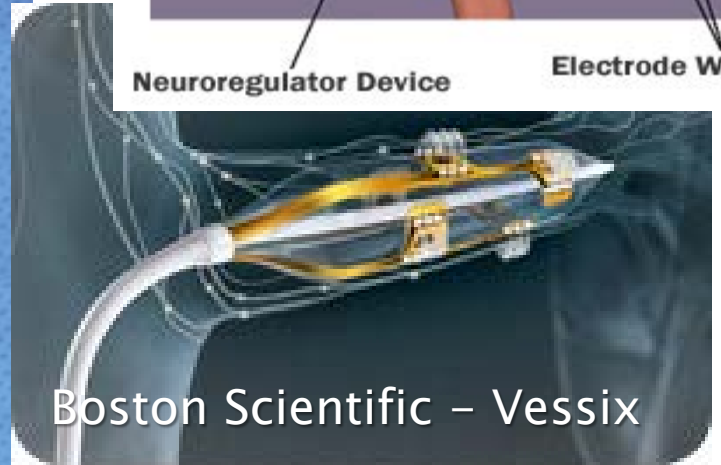
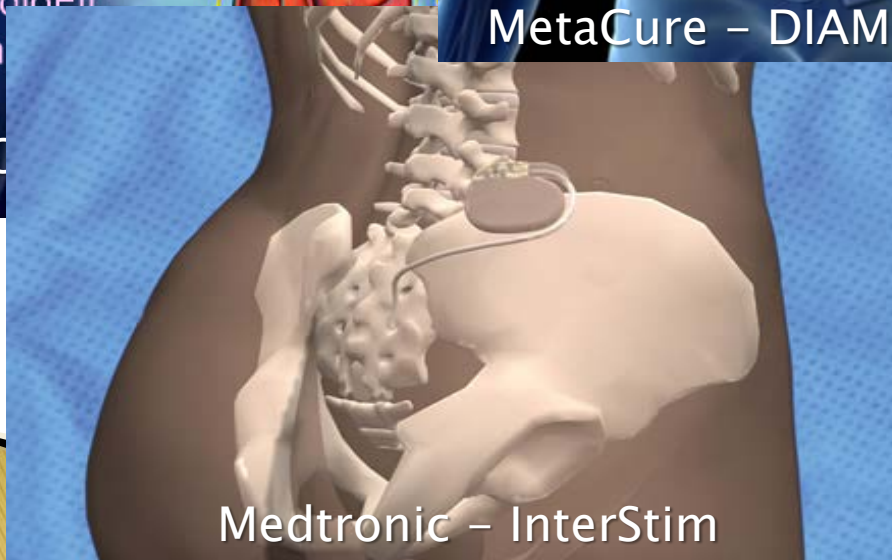
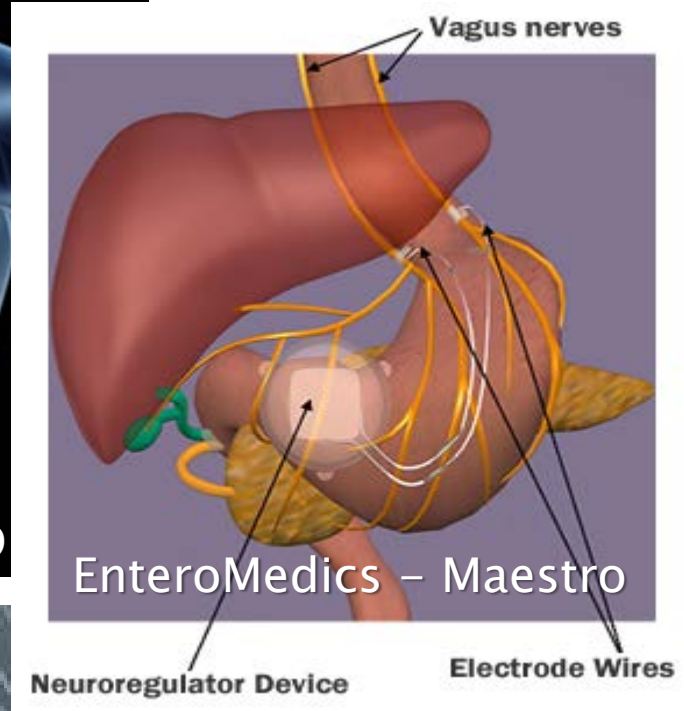
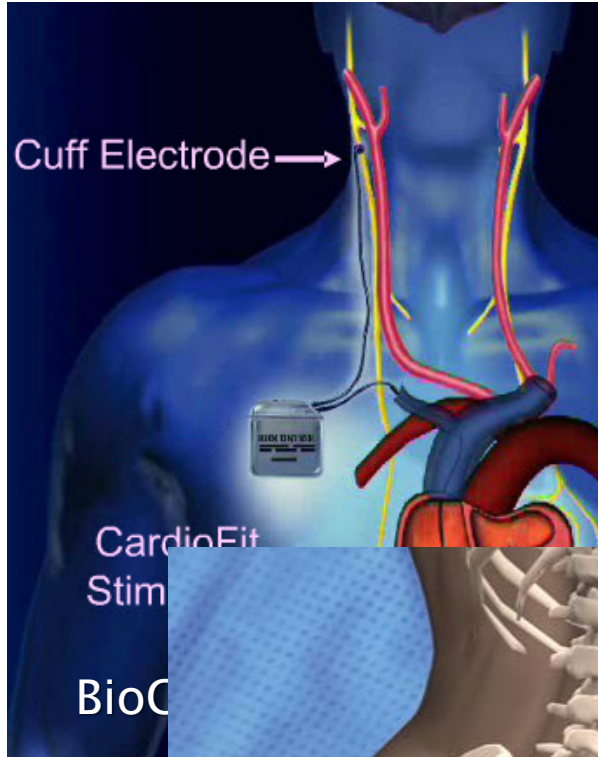
Neuropace – RNS System



Second Sight – Argus II



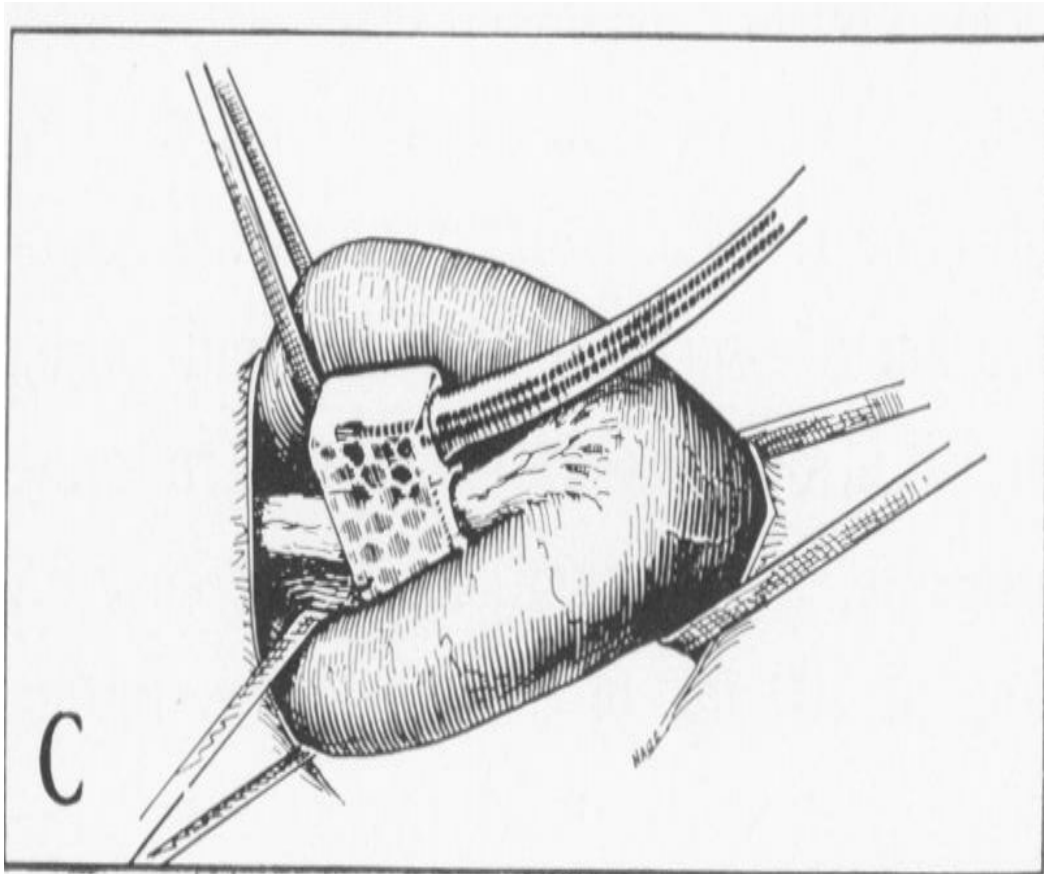
Neuromodulation – Not Just For The BRAIN



U.S. RCT Pivotal Trials Not Meeting Primary Efficacy Endpoint

- ▶ Medtronic SYMPLICITY (Renal Denervation)
 - 14 mmHg SAP Drop versus 12 mmHg in Sham Arm
- ▶ CVRx[®] DEBuT (Baroreceptor Stimulation for Hypertension)
 - Primary: 'On' 54%, 'Off' 46%, > -10 mmHg SAP at 6m
 - Secondary: 42% On, 24% 'Off' < 140 SAP at 6m
 - ~50% < 140 SAP at 12 months with both arms 'On'
- ▶ BROADEN/RECLAIM Trials for Depression
- ▶ Enteromedics EMPOWER
 - 24.4% versus 15.9% in sham Excess Weight Loss at 12 months. Primary endpoint > 10 percent difference
 - FDA Panel YESTERDAY!: 8 to 1 safety, 4 to 5 efficacy; 6 to 2 for approval (1 abstention)

Comparison: Clinical Nerve Cuffs Past and Present

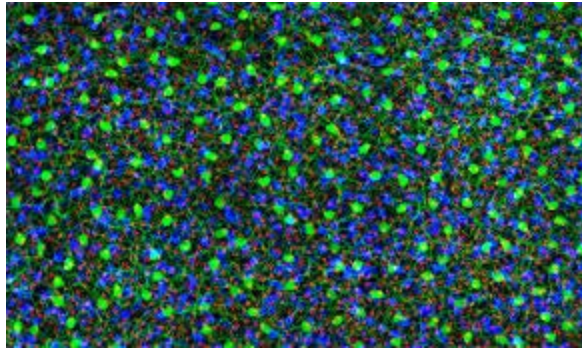


Braunwald 1970



Why No Higher Resolution Device?

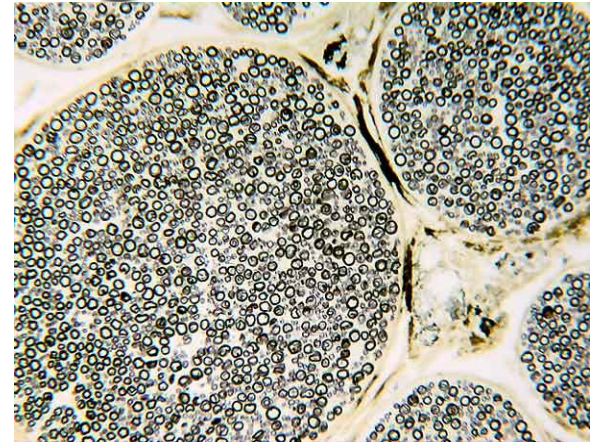
Retina vs. Vagus



Regular, identifiable retinal mosaic

<http://webvision.med.utah.edu/2012/02/retinal-half-mosaic/>

Retina/Cochlea: Consistent functional maps



~100,000 Fibers in Vagus Nerve

<http://vanat.cvm.umn.edu/neurLab1/nerves.html>

PNS: No technology to create high-resolution functional maps (until now)

- Manufacturing complexity
- Regulatory burden
- Start-ups: No revenue
- Benefits/Risks/Costs

NIH/NINDS New Programs

1. **Develop Academic and Clinical Tools to Observe and Understand Mechanisms of Action**
2. **Support Animal and Clinical Studies to Investigate Mechanisms of Action**
3. **Provide Targeted Support for Device Clinical Studies to Address Unknowns in Business Case**

The White House B.R.A.I.N. Initiative

- ▶ **Brain Research through Advancing Innovative Neurotechnologies**
- ▶ **\$100 Million in Key Investments to Jumpstart the Effort in FY2014:**
 - National Institutes of Health: ~ \$40 Million
 - Defense Advanced Research Projects Agency: ~ \$50 Million
 - National Science Foundation: ~ \$20 Million
- ▶ **Public/Private partnerships**
 - Allen Institute: ~ \$60 Million annually
 - Kavli Foundation: ~ \$4 Million annually
 - Howard Hughes Medical Institute: ~ \$30 Million annually
 - Salk Institute for Biological Studies: ~ \$28 Million

Brain Research through Advancing Innovative Neurotechnologies

1. **Generate a Census of Cell Types**
2. **Create Structural Maps of the Brain**
3. **Develop New Large-Scale Network Recording Capabilities**
4. **Develop A Suite of Tools for Circuit Manipulation**
5. **Link Neuronal Activity to Behavior**
6. **Integrate Theory, Modeling, Statistics, and Computation with Experimentation**
7. **Delineate Mechanisms Underlying Human Imaging Technologies**
8. **Create Mechanisms to Enable Collection of Human Data**
9. **Disseminate Knowledge and Training**

FY14 NIH B.R.A.I.N Funding Opportunities

1. **Transformative Approaches for Cell-Type Classification in the Brain (U01) (RFA-MH-14-215): 10M, 5-8 awards**
2. **Development and Validation of Novel Tools to Analyze Cell-Specific and Circuit-Specific Processes in the Brain (U01) (RFA-MH-14-216): 5M, 7-10 awards**
3. **New Technologies and Novel Approaches for Large-Scale Recording and Modulation in the Nervous System (U01) (RFA-NS-14-007): 7.5M, 10-15 awards**
4. **Optimization of Transformative Technologies for Large Scale Recording and Modulation in the Nervous System (U01) (RFA-NS-14-008): 7.5M, 10-15 awards**
5. **Integrated Approaches to Understanding Circuit Function in the Nervous System (U01) (RFA-NS-14-009): 10M, 10-15 awards**
6. **Planning for Next Generation Human Brain Imaging (R24) (RFA-MH-14-217): 4M, 7-9 awards**

Key Points: B.R.A.I.N. Initiative

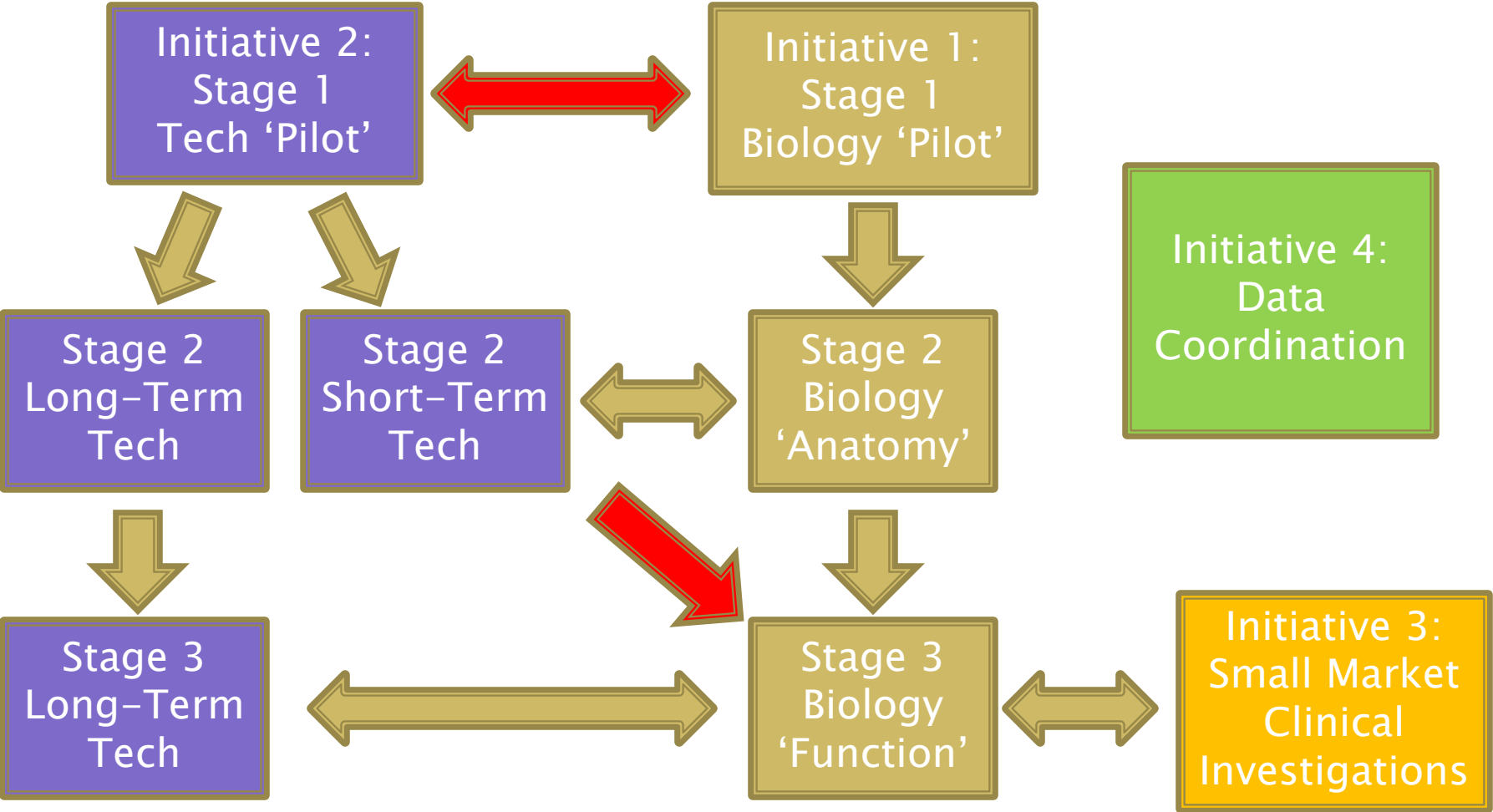
- ▶ **ACD Final Report Released in June**
 - “BRAIN 2025: A Scientific Vision”
 - Detailed set of goals and deliverables
 - Available on NIH Website (google ‘NIH BRAIN’ for details)
 - \$4.5 Billion in Funding over Twelve Years
- ▶ **Fiscal Year 2014 Funding Announcements**
 - <350 applications for 6 RFAs, Review in June/July
 - Two RFAs focused on technologies for large-scale recording/modulation
 - Highly competitive teams
- ▶ **Fiscal Year 2015**
 - President’s Budget Request – 100 million
 - New Funding Announcements likely

Common Fund: Functional Mapping for Neuromodulation of Visceral Organs

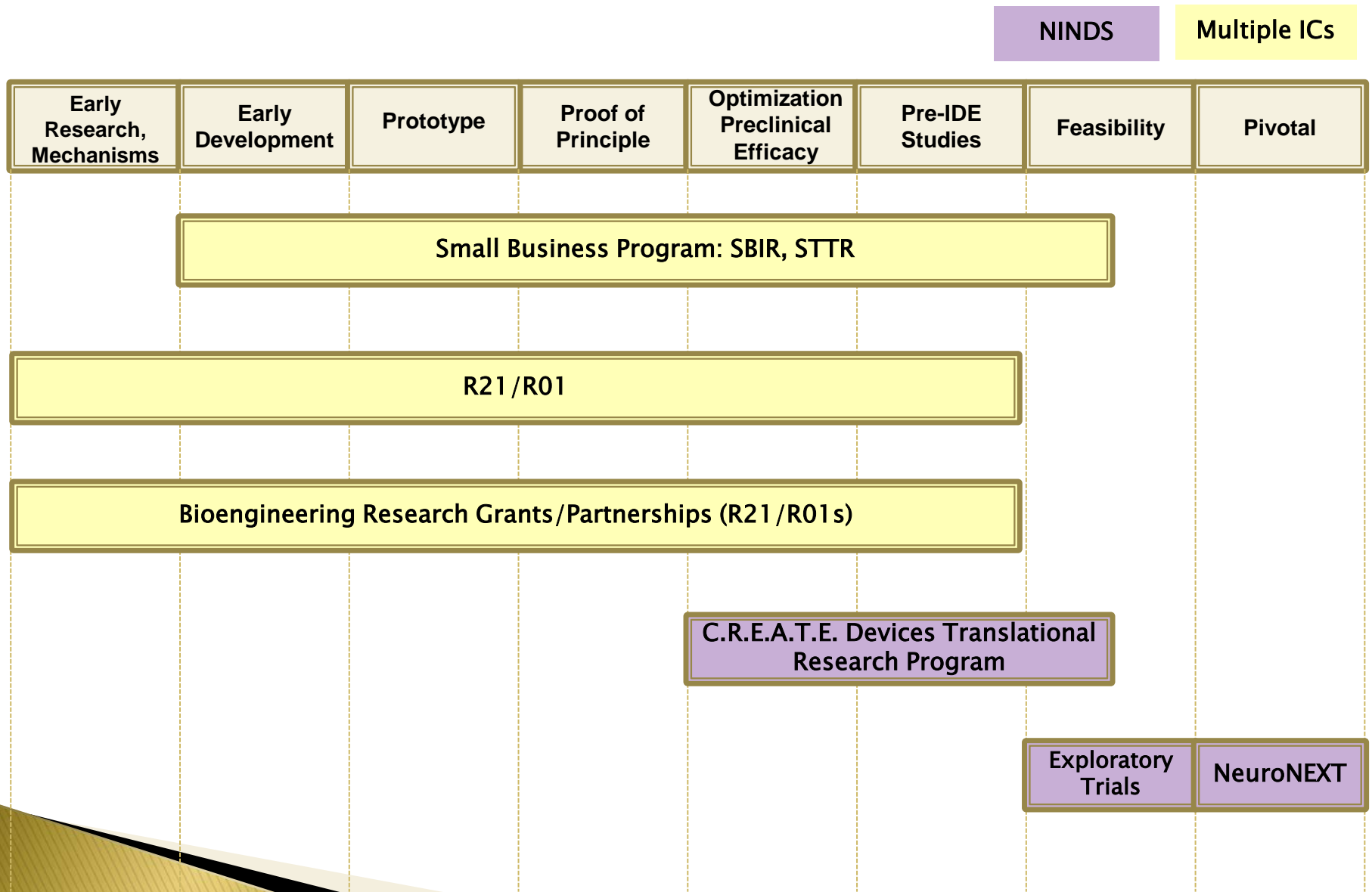
This Program will capitalize on recent advances in technology – and anticipated new technology developments facilitated by the Program – to deliver detailed, **integrated functional and anatomical neural circuit maps in five organ systems.**

These maps will be directly leveraged 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.

Program Outline: 4 Initiatives, 3 Stages



Translational Device Timeline and Funding Mechanisms



NINDS C.R.E.A.T.E. Devices Program

Research Device Development Track UH2/UH3



FDA Submission for IDE/or IRB Approval for NSR Study

510(k) Therapeutic UH2/UH3



FDA 510(k)
Market
Approval
Submission

FDA Submission for IDE/or IRB Approval for NSR Study

PMA/HDE Therapeutic Device Development Track UH2/UH3



FDA Pre-Submission Guidance FDA Submission

Looking for Feedback

kip.ludwig@nih.gov

- ▶ NIH Project Team Lead – The White House B.R.A.I.N. Initiative
 - ▶ NIH Lead – Neuromodulation Common Fund Initiative
 - ▶ NINDS Lead – C.R.E.A.T.E. Devices
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