Common Fund Venture Program Update

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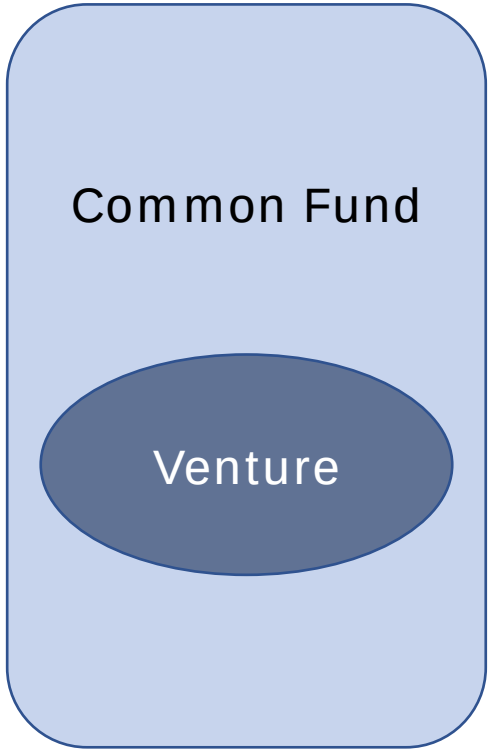
Venture Program

"Amazing things with modest funding"

Venture is enabling Common Fund support of **bold, short-term** initiatives.

- Adds flexibility to implement CF mission quickly, through small, innovative programs
- Launched in FY24 with 2 initiatives
  - Oculomics
  - Systems Biology Data Platform



Venture is part of Common Fund, not a separate activity

Venture Criteria

Proposals must meet Common Fund criteria:

- **Transformative** - exceptionally high and broad impact in biomedical/behavioral research
- **Catalytic** – time-limited investments, accelerate and enable subsequent research
- **Goal-driven** – defined goals to develop specific deliverables
- **Synergistic** –advance missions of multiple ICOs, relevant to multiple diseases/conditions
- **Novel** – innovative solutions to specific scientific challenges

Proposals must meet additional Venture Space criteria:

- **Bold** – daring investments with potential for significant, outsized impact
- **Nimble** – can be implemented rapidly in response to scientific opportunity
- **Focused** – 3 years, up to $5M/year in a clearly defined research topic

Development and Application of Imaging Technologies for Oculomics

Goal:

- To support development and application of novel, noninvasive ocular (eye) imaging technologies, machine learning algorithms, and other tools
- Enable identification of highly sensitive and specific **biomarkers** for diseases affecting the **whole body**

Status:

- Issued Research Opportunity Announcement in March
- Applications received in May
- Up to 3 awards anticipated by end of September

Update on current Venture initiative

Systems Biology Data Platform

Goal:

- To integrate multiple data types from the Accelerating Medicines Partnership (AMP) program
- Will allow researchers to explore the role of a **gene**, **molecule**, **cell**, or **pathway across tissues** involved in **different diseases**

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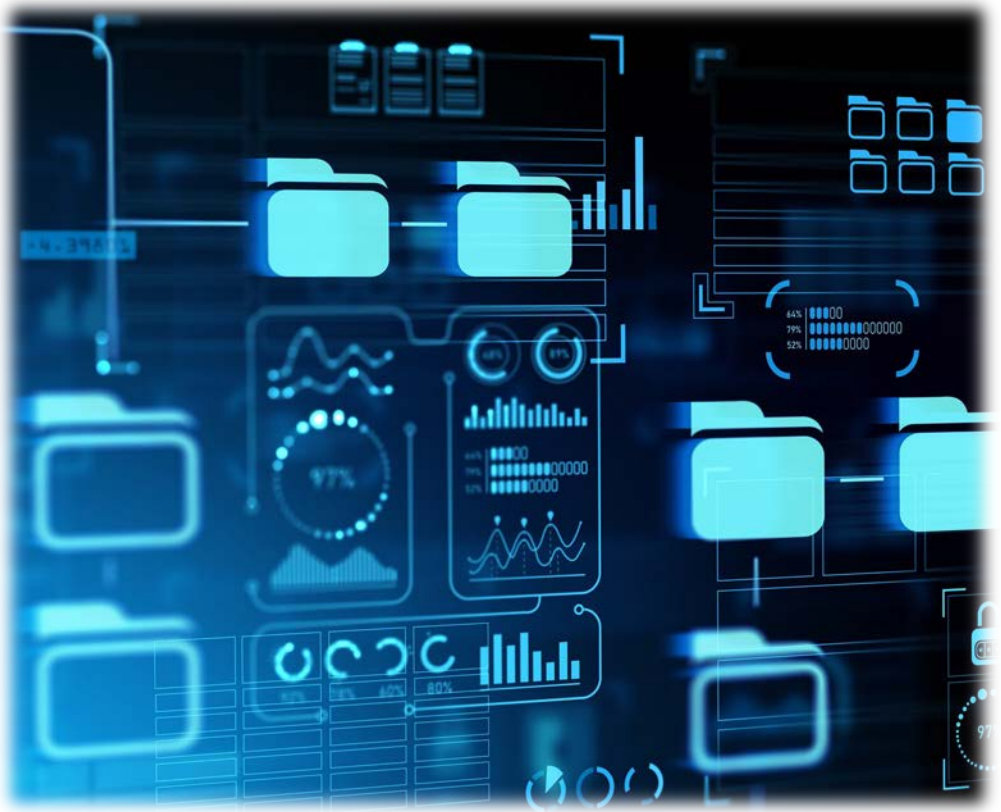


Improvements to Venture

- **Enhancing external engagement and transparency**
  - Leveraging public input in developing new initiatives through an annual request for ideas
  - Regular updates to Council with opportunity for discussion
  - Same transparency as with all CF programs – public websites with goals, purpose, leadership, funding opportunities, funded research, research results, etc.

- **Monitoring / reporting on milestone-driven progress**
  - Each project has defined milestones, monitored frequently, with formal reporting at least annually
  - Initiative websites will be updated with progress and achievements over time

Improvements to Venture

Clarifying language to avoid misunderstandings

- Explicit inclusion of biomedical and behavioral science; basic, translational, clinical, and community-based research
- Emphasize boldness of approach, rather than risk – we embrace bold approaches to ultimately result in impactful outcomes

Inclusion of diverse perspectives

- Leveraging the work of internal OSC committee focused on enhancing diversity and inclusion in our programs
- Various strategies including:
  - outreach to diverse groups of potential investigators and end users
  - requirements for plans to enhance diverse perspectives in applications
- Strategies for including diverse perspectives will be described in Council updates

New Venture Initiative–
Newborn Screening by Whole-Genome Sequencing (NBSxWGS)

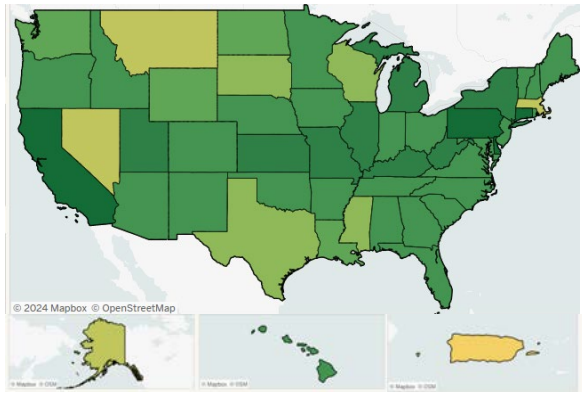
Objective: demonstrate feasibility of a collaborative model for NBS by WGS

- A single $5M annual investment over 3 years
- Demonstration project across multiple states, to show potential for a national NBSxWGS program
- Demonstrating feasibility of a national program would be an important advance:
  - **More equitable access**
  - Better able to **keep pace with therapeutic developments** for rare diseases

Current State-Run Newborn Screening (NBS) Programs

Core Disorders Screened

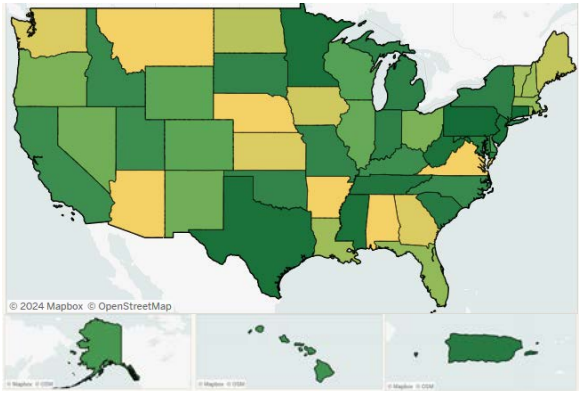
31 — 37



Last Updated: 8/6/2024

Secondary Disorders Screened

0 — 25



Last Updated: 8/6/2024

- ❑ Each year, 97% of newborns in the U.S. are screened by public health labs for various genetic disorders.
- ❑ Most screening is done via biochemical assays rather than DNA sequencing.
- ❑ Many states screen for at most 37* core conditions and 25 secondary conditions on the federally recommended screening panel (i.e., the RUSP).
- ❑ Thousands of rare genetic diseases are not screened.
- ❑ The diagnostic odyssey takes years for many of these diseases, precluding the possibility of early treatment.

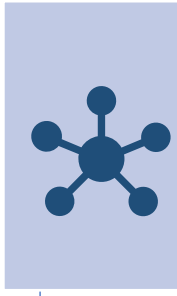
Source: Newborn Screening Technical assistance and Evaluation Program (NewSTEPs)
www.newsteps.org/resources/data-visualizations/newborn-screening-status-all-disorders

*Jan 2024: HHS Advisory Committee on Heritable Disorders in Newborns & Children (ACHDNC) voted to add infantile Krabbe disease to their Recommended Uniform Screening Panel (RUSP) for newborns, bringing the number of core conditions to 38 (doi: 10.1126/science.zsi5h5d).

Venture Initiative Goals for NBSxWGS

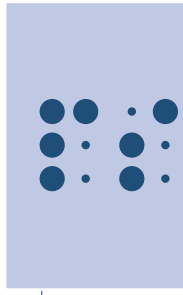
Overarching Aim: *Demonstrate feasibility of a collaborative model for NBS by WGS across 5-10 states - provide a roadmap to a national newborn genetic screening program.*

GOALS



Support a centralized lab for analysis and interpretation of genomic sequencing results.

Achieve equitable access to genomic sequencing in the newborn period.



Focus on a limited gene panel of serious / life-threatening rare diseases with early treatment options available.

Examine ethical, legal & social implications (ELSI) of population-wide genomic sequencing in the newborn period.

Strength in Diversity

NBSxWGS will:

- ❑ **Establish a Community Advisory Board (CAB)**
  - Solicit opinions on WGS for newborns from underrepresented communities and community leaders, interest groups and subject matter experts
  - Advise on community engagement approaches, informed consent, data sharing, research design, implementation barriers for study, community education, dissemination strategies, etc.
- ❑ **Attract new expertise to the NBS field**
  - Subject matter expertise to inform implementation of NBS X WGS at scale
  - Provide opportunities to make progress on diversification
- ❑ **Require Plans for Enhancing Diverse Perspectives**

Responsive to Common Fund and Venture Criteria

Common Fund Criteria

- ❑ **Transformative:** Enable early or even pre-symptomatic treatment of rare genetic diseases
- ❑ **Catalytic:** Answer questions to enable broad U.S. implementation of universal, socially acceptable, and equitable newborn genomic sequencing.

Venture Criteria

- ❑ **Bold:** Transform NBS in the U.S. to provide actionable genomic results for earlier intervention
- ❑ **Nimble:** Essential components already in place
  - Rapid genome sequencing technology
  - Gene lists for newborn sequencing
  - Small, state-specific pilot programs
- ❑ **Focused:** 3-year program implemented over 5-10 states to determine the feasibility of a nationwide program

Anticipated Impact

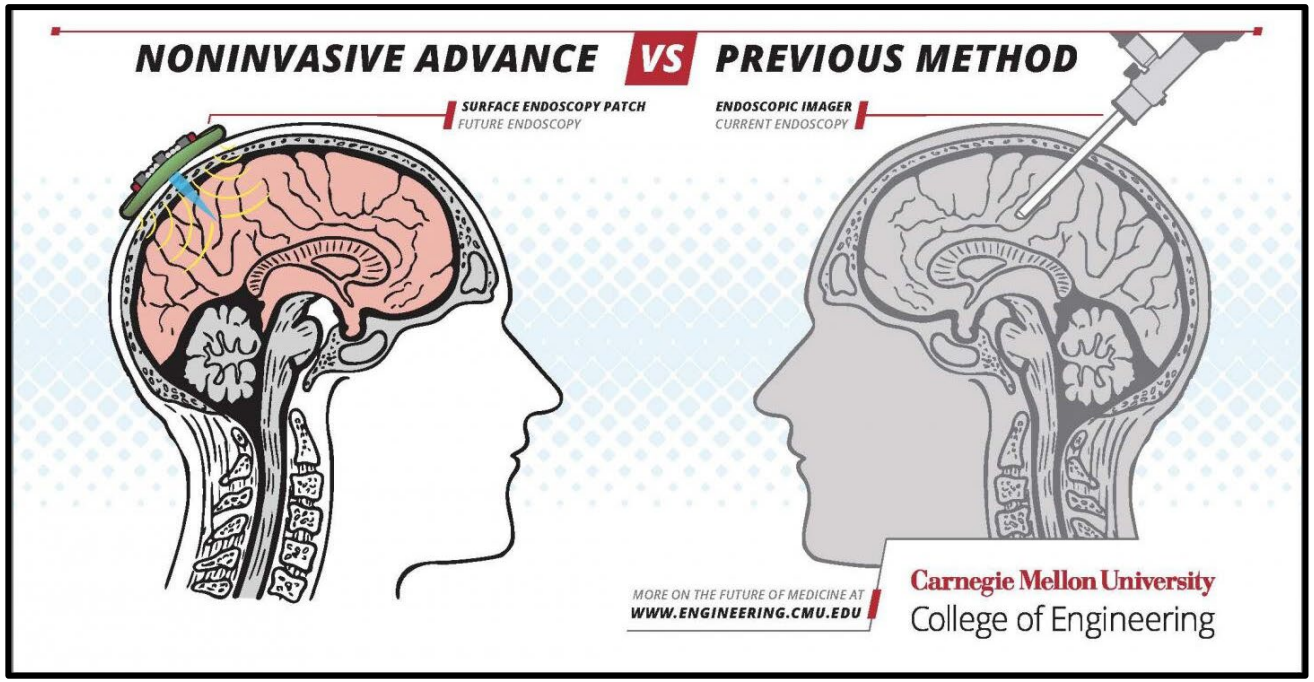
NBSxWGS will …

- Enable early treatment, improving health outcomes for newborns with rare genetic conditions
- Provide more equitable access to genomic sequencing for newborns
- Expand screening from <40 to hundreds of diseases
- Increase uniformity of screened conditions among states
- Decrease the diagnostic odyssey for individuals with rare diseases

New Venture Initiative:
Advancing Non-Invasive Optical Approaches for Biological Systems

Objective: Develop optical systems to noninvasively engage target regions within intact, live tissues

- Multiple awards totaling $5M annually, over 3 years
- **Temporal and spatial resolution** matching current state-of-the-art invasive approaches used in medicine and research
- Would permit non-invasive measurements at **multiple scales** (region, cell, subcellular, molecular)
- Reveal physiological and pathophysiological processes **in real time**

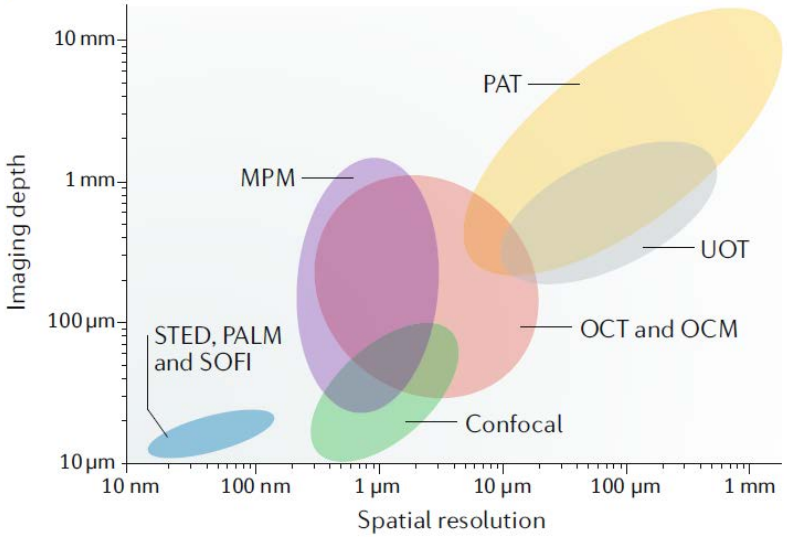


Chamanzar and Scopelliti, CMU
https://engineering.cmu.edu/news-events/news/2019/07/16-chamanzar-nature.html

Enabling Technology for Non-invasive Imaging

Our Challenge

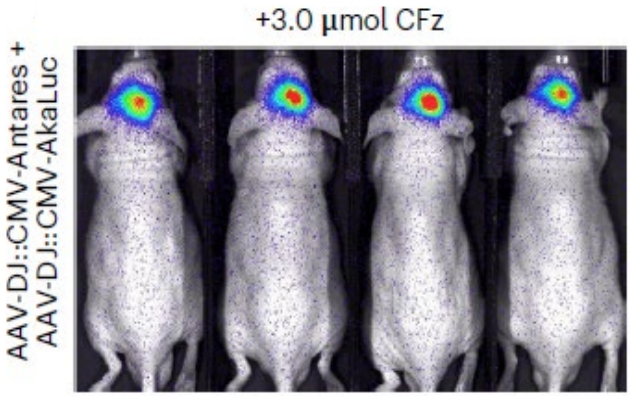
- Trade-offs between imaging depth and resolution
- Limited dynamic range
- Avoiding damage to living tissue



Yoon et al, Nat Rev Phys 2020

Current Research Approaches

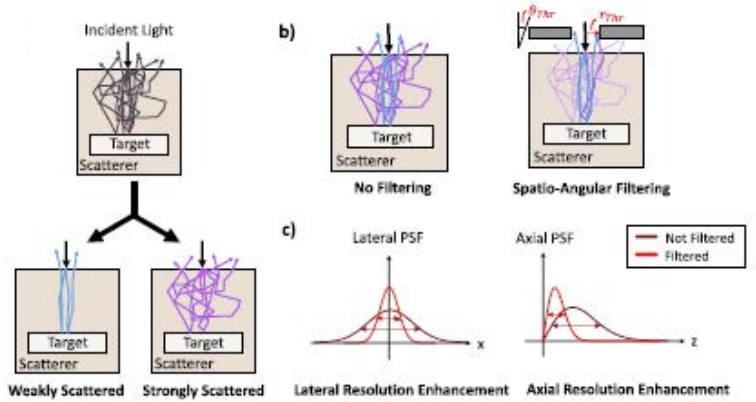
- *In vivo* signal systems and amplifiers



Su et al, Nat Chem Bio 2023

➢ Requires transgene expression

- Improving light penetration and detection



Cua et al, Biomed Optic Exp, 2022

➢ Requires validation and optimization *in vivo*

The Future

Advancing Non-Invasive Optical Approaches for Biological Systems

- **Capable of wide resolution dynamic range** (µm to cm)
- **Noninvasive** (no surgical access, transgenes or contrast agents)
- **Broadly applicable** (collect information from multiple tissue functions simultaneously)

Venture Initiative Goal

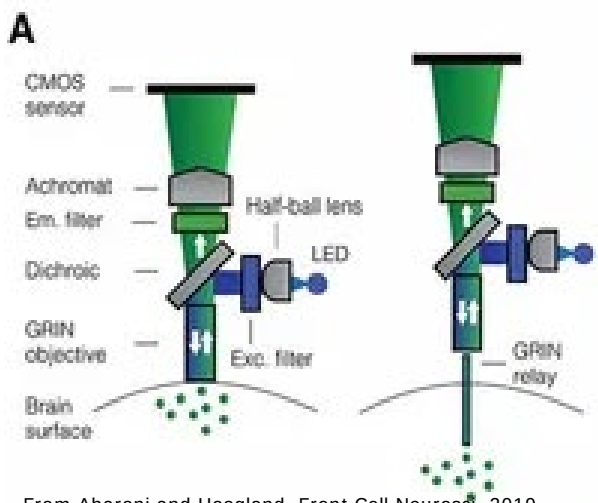
Program Goals:

- Enable development of next generation non-invasive imaging platforms toward many biological and biomedical applications
- Incorporate approaches that push optical interfaces beyond the limits of diffraction and address light scattering in tissue

Anticipated Work Products:

Phased approach (Years 1-2)

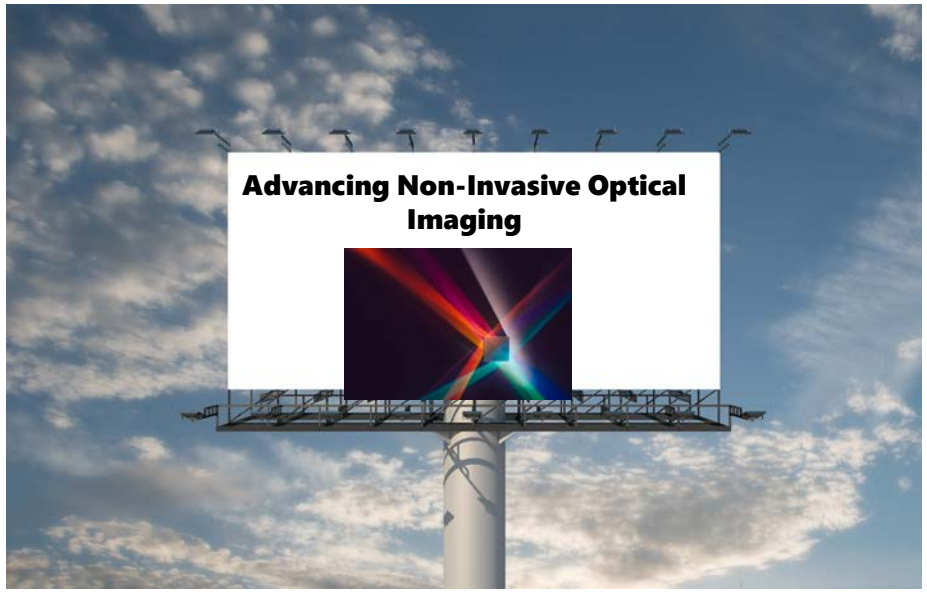
- **Hardware designs** that integrate novel forms of optical imaging data acquisition and processing
- **Prototypes** that overcome light-scattering barriers in complex biological systems
- *(Year 3)* **Optimization** and performance testing



From Aharoni and Hoogland, Front Cell Neurosci, 2019

Current *in vivo* imaging is cumbersome and invasive.

Workforce and Team Diversity are Essential for Success



Advertising broadly is key to broadening access

- ❑ Requires diverse teams including physicists, biologists, engineers, etc.
- ❑ Encourage partnerships across institutes and research organizations
- ❑ Provide research and training opportunities encouraging URM involvement
- ❑ Include outreach and advertising
  - Professional societies
  - Social media
  - Informational Webinar
- ❑ Require Plans for Enhanced Diverse Perspectives with milestones monitored throughout each project

Responsive to Common Fund and Venture Criteria

Common Fund Criteria

- **Catalytic:** Drive advances in:
  - *in vivo* biochemistry and cellular activity measurement
  - point-of-care advanced diagnostics and longitudinal monitoring
  - non-invasive procedures that replace surgery
- **Goal-driven:** Quantitative metrics to demonstrate *in vivo* improvements to tissue depth, contrast, and temporal and spatial resolution across scales
- **Synergistic:** Multidisciplinary approaches with widely applicable outcomes across NIH

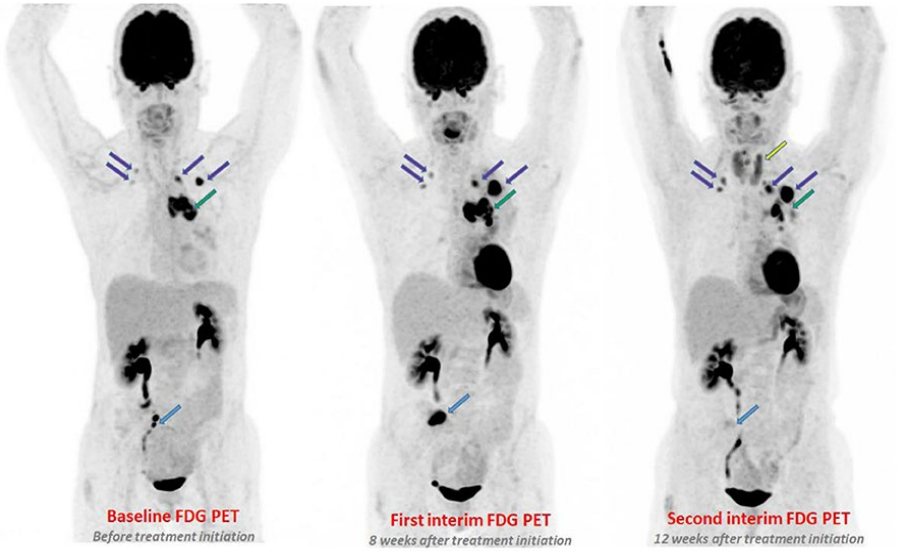
Venture Criteria

- **Bold:** Adapt fundamental principles of microscopy to non-invasive in vivo imaging
- **Nimble:** Combine key elements under active research to demonstrate and motivate additional development, including
  - Technologies already demonstrated in non-biological systems
  - Methods yet to be optimized in heterogenous tissues
- **Focused:** Phased awards for 2-year development and 1-year optimization

Anticipated Impact of Improved Optical Technologies Spans Basic, Clinical and Translational Research

- **Reveal physiological processes in real time at multiple scales**
- **Enable meaningful interactions with living systems without invasive manipulations**
  - *E.g., inflammatory processes, neuronal and muscular activity, fetal development*
- **Allow monitoring of clinical processes, including morphological and cellular features:**
  - *E.g., cancer progression and response to treatment, coronary artery disease, neurodegenerative diseases*

Response monitoring with FDG-PET



From Humbert and Chardin, Front Oncol, 2020

Current state of the art requires radioisotope tracers to monitor clinical treatment and progression.

Questions or comments?

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