



Neurodegeneration Challenge Network

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CZI Neuroscience

1. CZI Science Overview
2. Neurodegeneration Challenge Network
3. Lessons learned

Chan Zuckerberg Initiative

Our Mission

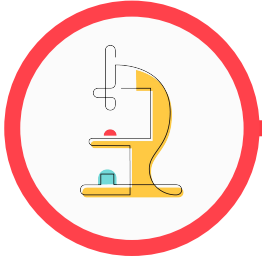
Supporting the science and technology that will make it possible to cure, prevent, or manage all disease by the end of the century.

Our Values

- People
- Technology
- Collaboration
- Open Science



Science Goals



80 YEARS

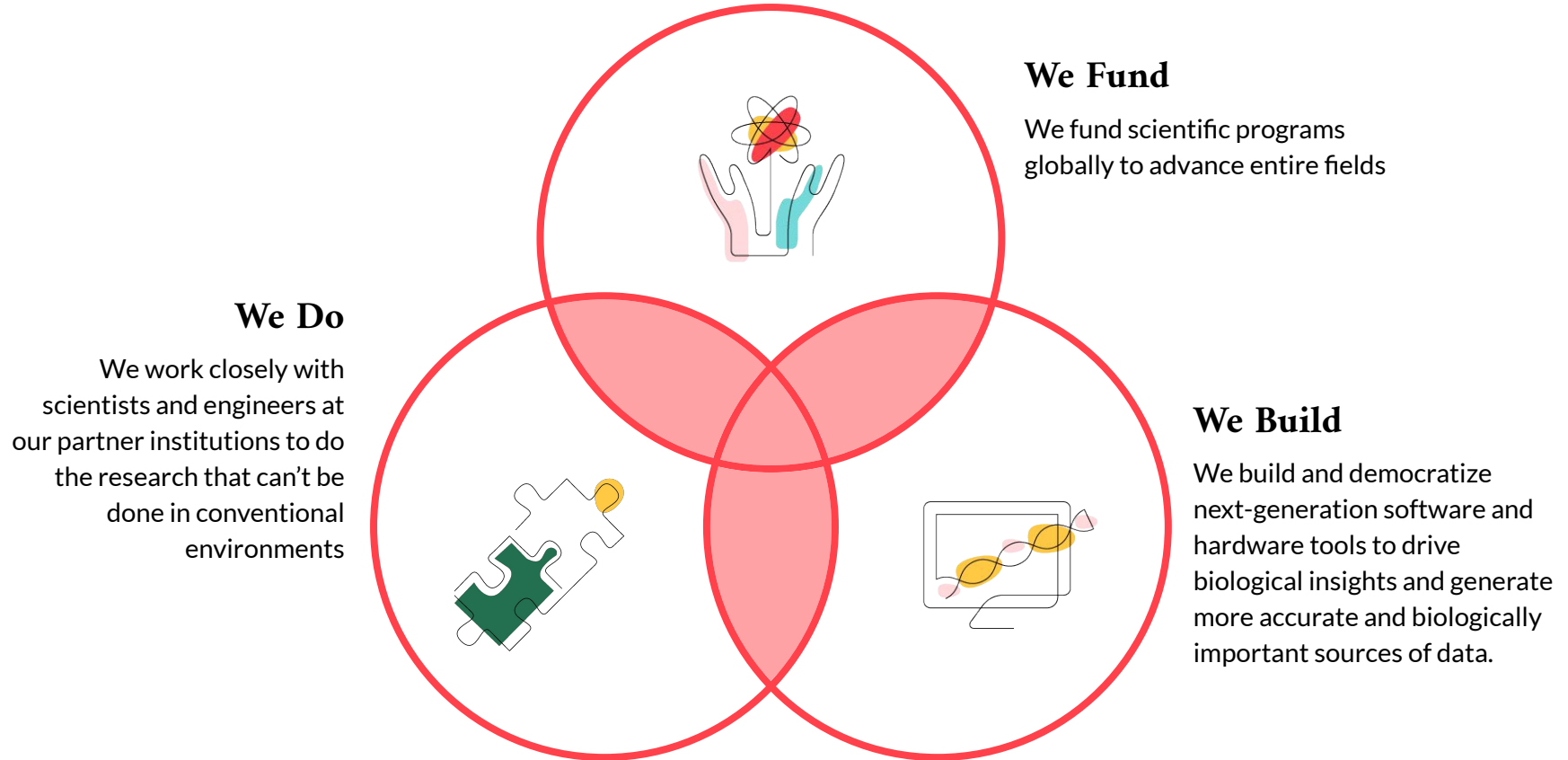
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10 YEARS

Advance research and develop technologies to measure human biology in action

Understanding the mysteries of the cell and how cells interact in systems.

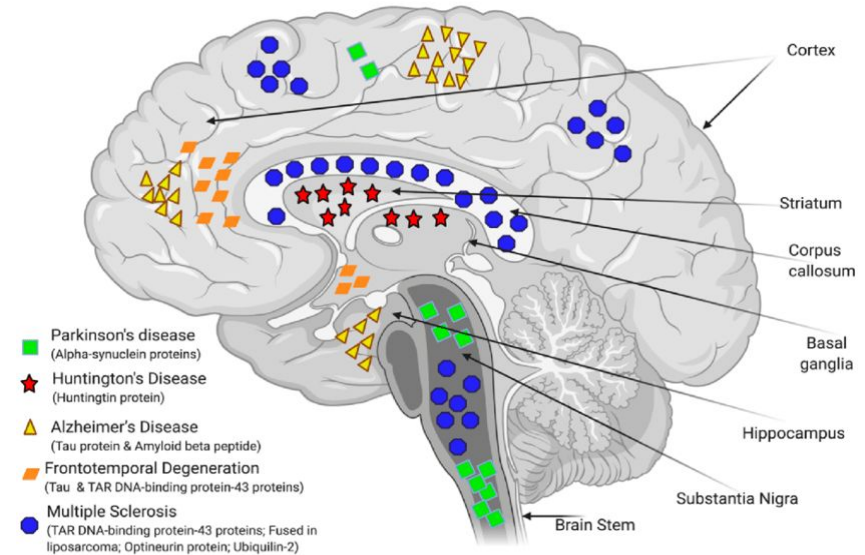
CZI Approach



Neurodegeneration Challenge Network (NDCN)

Why Neurodegeneration?

- Major unmet medical need
- 200+ disorders spanning the lifespan
- No (few) disease-modifying therapies to prevent, cure or treat disease
- Large gaps in our understanding of the basic biology and mechanisms underlying disease
- Field in need of a new approach that is less siloed



By understanding what goes wrong in disease, we will learn about fundamental principles

>> Neurodegeneration is at the core a **cell biological challenge**

>> aligned with CZI focus on *understanding mysteries of cell, measuring human biology in action*

Neurodegeneration Challenge Network (NDCN)

Challenge Network: a new model for collaborative research

**Program launched in 2018



- Network approach
- Foundational, discovery science
- Attract new talent, expertise & ideas to the neurodegeneration field
- Explicitly broad and interdisciplinary
- Cross-disease: break down disease and research silos
- Enable bold, innovative work
- Support collaboration & open science

"A network that is more than the sum of its parts"

First five years of the Neurodegeneration Challenge Network –

DIVERSE, HIGHLY INTERACTIVE NETWORK

- 138 RFA grants awarded (60% early career)
- Total program investment > \$90M (\$70M in RFA grants)
- Current: 151 principle investigators/labs
- 4 collaborative grant programs
- 500+ students/postdocs/staff affiliates
- Alumni program for previous grantees
- Various invited collaborators as Network affiliates

FUNDAMENTAL BIOLOGY & INTERDISCIPLINARY

- Basic science, mechanisms of disease >> cellular neuroscience focus
- Cross disease – rare and common disease
- Range of disciplines: clinicians, patients, computational biologists, engineers

COMMUNITY

- Engaged community that is more than a group of grantees
- Training, mentorship, venues for collaboration, cross-program Working Groups

IMPACT BEYOND THE NETWORK

- tools/resources (iPSC, computational, AAV tools), open science, community projects



NDCN Grant Mechanisms >> Collaboration at the Core

Collaborative Science Awards (2018-2022)

- Project based award supporting small team collaborations, including clinicians (9 projects)

Ben Barres Early Career Acceleration Awards (2018-2023)

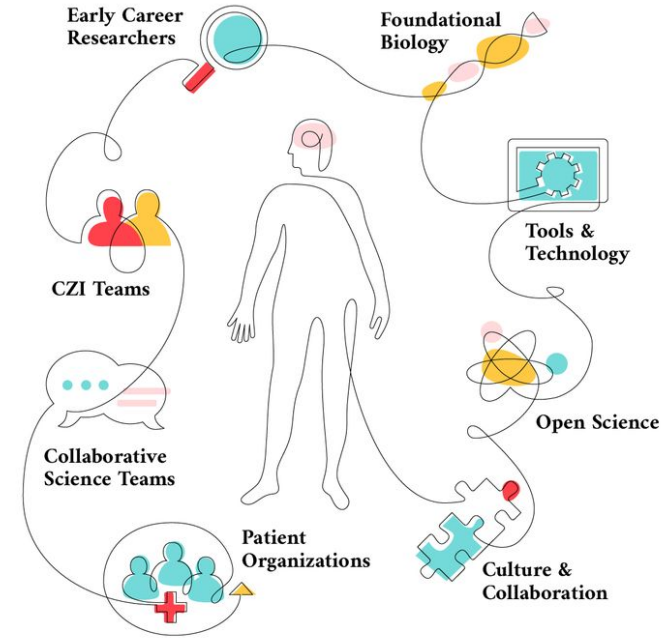
- Investigator award to support early stage PIs new to neurodegeneration (17 awards, Cycle1) ****Cycle 2 announced this week**

Collaborative Pairs Project Awards (2020-2026)

- High risk/reward collaborative projects between pairs of researchers. Pilot phase (30 projects, 2020-2022) + Phase 2 (16 projects, 2022-2026) ****Cycle 2 in final review**

Patient Partnered Collaborations for Rare Neurodegenerative Disease (2023-2027)

- Project based award supporting collaborations between research teams and patient advocacy organizations to understand mechanisms of rare neurodegenerative disorders (5 projects)



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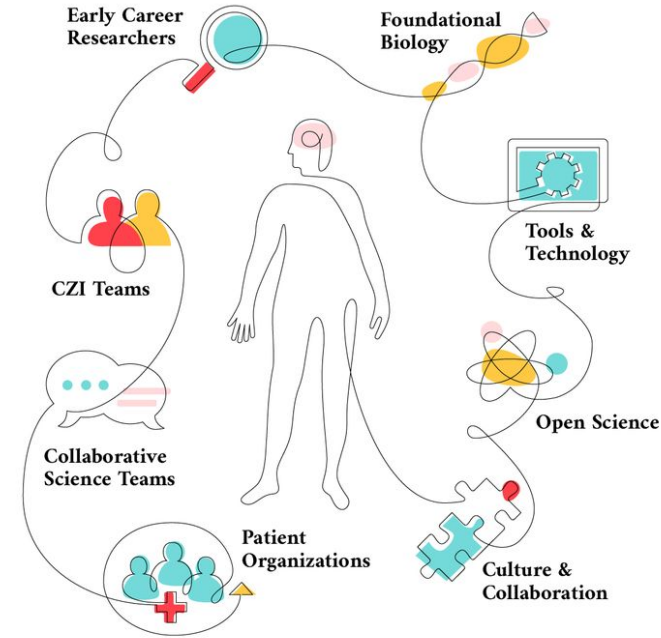
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Early career investigators: investing in a new generation of talent

Ben Barres Early Career Acceleration (ECA) Award

Cycle 1 (2018-2023): first cohort > 17 grantees

Cycle 2 in final review: expansion to fundamental neuroscience > 13 awards, announced this week

New ideas, new approaches to disease mechanisms



Ivan Marazzi (Mt. Sinai)
virologist/immunologist
Innate Immune system



Niang (Jenny) Jiang (Penn)
systems immunology
Single cell, high throughput
approaches to immune repertoire



Debora Marks (Harvard)
Computational biologist
Ai/ML modeling

Cutting edge technologies



Sergiu Pasca (Stanford)
Organoid modeling



Viviana Gradinaru (Caltech)
AAVs / viral vectors



Martin Kampmann (UCSF)
CRISPR / iPSCs

Meet the Ben Barres Early Career Acceleration Awards Cycle 2 Grantees



Ghazaleh Ashrafi
Washington University in St. Louis



Frederick Bennett
University of Pennsylvania



Christopher Douse
Lund University



Rune Enger
University of Oslo



Erin Gibson
Stanford University



Sabine Krabbe
*German Center for
Neurodegenerative Diseases*



Tal Laviv
Tel Aviv University



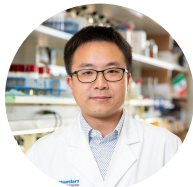
**Alba Diz
Muñoz**
*European Molecular
Biology Laboratory*



**Vidhya
Rangaraju**
*Max Planck Florida Institute
for Neuroscience*



Pengfei Song
University of Illinois



Lu Sun
*University of Texas Southwestern
Medical Center*



**Maria Antonietta
Tosches**
Columbia University



Li Ye
*The Scripps
Research Institute*

Collaborative Pairs – The Power of Two

TALENT:

- Bring new expertise and talent into the field
- Support early career researchers

COLLABORATION:

- Catalyze new collaborations and scientific partnerships
- Pairs as a nimble form of collaboration

NEW IDEAS:

- Bold, creative, “out-of-the-box” ideas
- Potential transformative science

ENCOURAGE RISK

- Seed funding – springboard early stage projects
- Phased process > Pilot phase + selection for second phase investment



Neurodegeneration Challenge Network

What we've learned so far

- **Impact of recruiting new talent, expertise and ideas into the field** – opportunities and challenges of this approach
- **Early career researchers:** strong pull towards novel collaborative models; **value of mentorship (peer and senior) to bridge transitioning researchers into new fields**
- **The power of networks to connect** – collaborations emerge in unpredictable ways
- **Collaboration is a powerful tool** to accelerate science and amplify impact
- Building collaborations between stakeholders from different expertise/perspectives requires the **right people** and the **right environment and context**
- **Importance of steady program management** high touch, “coaching rather than directing”; let researchers lead the science
- **Clinician scientists have been a valuable part of the network , critical as mentors and partners**, but face particular challenges that can constrain their capacities (and time) for collaboration
- **Strategic and selective focus:** even with generous support and funding, one program/organization can't do everything— CZI has strategic focus on fundamental science

Closing thoughts on critical challenges for the neurodegeneration field

Importance of strong basic and translational science for fueling clinical pipelines

Reconceptualizing how we think about neurodegenerative diseases

- neurodegenerative diseases as a disease class > look beyond single-disease approaches
- neurodegenerative diseases as more than disorders of the brain – systems-wide, whole-body disorders
- prevention, resilience
- need for broader interdisciplinary approaches, beyond biomedicine > social scientists, engineering, computer science

Investing in high quality, well-validated, accessible tools and resources

- biobanks / tissue resources / modernizing neuropathology
- models for human biology (iPSCs, organoids)

Supporting a strong scientific workforce and talent:

- science (this field) needs the best, brightest and most creative – *early career scientists and innovators*
- critical role of physician-scientists—*particular challenges faced by this career path*
- academic incentives/rewards systems are obsolete
- new ways of working: *interdisciplinary, collaborative science, team science require a different skill set than what we train for*
- science is global: *funding/programmatic mechanisms to support international collaborations*

Critical importance of Computational Biology / Big Data / AI

- data infrastructure, challenges of data integration, talent/workforce, incentives

Bridging the gap between basic and clinical science, and health care systems