Cancer Grand Challenges

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NCI Council of Research Advocates

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NIH NATIONAL CANCER INSTITUTE

Presentation Overview

CANCER GRAND CHALLENGES

- Why was **Cancer Grand Challenges** created?
- What is a cancer grand challenge?
- Funded research teams & projects (to date)
- CGC and patient advocacy
- An example of patient and public engagement

Why was Cancer Grand Challenges created?

CANCER GRAND CHALLENGES

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PROVOCATIVE QUESTIONS

- NCI established **Provocative Questions** in 2011 to stimulate research in areas that were perplexing, paradoxical or had not received sufficient attention
- New research questions developed periodically through extensive engagement with the cancer research community
- Funding mechanism = R01 and R21 awards ($275K - $500K)
- Projects usually led by a single investigator, 35 - 50 awards per year

CANCER RESEARCH UK

CRUK Grand Challenge

- CRUK launched the **CRUK Grand Challenge** initiative in 2015 to support international, multidisciplinary teams tackling major research challenges
- **Strategy:** Combine the problem identification process of Provocative Questions with a team science approach to address big problems
- Between 2017-2019, CRUK funded 7 project teams (£16-20M per team)

NCI & CRUK Partnership

CANCER GRAND CHALLENGES

CANCER RESEARCH UK

NIH NATIONAL CANCER INSTITUTE

- In 2020, NCI and CRUK partnered to expand CRUK's Grand Challenge initiative through a collaborative funding initiative called **Cancer Grand Challenges (CGC)**
- CGC sets ambitious challenges in cancer research and provides awards up to $5M/year over 5 years ($25M total) that support international teams to address these challenges
- The initiative is guided by an international scientific committee with inputs from the global research community and people affected by cancer
- NCI and CRUK agreed to co-fund 3 rounds of awards, up to 4 new teams per round

What is a Cancer Grand Challenge?

CANCER GRAND CHALLENGES

- Important and complex problem in cancer research, which, if solved, would have significant benefit for patients
- Problem related to understanding, preventing, detecting and/or treating cancer
- Addressed through basic, translational, clinical and/or population research
- Can be a new problem or one that has existed for many decades
- Scale and scope of the problem should **demand** intellectual inputs from multiple investigators
- Problem for which researchers are poised to make significant progress (timely)

See previous challenges:

cancergrandchallenges.org/challenges

Round 1 Teams (2022)

CANCER GRAND CHALLENGES

eDyNAmiC

Team Lead
Paul Mischel (Stanford)

Challenge
Understand the biology of extrachromosomal DNA (ecDNA) in cancer

Approach
- Identify mechanisms involved in the generation and action of ecDNAs in cancer
- Understand how ecDNAs drive drug resistance to identify new therapeutic targets

NEXTGEN

Team Leads
Martin Pule (UCL)
Catherine Bollard (Children's Natl)

Challenge
Develop novel therapies to target solid tumors in children

Approach
- Discover new targets for CAR T-cell therapies and develop components that target tumour cells
- Conduct clinical trials to guide the iterative design and improvement of novel CAR-T therapies

CANCAN

Team Leads
Eileen White (Rutgers)
Marcus Goncalves (Weill Cornell)
Tobias Janowitz (Cold Spring Harbor)

Challenge
Understand and reverse cachexia in cancer patients

Approach
- Establish classification of molecular and clinical subtypes of cachexia
- Develop mechanistically informed treatments for cachexia to improve quality of life and life expectancy

PROMINENT

Team Leads
Allan Balmain (UCSF)
Paul Brennan (IARC)
Nuria Lopez-Bigas (IRB, Barcelona)

Challenge
Understand how cells harboring oncogenic mutations maintain normal phenotypes and transition to tumors

Approach
- Understand differences between normal human tissues at high or low risk of neoplastic growth
- Identify factors that promote the growth of mutated cells in normal tissue to aid in cancer prevention

Round 2 Teams (2024)

CANCER GRAND CHALLENGES

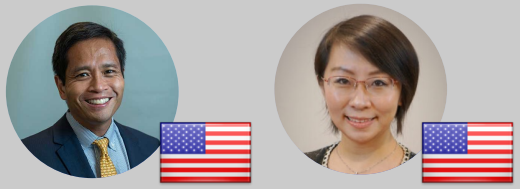
MATCHMAKERS

Team Lead
Michael Birnbaum (MIT)

Challenge
Decipher the T-cell receptor cancer recognition code

Approach
- Conduct high throughput methods to characterize thousands of TCR-peptide/MHC pairs
- Train computational models to predict which tumor (neo)antigens T-cell receptors recognize

PROSPECT



Team Leads
Andrew Chan (Mass General)
Yin Cao (Wash U)

Challenge
Determine why the incidence of early-onset cancers in adults is rising globally

Approach
- Define the early-onset exposome associated with early onset colorectal cancer
- Conduct -omics profiling, systems epidemiology, and community trials to understand mechanisms

PROTECT

Team Lead
Stefan Pfister (DKFZ)

Challenge
Develop therapeutics to target oncogenic drivers of solid tumors in children

Approach
- Pursue 12 pediatric-specific drug targets including oncogenic fusions and other difficult targets
- Develop molecular glue degraders and PROTACs to deliver at least one candidate for clinical testing

SAMBAI

Team Lead
Melissa Davis (Morehouse)

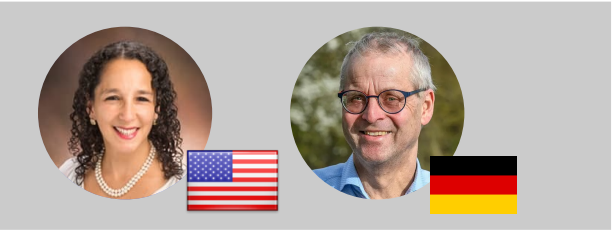
Challenge
Understand mechanisms through which genetics, biology, and social determinants affect cancer risk and outcomes in diverse populations

Approach
- Build a repository that contains social, environmental, genetic, and biological data from 40,000 patients
- Study 3 cancer types to define the causes of disparate health outcomes in the global African diaspora

Round 2 Teams (2024)

CANCER GRAND CHALLENGES

KOODAC



Team Leads

Yaël Mossé (CHOP)

Martin Eilers (Universitat Wurzburg)

Challenge

Develop therapeutics to target oncogenic drivers of solid tumors in children

Approach

- Develop orally bioavailable drugs targeting 5 previously undruggable oncoproteins for pediatric tumors
- Develop molecular glue degraders and PROTACs, and perform IND-enabling studies for lead candidates

- CRUK is a private charity that supports research awards through donations and partnerships
- Funding support from CRUK's other donors will allow CRUK to fully fund a 5th team (KOODAC) in round 2

➢ **NCI does not participate in private fundraising**

fundación científica asociación española contra el cáncer

The Spanish Association Against Cancer

RÉPUBLIQUE FRANÇAISE Liberté Égalité Fraternité

INSTITUT NATIONAL DU CANCER

The French National Cancer Institute

KWF

KWF Dutch Cancer Society

The Mark Foundation® for Cancer Research

Patient Advocacy

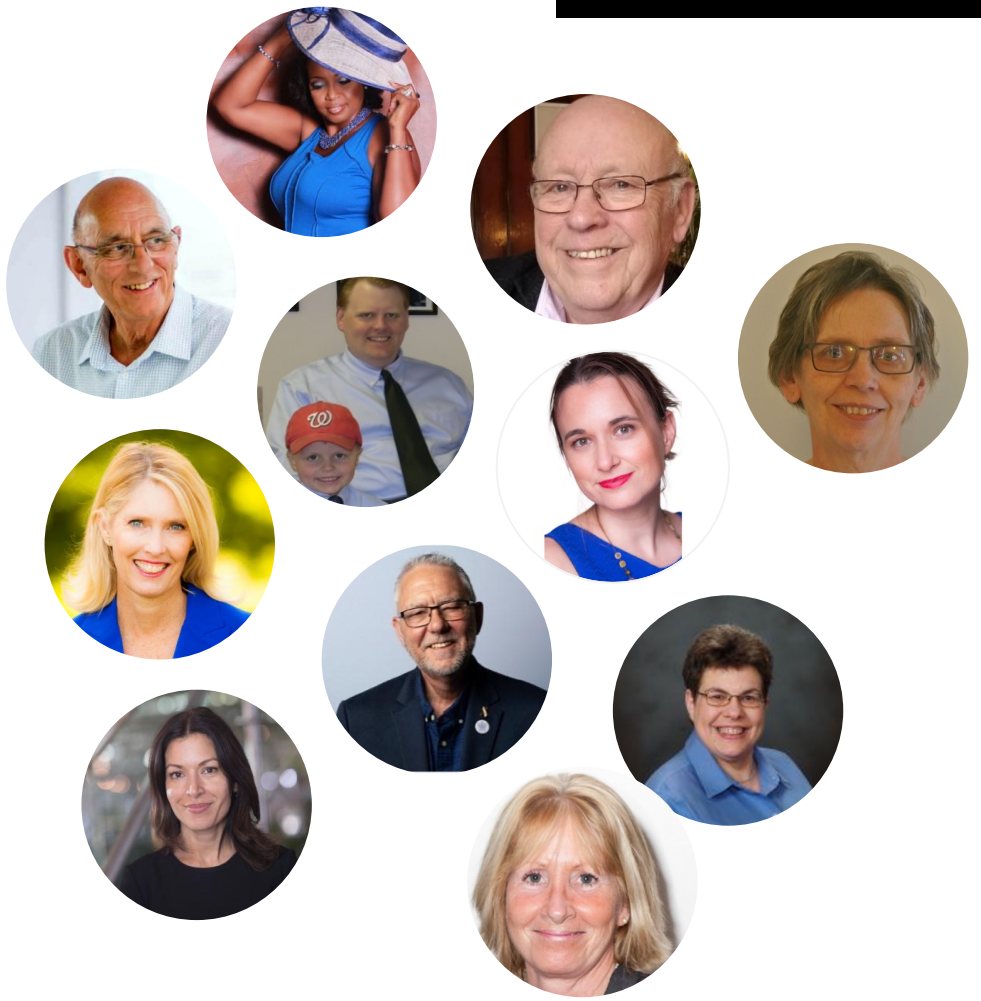
CGC requirements

Teams are required to involve patient advocates (patients, survivors, caregivers) in their research

CGC teams are expected to recruit a minimum of one patient advocate with a clearly defined role

Advocates should represent people affected by cancer as a group – not just provide their individual viewpoint or that of any advocacy organization

Teams should collaborate with their advocate(s) throughout the research, where such interaction can add clear value and advance progress



CGC patient advocates

Definitions

CANCER GRAND CHALLENGES

Patient Advocacy

Involvement

- When patient advocates use their experiences of cancer to help shape research
- Carried out with or by patient advocates, rather than to or for them
- Enables patient advocates to have a voice that is listened to and reflected in the scientific strategy

Engagement

- When information and knowledge about research is shared with other patient advocates and the public who are not associated with the CGC research program
- Design and delivery of engagement activities provides an opportunity to involve patient advocates

Participation

- When a person is part of a research study or clinical trial but does not work directly with the researcher(s)
- Research is being done to the patient, not with them

CGC Advocacy Panel

Margaret Grayson
(Chair) (UK)

Yelak Biru
(US)

Ivana Cattaneo
(Italy)

Anjee Davis
(US)

Joya Harris
(US)

Dirk Hellrung
(Germany)

Claire James
(UK)

Patrick McGuire
(UK)

Gita Patel
(UK)

Chris Stewart
(US)

Christine Qiong Wu
(Canada)

Responsibilities

- Assist CGC program team in developing strategies to involve patient advocates in CGC research
- Provide feedback on the CGC teams' proposed approaches for involvement and engagement
- Engage with patient advocates on the funded teams throughout the research projects to help them refine and enhance patient advocacy efforts

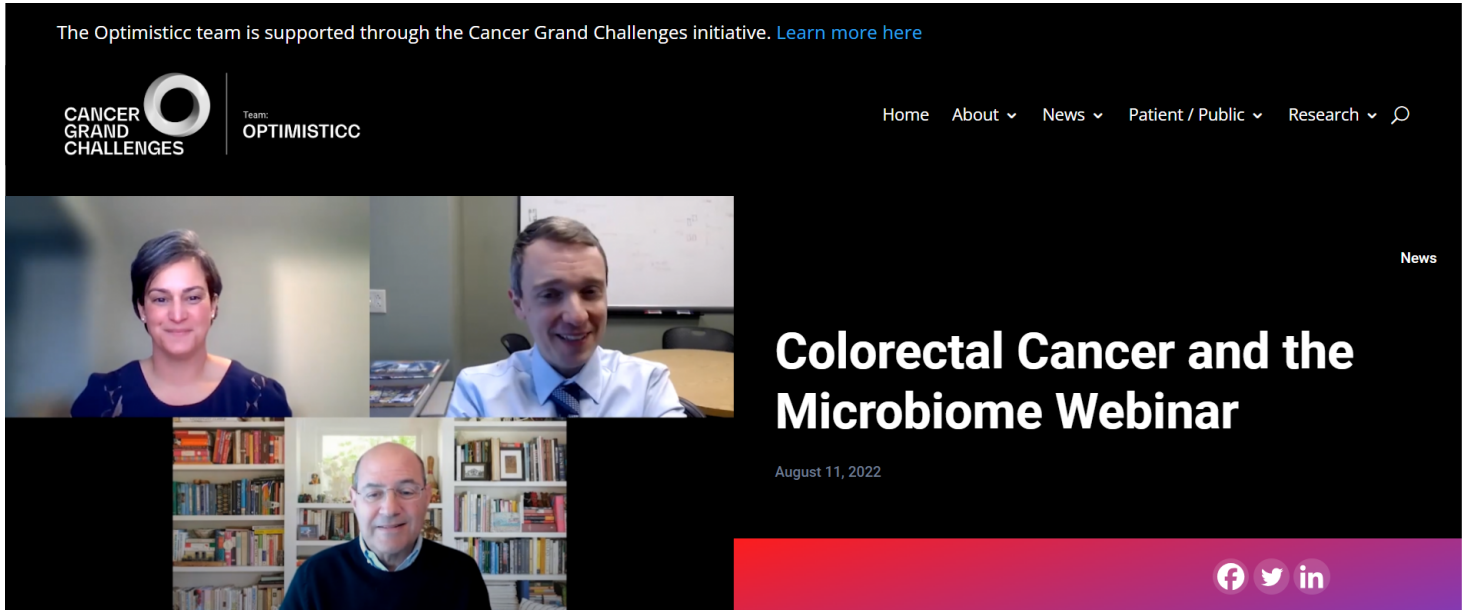
Example of patient and public engagement

CANCER GRAND CHALLENGES

Team OPTIMISTICC

OPportunity **T**o **I**nvestigate the **M**icrobiome's **I**mpact on **S**cience and **T**reatment **I**n **C**olorectal **C**ancer

Educational webinars to share knowledge about the research



https://optimisticc.org/colorectal-cancer-and-the-microbiome-webinar/

Webinar format

A series of informal conversations between the OPTIMISTICC researchers and patient advocates discussing the role of the gut microbiome in human health and disease and its association with colorectal cancer.

Acknowledgements

Management Group

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Tiffany Wallace, NCI, CRCHD
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Award Management

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