Cancer Grand Challenges

A New NCI Program in Collaboration with Cancer Research UK (CRUK)

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December 3, 2019
NCI Approaches to Address Specific Problems and Challenges

- Established in 2011 to stimulate research in areas that are perplexing, paradoxical or have not received sufficient attention
- New research questions are developed periodically through extensive engagement with the cancer research community

<table>
<thead>
<tr>
<th>Provocative Questions</th>
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<tbody>
<tr>
<td><strong>Investigators</strong></td>
<td>Individual principal investigator (PI) or multi-PIs, foreign participation allowed</td>
</tr>
<tr>
<td><strong>Funding Scale</strong></td>
<td>R21 ($275K); R01 (~$500K)</td>
</tr>
<tr>
<td><strong>Number of Awards</strong></td>
<td>R21 (10-15/year); R01 (25-35/year)</td>
</tr>
<tr>
<td><strong>Award Period</strong></td>
<td>R21 (≤ 2 years); R01 (≤ 5 years)</td>
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**Opportunity:** Combine the problem-identification process of the Provocative Questions initiative with a multidisciplinary team-based approach to attack major cancer problems from new perspectives
Cancer Research UK (CRUK)

- World’s largest independent cancer research charity
- £413 million ($531 million), financial year 2017-18
- Mission to promote public health by research into the causes, diagnosis, prevention and treatment of cancer
- Research funding through various mechanisms:
  - Investigator-initiated grants
  - Training fellowships
  - Research infrastructure (institutes and centers)
- 150+ research partnerships worldwide

“…partnerships enable mutually beneficial research collaborations with like-minded organisations…accelerating progress in the fight against cancer.”
Major Goals

- Identify specific barriers that, if removed, would be transformative and unlock the potential for patient benefit
- Fund a portfolio of novel and innovative research to address the challenges
- Encourage multi-disciplinary approaches and attract new thinking to cancer research
- Train future leaders in cancer research
- Facilitate global collaboration among researchers

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<th>Funded Awards (2017-2019)</th>
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<tbody>
<tr>
<td>Investigators</td>
<td>International teams; 8-15 investigators; 5-8 institutions; 3+ countries (on average)</td>
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<tr>
<td>Funding Scale</td>
<td>~ £20 million ($26 million)</td>
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<tr>
<td>Number of Awards</td>
<td>3-4 per funding round (biennial)</td>
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<tr>
<td>Award Period</td>
<td>Generally 5 years (flexible)</td>
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Previous Grand Challenges Align with NCI Priorities

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<tr>
<th>CRUK Grand Challenge</th>
<th>NCI Scientific Interest (NCI Program)</th>
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<tr>
<td>Map the molecular and cellular tumour microenvironment to define new targets for therapy and prognosis</td>
<td>Establishing a tumor atlas (Human Tumor Atlas Network)</td>
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<td>Distinguish between lethal cancers which need treating, and non-lethal cancers that don’t</td>
<td>Characterizing screen-detected lesions (MCL)</td>
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<td>Develop innovative approaches to target the cancer super-controller MYC</td>
<td>Characterizing RAS oncogenic mutants (Ras initiative)</td>
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<tr>
<td>Define mechanistic rules for combinatorial treatments to overcome resistance and avoid toxicity</td>
<td>Defining the basis for intrinsic and acquired drug resistance (DRSN)</td>
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<tr>
<td>Create novel tumour vaccinology approaches that establish or enhance successful immune responses beyond what is revealed by current checkpoint therapy</td>
<td>Improving immuno-oncology through the identification of new antigens and approaches (IOTN)</td>
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Grand Challenge Process

International Workshops

- Milan
- Amsterdam
- London
- Edinburgh
- NCI

Grand Challenge Award Panel (GCAP)

- GCAP Set Grand Challenges (Jan 2020)
- Public Launch (Feb 2020)
- Expression of Interest letters due (Jul 2020)
- GCAP Select finalists for full applications (Sep 2020)
- £30K ($39K) awards
- GCAP Final review & funding selections (May 2021)

Grand Challenge Awards

- Full applications are due

2019 2020 2021
<table>
<thead>
<tr>
<th>PI</th>
<th>Countries (# of investigators)</th>
<th>Title</th>
<th>Funding</th>
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<tbody>
<tr>
<td>Greg Hannon</td>
<td>UK, Switzerland, US, Canada and Republic of Ireland (15)</td>
<td>Creating Virtual Reality Maps of Tumors</td>
<td>£20M</td>
</tr>
<tr>
<td>Josephine Bunch</td>
<td>UK (12)</td>
<td>Studying Tumor Metabolism from Every Angle</td>
<td>£20M</td>
</tr>
<tr>
<td>Jelle Wesseling</td>
<td>The Netherlands, UK and US (13)</td>
<td>Preventing Unnecessary Breast Cancer Treatment*</td>
<td>£15M</td>
</tr>
<tr>
<td>Mike Stratton</td>
<td>France, UK and US (8)</td>
<td>Identifying Preventable Causes of Cancer</td>
<td>£16M</td>
</tr>
<tr>
<td>Thea Tlsty</td>
<td>Canada, Israel, UK and US (14)</td>
<td>A New Way to Tackle Inflammation-Associated Cancer</td>
<td>£20M</td>
</tr>
<tr>
<td>Matthew Meyerson,</td>
<td>Canada, The Netherlands, Spain, UK and US (14)</td>
<td>Manipulating the Microbiome to Beat Bowel Cancer</td>
<td>£19M</td>
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<tr>
<td>Wendy Garrett</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Stephen Elledge</td>
<td>The Netherlands, UK and US (13)</td>
<td>Understanding Why Cancers Grow in Some Tissues and Not In Others*</td>
<td>£20M</td>
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<tr>
<td><strong>TOTAL</strong></td>
<td></td>
<td></td>
<td><strong>£131M</strong></td>
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*Co-funded through partnerships

https://www.cancerresearchuk.org/funding-for-researchers/how-we-deliver-research/grand-challenge-award/funded-teams
Partnership Agreement with CRUK

- NCI will partner with CRUK to co-fund approximately four Grand Challenge awards per biennial funding round (×3 rounds)

- NCI funding will be awarded using the Other Transactions Authority (OTA) mechanism

- Funded teams will sign a master Funding and Collaboration Agreement (FCA) co-developed by CRUK and NCI

- All decisions regarding the Partnership will be approved by a Joint Steering Committee comprising CRUK and NCI leadership
CRUK is responsible for convening the GCAP and setting the agenda

GCAP advises CRUK only

NCI may attend GCAP meetings and may share NCI views during GCAP meeting

NCI may not exercise control over the GCAP or make decisions about its membership

NCI may not accept advice or recommendations from the GCAP

CRUK considers GCAP advice. CRUK subsequently engages in conversations with NCI

NCI staff may observe GCAP discussions and participate to convey NCI priorities and views

Virtual Core Team makes joint recommendations to the JSC on:
1. Setting Grand Challenges
2. Funding recommendations (short-listed teams and final awards)
3. Post-award monitoring, continued funding and adjustments

Before the JSC convenes, CRUK and NCI staff brief their leadership on recommendations

JSC must unanimously approve decisions at each step (1, 2, 3), upon the recommendation of the Virtual Core Team
Funding and Operations

- **Operational Manager**
  - CRUK

- **Virtual Core Team**
  - NCI

- **Cancer Grand Challenges Team**
  - U.S. Institution
  - U.S. Institution
  - Non-U.S. Institution
  - Non-U.S. Institution

- **Total includes ≤10% indirect costs**
- **Direct only**

- **$15M per year (total costs)**

- **~50% of direct costs**

- **Direct + full indirect**

- **Direct only**
NCI Budget Impact

Provocative Questions (ACTUALS)

Future Estimates
- Cancer Grand Challenge (~$15M)
- Provocative Questions (~$17M)
- Alternating years

New competing PQ awards

Millions ($)


New competing CGC awards

Millions ($)

2022 2023 2024 2025 2026 2027

15 17 15 17 15 17
Looking Ahead

• Grand Challenge is a new approach to identify scientific opportunities and support team-based cancer research

• CRUK and NCI will work collaboratively to develop a program evaluation framework

• Opportunity to further engage with the US cancer research community to advance scientific progress

• NCI Grand Challenge Consultation Workshop (Dec 4)

• Thank you