NIH NATIONAL CANCER INSTITUTE

Provocative Questions Initiative

Identifying Perplexing Problems to Drive Progress Against Cancer

The purpose of this Funding Opportunity Announcement is to support innovative research projects designed to solve specific problems and paradoxes in cancer research. Provocative Questions (PQs) are meant to challenge researchers to elucidate specific problems in key areas of cancer research that are important but have not received sufficient attention. As in previous years, one of the PQs addresses cancer health disparities.

PQ – 2: How do variations in immune function caused by comorbidities or observed among different populations affect response to cancer therapy?

Intent

Although the immune system has the potential to detect and eliminate cancer, considerable variability in immune function exists among populations and in response to comorbidities. These variations may help to explain observed differences in response to cancer therapies among patients and different populations. This PQ seeks applications that will identify and/or validate immune response variations among cancer patients (including tumor-associated immune responses and/or host immune responses) and investigate how these variations may positively or negatively affect response to cancer therapy Successful applications might include mechanistic or epidemiological studies to investigate how population-based differences in immune traits (e.g., across such populations as racial/ethnic groups, age groups, and/or gender) can influence therapeutic outcomes. Furthermore, applications may seek to determine how comorbid conditions (e.g obesity, heart disease, diabetes, etc.) may influence immune function and elucidate mechanism(s) by which this influence may affect therapeutic responses.

Feasibility

Responsive applications may include mechanistic, epidemiological, or comparative-based studies investigating variations in immune responses, either in response to chronic comorbid conditions or among well-defined population groups. Demonstrated differences in immune signatures including immune cell infiltration, chemotaxis, and cytokine profiles; studies directed at characterization of immune response markers related to therapeutic targets; and pathways differentially activated or inhibited in individuals or among diverse well-defined populations could provide starting points for these studies. The goal of this work should be to explain how these immune variations contribute to positive, negative, or no response to cancer therapy amongst diverse population groups (i.e., racial/ethnic groups, various age groups, etc.).

AT A GLANCE

Submission Deadlines

- Applications due October 30, 2017, June 28, 2018, and October 30, 2018
- Letter of Intent due 30 days before application due dates

Award Mechanisms

R01 and R21 awards for each PQ

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Implications of Success

Successful applications should propose studies to increase understanding of immunological mechanisms that affect response to cancer therapy among patients suffering from comorbidities and/or among diverse populations. Results from funded projects are expected to serve as a solid foundation for developing tangible strategies to manipulate the immune responses that influence favorable response to cancer therapy.

For the full text of these RFAs, visit:

R01
grants.nih.gov/grants/guide/rfa-files/RFA-CA-17-017.html

R21
grants.nih.gov/grants/guide/rfa-files/RFA-CA-17-018.html

Provactative Questions

R01 and R21 awards are available for each Provocative Question.

PQ – 1
What molecular mechanisms influence disease penetrance in individuals who inherit a cancer susceptibility gene?

PQ – 2
How do variations in immune function caused by comorbidities or observed among different populations affect response to cancer therapy?

PQ – 3
Do genetic interactions between germline variations and somatic mutations contribute to differences in tumor evolution or response to therapy?

PQ – 4
Can we develop tools to directly change the expression or function of multiple chosen genes simultaneously and use these tools to study the range of changes important for human cancer?

PQ – 5
How does mitochondrial heterogeneity influence tumorigenesis or progression?

PQ – 6
How do circadian processes affect tumor development, progression, and response to therapy?

PQ – 7
How do cancer-specific subcellular pathognomonic structures develop, what is their function, and can they be a source of novel therapeutic targets?

PQ – 8
What are the predictive biomarkers for the onset of immune-related adverse events associated with checkpoint inhibition, and are they related to markers for efficacy?

PQ – 9
Can we develop bifunctional small molecules that will couple oncoproteins or other cancer causing molecules of interest to inactivating processes such as degradation and achieve tissue-specific loss of function?

PQ – 10
How do microbiota affect the response to cancer therapies?

PQ – 11
Through what mechanisms do diet and nutritional interventions affect the response to cancer treatment?

PQ – 12
What are the molecular and/or cellular mechanisms that underlie the development of cancer therapy-induced severe adverse sequelae?

For more information, please visit:
https://provocativequestions.nci.nih.gov/