Provocative Questions RFA

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BSA Meeting
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THE PROVOCATIVE QUESTIONS PROJECT

- Challenge the scientific community to think about and answer important but non-obvious questions that will stimulate NCI’s research communities to use laboratory, clinical, and population research in especially effective and imaginative ways.
  - The power of a good question: excite the research community

- The proposals should:
  - Build on specific advances in our understanding of cancer and cancer control
  - Address broad issues in the biology of cancer that have proven difficult to resolve
  - Take into consideration the likelihood of progress in the foreseeable future (e.g. 5 to 10 years)
  - Address ways to overcome obstacles to answering the question
DEVELOPMENT OF THE PQ’S

• An interactive, iterative process still in progress

• A series of small workshops + website

• Four workshops held thus far (Oct, Feb):
  – Exploratory
  – Clinical and translational sciences
  – Behavior, population, epidemiology, and prevention sciences
  – Basic sciences

• More workshops planned (July, Aug)
  – Seattle, San Francisco, Los Angeles, San Diego, Bethesda
SELECTION OF PQ’S

• PQ’s developed and selected from meetings and those submitted to website
  – Goal for this RFA: 15-20 PQ’s

• Many types of PQ’s: e.g., epidemiology, pathogenesis, prognosis, risk modification, prevention, diagnosis, therapeutics, and behavior

• Verify the PQ’s are understudied: portfolio analysis by the Office of Science Policy and Analysis (OSPA)
RFA, R21, R01, BUDGET

- RFA: To highlight research issues that are not well studied
  - To move research into these areas quickly and effectively
- R21 and R01: Well understood formats
  - R21: 2 years funding; R01: 4 years funding
- Budget: up to $15 million
  - Sufficient to generate community interest and make multiple awards
  - Total amount awarded will depend on the number of highly meritorious applications
REVIEW CRITERIA

• The 5 standard review criteria (Significance, PI, Innovation, Approach, and Environment)

• Applications may come from PI’s new to a field
  – strength of the applications judged in large part on the power of the ideas behind the proposed research
  – preliminary data unnecessary
  – track record in the field should not be weighed as heavily as in other reviews
HOW DOES OBESITY CONTRIBUTE TO CANCER RISK?

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LONG-TERM MORTALITY AFTER GASTRIC BYPASS SURGERY

<table>
<thead>
<tr>
<th>End Point</th>
<th>Matched Subjects</th>
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<tbody>
<tr>
<td></td>
<td>Surgery Group</td>
<td>Control Group</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(N=7925)</td>
<td>(N=7925)</td>
<td></td>
</tr>
<tr>
<td>All causes of death</td>
<td>213</td>
<td>321</td>
<td></td>
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<tr>
<td>no./10,000 person-yr</td>
<td>37.6</td>
<td>57.1</td>
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<tr>
<td>Cardiovascular disease</td>
<td>55</td>
<td>104</td>
<td></td>
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<tr>
<td>no./10,000 person-yr</td>
<td>9.7</td>
<td>18.5</td>
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</tr>
<tr>
<td>Diabetes</td>
<td>2</td>
<td>19</td>
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</tr>
<tr>
<td>no./10,000 person-yr</td>
<td>0.4</td>
<td>3.4</td>
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</tr>
<tr>
<td>Cancer</td>
<td>31</td>
<td>73</td>
<td></td>
</tr>
<tr>
<td>no./10,000 person-yr</td>
<td>5.5</td>
<td>13.3</td>
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<tr>
<td>Other diseases</td>
<td>62</td>
<td>89</td>
<td></td>
</tr>
<tr>
<td>no./10,000 person-yr</td>
<td>11.0</td>
<td>15.5</td>
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<tr>
<td>All non-disease causes</td>
<td>63</td>
<td>36</td>
<td></td>
</tr>
<tr>
<td>no./10,000 person-yr</td>
<td>11.1</td>
<td>6.4</td>
<td></td>
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</tbody>
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*Deaths that were caused by disease include all deaths minus those caused by accidents unrelated to drugs, poisonings of undetermined intent, suicides, and other non-disease deaths.

DO DRUGS THAT ARE COMMONLY AND CHRONICALLY USED FOR OTHER INDICATIONS PREVENT CANCERS AND, IF SO, HOW?

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Weak or No Effect

WHAT PROPERTIES OF NON-MALIGNANT LESIONS (IN SITU CA’S) PREDICT THE LIKELIHOOD OF INVASIVE DISEASE?

- Prostatic Intraepithelial Neoplasia (PIN)
- Ductal Carcinoma In Situ (DCIS)
- Pancreatic Intraepithelial Neoplasia (PanIN)
WHAT IS THE CLINICAL SIGNIFICANCE OF FINDING CELLS FROM A PRIMARY TUMOR AT ANOTHER SITE?

Lymph node invaded by ductal breast carcinoma
WHAT ENVIRONMENTAL FACTORS CHANGE THE RISKS OF VARIOUS CANCERS WHEN PEOPLE MOVE FROM ONE GEOGRAPHIC REGION TO ANOTHER?

WHY DON’T MORE PEOPLE ALTER BEHAVIORS KNOWN TO INCREASE THE RISK OF CANCERS?

• The message itself is not designed optimally for impact
• The message is not effectively delivered
• The interventions to facilitate behavior change are not optimal
Why are different animals with different sizes and different life spans so different with respect to cancer incidence?

Turtles

Mice

Sharks

Whales….except belugas from the SLE!
WHY ARE SOME DISSEMINATED CANCERS CURED BY CHEMOTHERAPY ALONE?
SUMMARY

• Stimulate research in compelling, understudied areas

• Evaluation of success
  – Shorter term:
    • A plethora of exciting applications—reissuance
  – Intermediate term:
    • PI’s continue their studies through traditional grant mechanisms
  – Longer term
    • Answers to the questions
    • Better understanding of neoplasms
    • Improved risk assessment, prevention, treatment, etc.
THANKS

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RFA Concept: Dinah Singer, Barbara Spalholz, Judy Mietz, Anne Lubenow, Jerry Lee
BSA SUBCOMMITTEE QUESTIONS

“The PQ RFA is an excellent idea but….”

• Analogous NCI/NIH programs?
• Complexity and challenge of the review process
  – Getting enough competent reviewers for the two-tiered process?
  – “Non-responsive” to RFA: stringent or permissive?
  – “Enforcing” the importance of ideas vs. preliminary data?
    • Proscribe preliminary data?
  – Automatic submission of triaged applications to a regular CSR study section?