Trans-NIH
US-China Program for Biomedical Collaborative Research (R01)

June 2018 BSA

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Tram Kim Lam (DCCPS)
Dan Xi (DCTD)
NCI Participation in Trans-NIH U.S.-China Joint Collaborative Research Program
Summary of First Seven Years (2011-2017)


<table>
<thead>
<tr>
<th>Type</th>
<th>Year(s)</th>
<th>Extramural</th>
<th>Intramural</th>
<th>Funds (US)</th>
<th>Funds (China)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Administrative Supplement</td>
<td>2011</td>
<td>11</td>
<td>2</td>
<td>$1M/yr (NIH: $2M/yr)</td>
<td>$1M/yr</td>
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<tr>
<td></td>
<td>2012</td>
<td>8</td>
<td>1</td>
<td>$1M/yr (NIH: $3M/yr)</td>
<td>$2.02M/yr</td>
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<tr>
<td>R01</td>
<td>2013-2015</td>
<td>5</td>
<td>2</td>
<td>$1M/yr (NIH: $5M/yr)</td>
<td>$3.2M/yr</td>
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<tr>
<td></td>
<td>2017-2022</td>
<td>5 (1 paid by OAR)</td>
<td>1</td>
<td>$1M/yr (NIH: $4.5M/yr)</td>
<td>$3.0M/yr</td>
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</tbody>
</table>

- Cancer-specific Topics:
  - 2011: Broad emphasis on all basic research applicable to cancer, with additional emphasis on HIV-associated malignancies, rare/regionally-associated cancers, studies of TCM.
  - 2012: Topics from 2011 + focus on infection-associated cancers, epidemiology and population sciences, cancer prevention, and preclinical development of novel cancer therapeutics and imaging agents.
  - 2013: Focus exclusively on infection-associated cancers. Emphasis on EBV, H. pylori, HBV/HCV, HPV, and Kaposi-Associated Herpes Virus
  - 2017: Focus on genomics/proteomics, nanotechnology, immunotherapy, liver cancer.
  - Proposed topics for 2018: Cancer sites with regionally high prevalence (Liver, NPC, Upper GI); environmental risk factors for cancer; and Traditional Chinese Medicine and Natural Products
**Process**

1. **CGH identifies partner and potential research areas.**
2. **trans-NCI or trans-NIH team crafts FOA.**
3. **CGH negotiates funding plan with foreign counterpart.**

**DOCs**
- Science driven by the DOCs*.
- FOAs negotiated with partner to represent DOC priorities.
- Applications referred to DOCs.

**CGH**
- Manages negotiations.
- Provides trans-NCI program coordination.
- Works across inter-agency (State, Missions, other ICs.).

*FOA topics are based on a consensus between NCI and partner agency.

**Staff Contributing to this Issuance**

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<td>DCCPS</td>
<td>Tram Kim Lam</td>
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**Note:** Bulk of past awards have gone to DCB.
What does success look like?

New collaborations.
Novel work funded.
Training exchanges take place.

Publications.
Continuation of Work.

Continuation of work without need for dedicated funding.
Evaluation of the Trans-NIH US China Program

Evaluation of 1st Three Rounds

- 37% (32 of 85) Administrative Supplement surveys received.
- 51% (20 of 39) R01 surveys (approximately one year into award period).

- Award created opportunities to:
  - Build Research Capacity
    - Expand the knowledge and abilities, train fellows and perform novel research
    - Enable cross-cultural analyses
  - Foster collaborations and accessibility to unique populations
    - Accelerate research from bench to bedside
  - Establish a foundation for future collaborative research studies
Cancer-Related Publications

75* publications, associated with 2013 NCI Extramural R01s, published in 33 distinct journals

- 57 manuscripts published in journals with an impact factor < 9.999
- 9 in journals with an impact factor between 10.000 and 19.999
- 1 in a journal with an impact factor > 20.000

High-Impact Journal Citations:


*8 manuscripts published in journals with no impact factor
Proposed Topics and Budget for FY19
IC Participation

- ICs planning to Sign on:
  - NCI
  - NIEHS
  - NINDS
  - NIMH
  - NEI

- Discussing participation:
  - NIA, NHLBI, NIBIB
  - FIC helping recruit more…

April 10th, 2018 – NIH-NSFC Joint Working Group on U.S.-China Biomedical Collaborative Research
1. Cancer Sites with Regionally High Prevalence
   ▪ Nasopharyngeal Carcinoma
   ▪ Liver Cancer
   ▪ Upper GI Cancers
2. Environmental Risk Factors
3. Traditional Chinese Medicine (TCM) and Natural Products
Cancer Sites with Regionally High Prevalence

- **Nasopharyngeal Carcinomas (NPC)**
  - Underlying mechanisms not fully understood.
  - Incidence and mortality declining globally, but EBV-associated NPC still high in Southern China.
  - Refining screening/treatment strategies, and the development of therapeutics for recurrent disease.

- **Upper GI Cancers**
  - Research on early detection and treatment of pre-neoplastic lesions.
  - Biomarker research to distinguish invasive tumors from benign lesions.
  - Research to identify modifiable risk factors.
  - Develop non-invasive methods to primary screen to identify high risk individuals who need screening.
Cancer Sites with Regionally High Prevalence

- **Liver Cancers**
  - Viral hepatitis, fatty liver disease, NASH, and alcoholic liver disease are major etiologic factors for liver cancer in the U.S. and China.
  - Research Topics:
    - Does the cell of origin influence liver tumor type?
    - Do liver cancer stem cells arise and are they found in all liver tumors?
    - What is the role of the hepatic stellate cell in cancer progression?
    - How do individual cell types/stromal components in the microenvironment influence tumor development or progression?
    - Identifying cohorts of cirrhotic patients to study risk(s) for cancer associated with viral (HBV, HCV) and/or non-viral (NASH, ALD) etiologies
    - Identify the independent and synergistic role of non-viral risk factors in liver cancer etiology.
    - Identifying/validation factors for liver cancer associated with specific underlying liver pathology (e.g. NASH, ALD, viral hepatitis)
    - Integration of imaging approaches with early detection of liver cancers.

Liver Cancer Incidence

Collaborative Effort with the NCI that will be leveraged to strengthen applicant pool.
Environmental Risk Factors

- The Ministry of Environmental Protection recently admitted the existence of toxic ‘cancer villages’ in China caused by or at least linked to uncontrolled environmental pollution.
  - Particulate matter in the air linked with increased mortality rates in the general population and contributes to lung cancer incidence,
  - Aflatoxin is a common food contaminant,
  - Arsenic present in many types of seafood.

Topics:
- The role of air pollution in cancer.
- The role of chemical exposures, including those derived from e-waste and pesticide exposures, in cancer.
About 60% of cancer patients in the US seek some form of CAM approach or consultations, including TCM.

Topics:
- Mechanisms and translational research on novel therapeutics development including combination approaches with conventional cancer care, immunotherapy, and investigational drug/treatment;
- Computation and experimental approaches to improve the accuracy of predicting advanced therapeutic effects and adverse effects due to interactions with conventional medicine;
- NCI OCCAM and NSFC to host integrative oncology workshop in October.

Acupuncture chart from Hua Shou (fl. 1340s, Yuan Dynasty).
Biospecimen Transfer and Data Sharing

- Experience with last issuance positive.
- Review criteria inclusive of biospecimen transfer and data sharing agreements.
  - Complementary biospecimen and data sharing language will be in both the NIH and NSFC FOAs.

**Biospecimen Transfer**

- Program can assist applicants navigate heavily bureaucratic biospecimen transfer process.
- FOA will require biospecimen sharing plan in the research strategy section.
  - Type and nature of samples.
  - Plan to obtain approval for exchange or shipping from Chinese government.
  - Plan to address aims if specimen transfer is not approved.

**Data Sharing**

- FOA will require resource sharing plan between NIH and NSFC investigator similar to a multi-PI grant.
- Applicants must plan to **share all final research data** in these
Proposed NCI Budget

- Up to 5 awards (R01) at a maximum of $200,000 total costs per year/per award for 5 years.
  - NSFC understands we cannot fund unless we receive meritorious applications.
- Budget (in total costs) of $1 million/year for 5 years.
- As was the case in previous bilateral funding opportunities, 10% of funds will be set aside to support intramural research collaborations (to support CCR and DCEG collaborations).
  - CSR has agreed to review intramural applications using the same study sections that review the extramural applications.
- Funded awards determined after parallel NCI and NSFC review.
  - NCI and NSFC must reach consensus to fund.
  - Only applications with high scores from both agencies will be funded.
Thank You
谢谢

cancer.gov
cancer.gov/espanol
Additional Reference Slides
Breadth of Existing NCI Work in China

- 114 Active Extramural Grants with Performance Sites in China.
- 58 Intramural Projects.
  - DCEG: 33
  - CCR: 25

*Detailed analysis included as attachment to concept.*
Distribution of Existing Awards

- ~50% of ongoing extramural funding of projects in China are R awards (37% R01).
  - Majority of the remaining grants are U-awards and the international work of the P30s and SPOREs.
  - Evenly spread across CSO codes with larger concentrations in etiology and treatment.
  - Evenly distributed across cancer sites, except for breast and lung.
- Contribution of past US-China grants
  - The bulk of the US-China grants have gone to DCB and represent a substantial portion of their work in China.
  - By cancer site, US-China grants largely mirror other grants with performance sites in China.

*Detailed analysis included as attachment to concept.*
### US-China versus NCI’s China Portfolio

- **All-China Portfolio**: All grants in the China Portfolio minus the U.S.-China Bilateral Program grants
- Projects can be coded to more than one Cancer Site.
- List reflects all cancer sites coded to China portfolio grants.

<table>
<thead>
<tr>
<th>NCI DOC</th>
<th># of Grants</th>
<th># of Supplements</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All-China</td>
<td>U.S.-China</td>
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<tr>
<td>CCT</td>
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<td>Office of Cancer Complementary &amp; Alternative Medicine</td>
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<tr>
<td>OHAM</td>
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<td>SBIR</td>
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### Cancer Site

<table>
<thead>
<tr>
<th>Cancer Site</th>
<th>All China Portfolio</th>
<th>US-China Portfolio</th>
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<tbody>
<tr>
<td>Bladder</td>
<td>3</td>
<td>0</td>
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<tr>
<td>Brain</td>
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<tr>
<td>Breast</td>
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<td>7</td>
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<tr>
<td>Cervical</td>
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<tr>
<td>Colorectal</td>
<td>6</td>
<td>3</td>
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<tr>
<td>Endometrial</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Esophageal</td>
<td>9</td>
<td>1</td>
</tr>
<tr>
<td>Head and Neck</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Kaposi’s Sarcoma</td>
<td>6</td>
<td>4</td>
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<tr>
<td>Kidney</td>
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<tr>
<td>Leukemia</td>
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<td>1</td>
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<tr>
<td>Liver</td>
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<tr>
<td>Lung</td>
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<tr>
<td>Melanoma/Skin</td>
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<td>2</td>
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<tr>
<td>Urinary System</td>
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</tbody>
</table>

***The bulk of the US-China grants have gone to DCB and represent a substantial portion of their work in China.***

***Current US-China grants largely mirror other grants with performance sites in China.***
Process – Most Components in Parallel

- Agree to produce a joint funding opportunity.
  - Prepare and sign an MOU, if necessary.
- Agree on scope.
  - Agree on budgets and funding levels in each country.
- Draft a concept.
- Agree on scope.
- Agree on budgets and funding levels in each country.
- Draft a concept.
- NCI seeks concept approval from scientific program leadership.
- Partnering agency seeks approvals.
- Produce language for funding opportunity announcement.
  - *Same for both parties.*
- NCI announces opportunity, requiring applicants’ collaborators submit same application to partner.
- Partner announces opportunity, requiring applicants’ collaborators submit same application to NCI.
- NCI conducts, scientific review.
- Partnering conducts scientific review.
- Scores from each review are used to seek programmatic consensus on funding.
- NCI funds grants.
- Partner funds grants.

***NOTE: There is an ongoing negotiation with CSR support towards bringing review fully into the NIH.***
US-China Bilat Eval
Did the U.S.-China Bilateral Program Produce New Collaborations?

Admin. Supplements: Had you collaborated with your fellow principal investigator prior to this project?

- I have not collaborated with him/her before:
  - Non-NCI Responses: 7
  - NCI Responses: 7

- I have collaborated with him/her before:
  - Non-NCI Responses: 15
  - NCI Responses: 3

R01s: Had you collaborated with your fellow principal investigator prior to this project?

- I have not collaborated with him/her before:
  - Non-NCI Responses: 5
  - NCI Responses: 2

- I have collaborated with him/her before:
  - Non-NCI Responses: 10
  - NCI Responses: 3
Do U.S.-China Bilateral Program Collaborators Plan to Work Together in the Future?

Admin. Supplements: What plans, if any, do you have to continue collaborating with your fellow investigator on other projects?

*Pls selected all answers that applied

- Discussed ways to collaborate on another project: 16 Non-NCI, 7 NCI
- Applying for funding to collaborate on another project together: 3 Non-NCI, 3 NCI
- Received funding to collaborate on another project together: 4 Non-NCI, 12 NCI
- We have no plans to continue to collaborate: 12 Non-NCI, 2 NCI
- Don’t know: 2 Non-NCI, 1 NCI
- N/A: 1 Non-NCI

R01s: What plans, if any, do you have to continue collaborating with your fellow principal investigator on other project(s)?

*Pls selected all answers that applied

- We have discussed ways to collaborate on another project together: 5 Non-NCI, 1 NCI
- We are applying for funding to collaborate on another project together: 7 Non-NCI
- We have received funding to collaborate on another project together: 1 Non-NCI, 1 NCI
Did the U.S.-China Bilateral Program Increase Teams’ Capacity/Skills?

Admin. Supplements: Laboratory/Team Capacity Building

- Number trained in lab or bench science techniques
- Number trained in administrative and financial grant management
- Number trained in medical procedures
- Number trained (either through mentoring or training courses) in scientific manuscript writing
- Number trained (either through mentoring or training courses) in grant writing
- Number trained in bioethics or IRB rules and regulations
- Number trained in qualitative data collection and analysis (e.g. focus group discussion,...)
- Number trained in quantitative data collection and analysis

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NCI Responses Only
Outcomes from the U.S.-China Bilateral Program (Supplements Only)

Admin. Supplements: Outcomes from Collaboration

- Publications: 29 Non-NCI Responses, 20 NCI Responses
- A manuscript is being prepared: 4 Non-NCI Responses, 1 NCI Response
- Presentations: 22 Non-NCI Responses, 8 NCI Responses
- Patents: 1 Non-NCI Response, 0 NCI Responses