



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

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NCI Participation in Trans-NIH U.S.-China Joint Collaborative Research Program

Summary of First Seven Years (2011-2017)

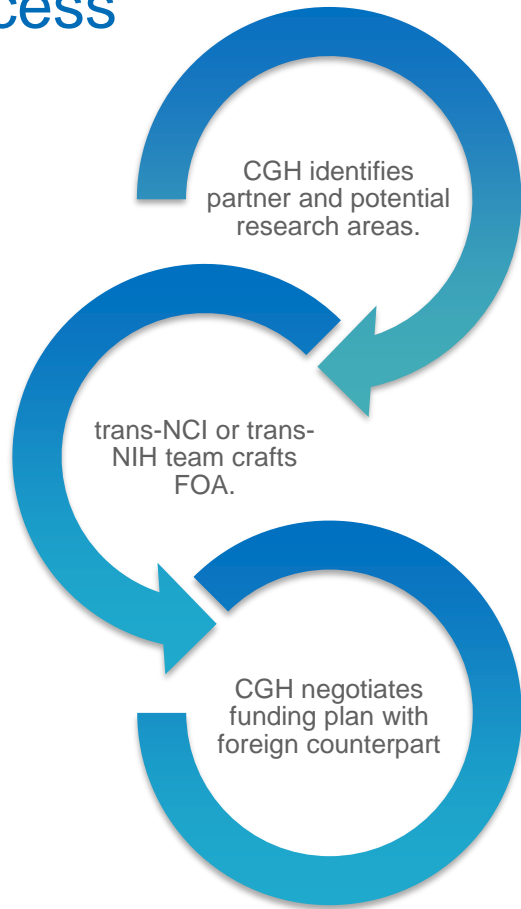


- 4 FOAs: Admin Supplements (2011, 2012), R01s (2013-2015, 2017-2022)

Type	Year(s)	Extramural	Intramural	Funds (US)	Funds (China)
Administrative Supplement	2011	11	2	\$1M/yr (NIH: \$2M/yr)	\$1.63M/yr
	2012	8	1	\$1M/yr (NIH: \$3M/yr)	\$2.02M/yr
R01	2013-2015	5	2	\$1M/yr (NIH: \$5M/yr)	\$3.2M/yr
	2017-2022	5 (1 paid by OAR)	1	\$1M/yr (NIH: \$4.5M/yr)	\$3.0M/yr

- 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



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.**

DOC	Staff Contributing to this Issuance
DCB	Betsy Read-Connole
DCP	Jo-Ann Rinaudo, Ping Hu, and Wendy Wang
DCTD	Dan Xi
DCCPS	Tram Kim Lam

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

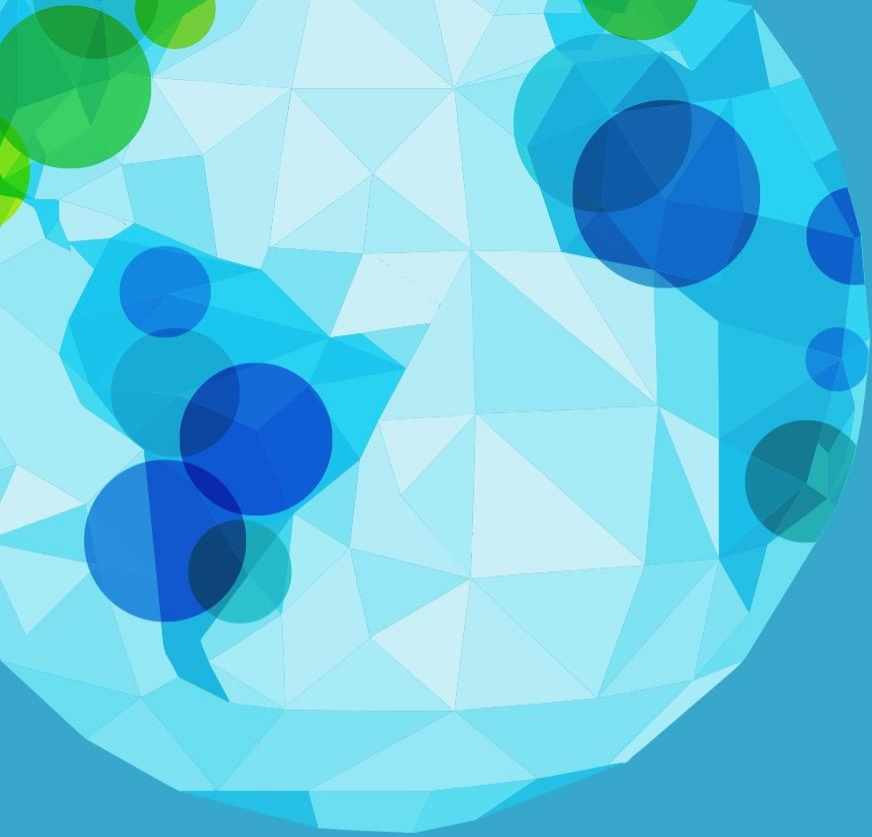
Cancer-Related Publications

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:

- Liu K, Lee J, Kim JY, Wang L, Tian Y, Chan ST, Cho C, Machida K, Chen D, Ou JJ. Mitophagy Controls the Activities of Tumor Suppressor p53 to Regulate Hepatic Cancer Stem Cells. **Mol Cell**. 2017 Oct 19;68(2):281-292.e5. doi: 10.1016/j.molcel.2017.09.022. Epub 2017 Oct 12. PMID: 29033320
- Gruffaz M, Vasan K, Tan B, Ramos da Silva S, Gao SJ. TLR4-Mediated Inflammation Promotes KSHV-Induced Cellular Transformation and Tumorigenesis by Activating the STAT3 Pathway. **Cancer Res**. 2017 Dec 15;77(24):7094-7108. doi: 10.1158/0008-5472.CAN-17-2321. Epub 2017 Oct 19. PMID: 29051178
- Tian Y, Kuo CF, Akbari O, Ou JH. Maternal-Derived Hepatitis B Virus e Antigen Alters Macrophage Function in Offspring to Drive Viral Persistence after Vertical Transmission. **Immunity**. 2016 May 17;44(5):1204-14. doi: 10.1016/j.immuni.2016.04.008. Epub 2016 May 3. PMID: 27156385
- Bao Y, Wu X, Chen J, Hu X, Zeng F, Cheng J, Jin H, Lin X, Chen LF. Brd4 modulates the innate immune response through Mnk2-eIF4E pathway-dependent translational control of I κ B α . **Proc Natl Acad Sci U S A**. 2017 May 16;114(20):E3993-E4001. doi: 10.1073/pnas.1700109114. Epub 2017 May 1. PMID: 28461486



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

Topics

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

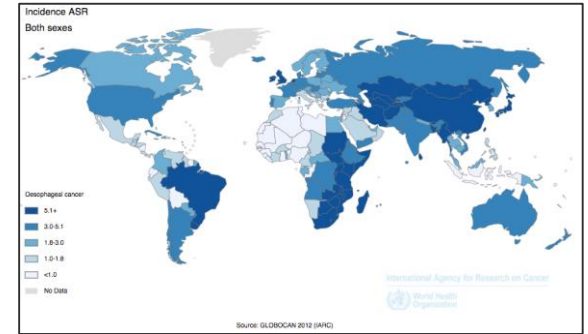
■ Nasopharyngeal Carcinomas (NPC)

- 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.

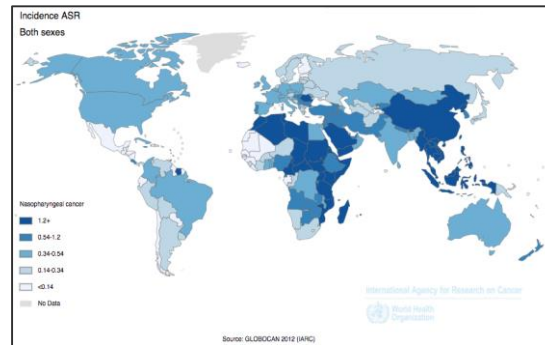
■ Upper GI Cancers

- 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.

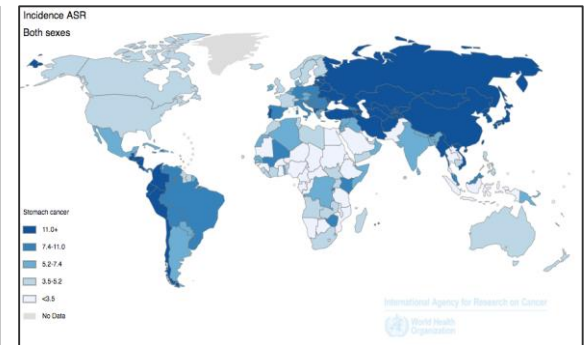
Esophageal Cancer



NPC Incidence



Gastric Cancer

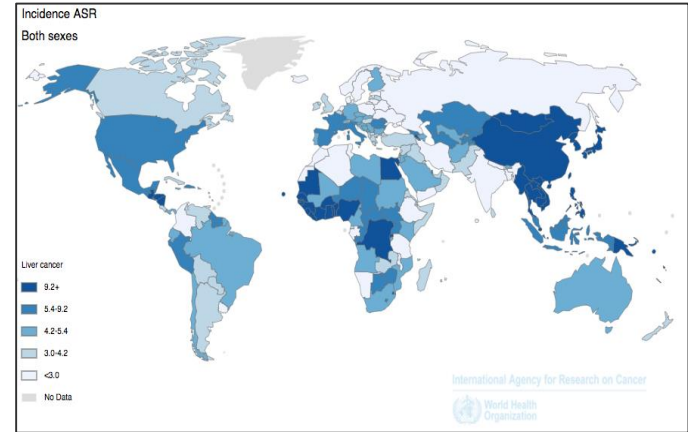


Cancer Sites with Regionally High Prevalence

▪ 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/validating 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



2018 Beijing Liver Cancer International Conference (BLCIC)

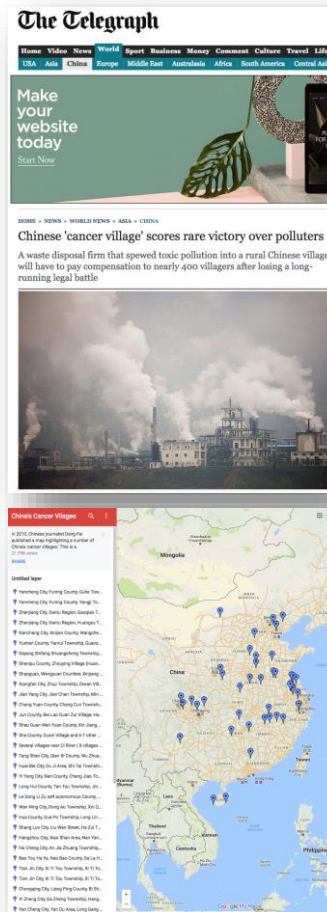
Co-Sponsors: Peking University Health Science Center & NIH/NCI
Organizer: Peking University 302 Hospital

Co-Organizers: Western Returned Scholars Association /Medical Doctors Association Youth Committee/NH Chinese Scholarship Association
Asia-Pacific Alliance of Liver Diseases (APALD)
China Research Hospital Society / Molecular Diagnostic Association
Tongji University / Center for Synthetic and Systems Biology (CSSB)
Beijing Medical Association Liver Disease Branch

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.



Traditional Chinese Medicine (TCM) & Natural Products Research

- 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



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CANCER
INSTITUTE**

cancer.gov

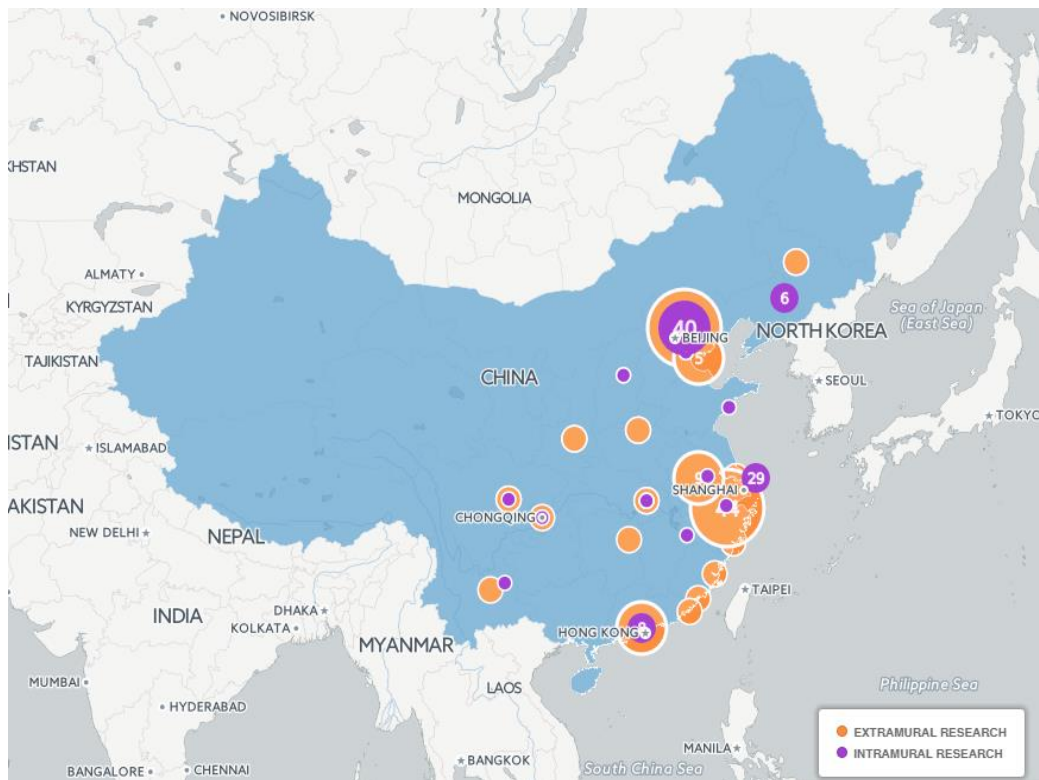
cancer.gov/espanol

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.

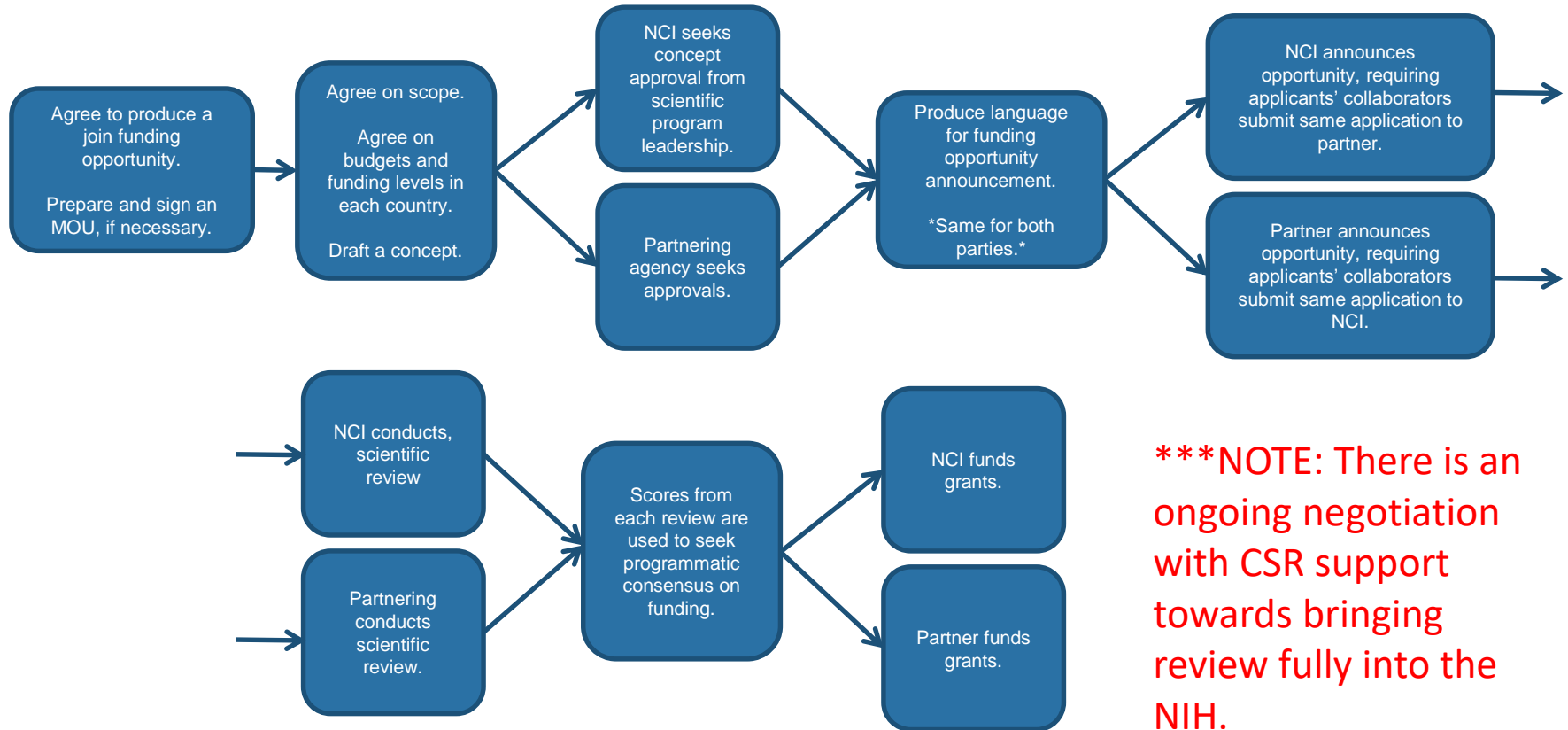
NCI DOC	# of Grants		# of Supplements	
	All-China	U.S.-China	All-China	U.S.-China
CCT	3		1	
CGH	1			
CRCHD				2
CSSI	1			
DCB	11	7	1	7
DCCPS	15	1	3	3
DCP	3	1	2	4
DCTD	11	2	11	2
Office of Cancer Complementary & Alternative Medicine			1	
OHAM	8		2	
SBIR	1			

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

Cancer Site	All China Portfolio	US-China Portfolio
Bladder	3	0
Brain	5	1
Breast	13	7
Cervical	10	2
Colorectal	6	3
Endometrial	1	0
Esophageal	9	1
Head and Neck	6	1
Kaposi's Sarcoma	6	4
Kidney	3	0
Leukemia	3	1
Liver	5	2
Lung	19	2
Melanoma/Skin	4	1
Myeloma	2	0
Nervous System	2	0
Neuroblastoma	1	0
Non Site-Specific Cancer	17	5
Non-Hodgkin's Lymphoma	9	1
Oral Cavity and Lip Cancer	2	0
Ovary	2	1
Pancreas	8	1
Pharyngeal	3	0
Prostate	8	1
Salivary Gland	1	0
Small Intestine Cancer	1	0
Stomach	2	2
Urinary System	2	0

***Current US-China grants largely mirror other grants with performance sites in China.

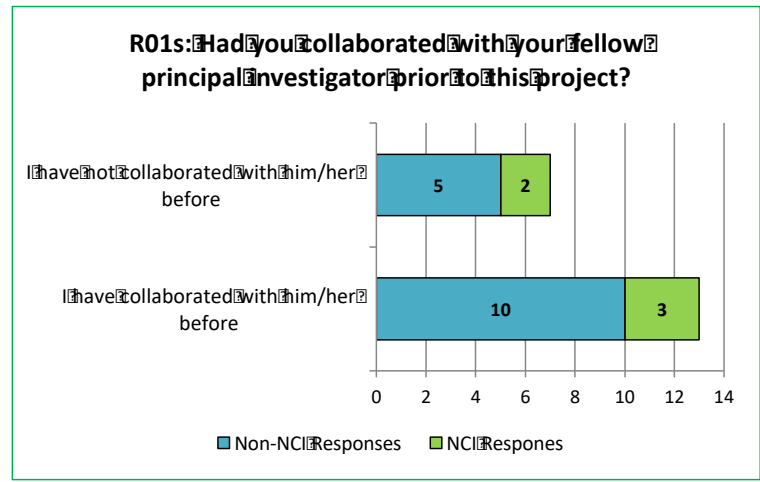
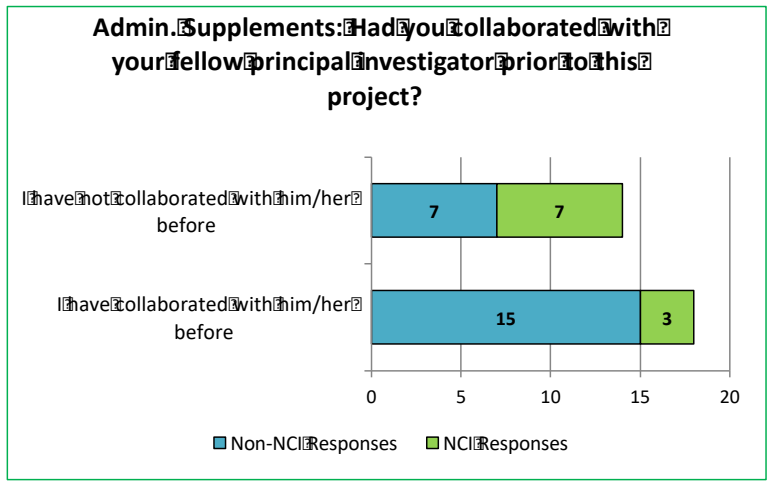
Process— Most Components in Parallel



*****NOTE: There is an ongoing negotiation with CSR support towards bringing review fully into the NIH.**

US-China Bilat Eval

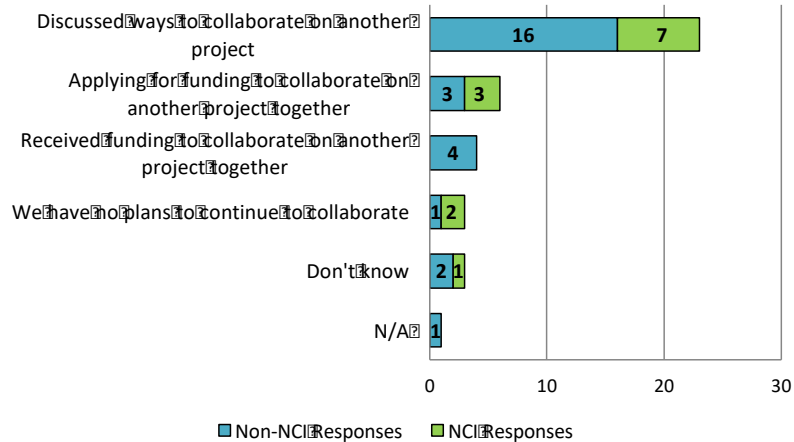
Did the U.S.-China Bilateral Program Produce New Collaborations?



Do U.S.-China Bilateral Program Collaborators Plan to Work Together in the Future?

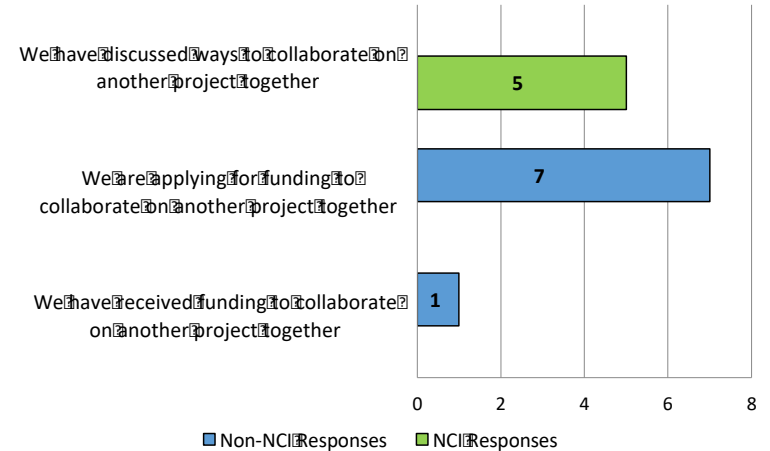
Admin. Supplements: What plans, if any, do you have to continue collaborating with your fellow investigator on other projects?

*Pls Selected All Answers that Applied



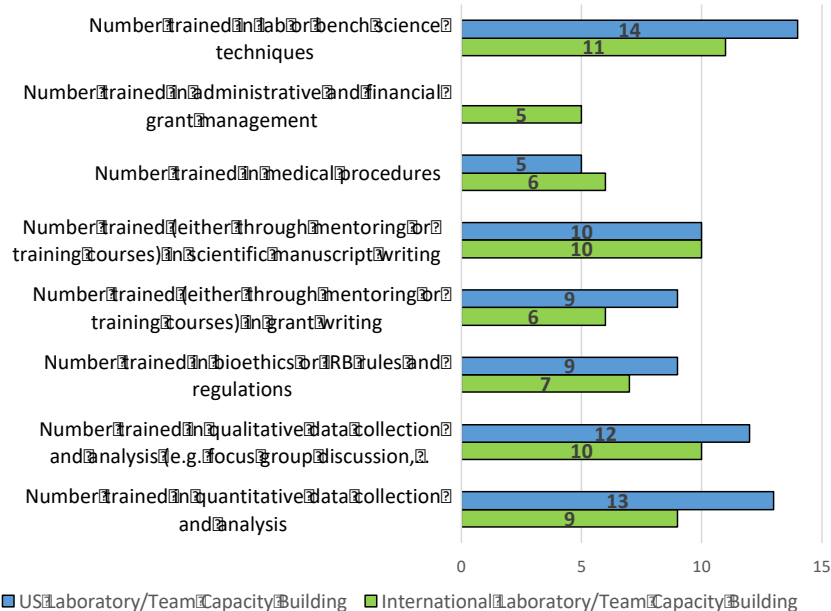
R01s: What plans, if any, do you have to continue collaborating with your fellow principal investigator on other project(s)?

*Pls Selected All Answers that Applied

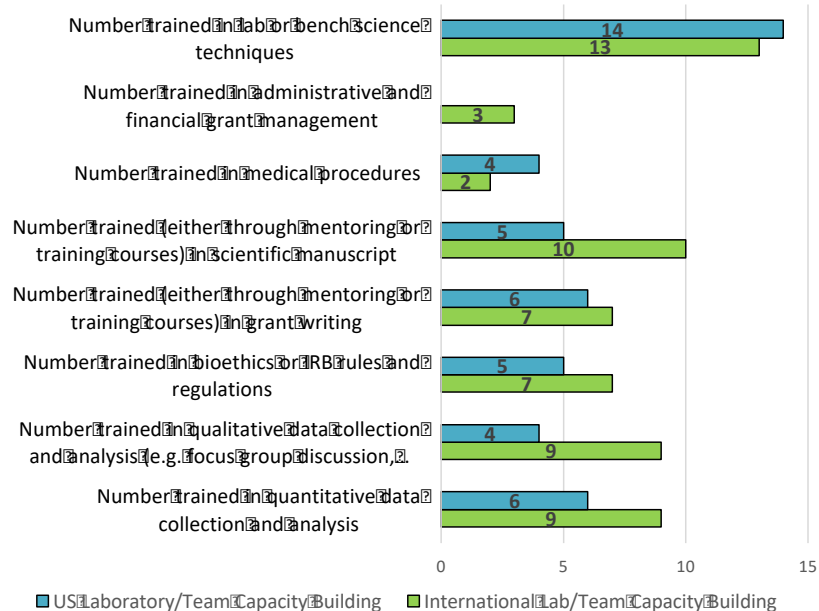


Did the U.S.-China Bilateral Program Increase Teams' Capacity/Skills?

Admin. Supplements: Laboratory/Team Capacity Building



R01s: Laboratory/Team Capacity Building



NCI Responses Only

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

