NCI's Alliance for Nanotechnology in Cancer Program: Phase III and Data Sharing Plans

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NCIP Nanotechnology Working Group
February 18, 2016

National Cancer Institute

U.S. DEPARTMENT
OF HEALTH AND
HUMAN SERVICES

National Institutes
of Health

NCI Alliance for Nanotechnology in Cancer (Alliance)

Alliance for Nanotechnology in Cancer:

- Supported by NCI's Office of Cancer Nanotechnology Research

- The Alliance works in concert with other NCI advanced technology initiatives to provide the scientific foundation and team science required to transform cancer research and benefit the patient

Nanotechnology Applications to Cancer:

- Potential to revolutionize biomedicine by manipulating materials at the nanoscale (unique physical, chemical, biological features that differ from bulk)

- Combine innovations in nanomaterials and cancer biology to develop new cancer solutions

- Early detection of disease
  - Sensors
  - Imaging

- Delivery of therapeutics
  - Local and systemic
  - Improved efficacy
  - Post-therapy monitoring

- New research tools to enhance understanding of disease

13 nm
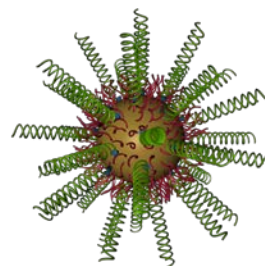
RNAi-functionalized gold nanoparticles (Mirkin, Northwestern)

NCI **Alliance** for **Nanotechnology** in Cancer

Phase II Alliance Organization
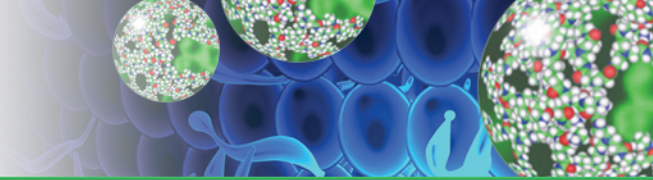
External Steering Committee

NCI Alliance Phase II

Centers for Cancer Nanotechnology Excellence (CCNEs) U54 Cooperative Agr.

Multi-disciplinary Training K99/R00 Awards, R25 Awards

Cancer Nanotechnology Platform Partnerships U01 Cooperative Agr.

Nanotechnology Characterization Laboratory (NCL)

Serves as national resource to aid regulatory review of cancer nanotechnologies

Coordination and Governance Committee (CGC)

Alliance Industrial Committee (AIC)

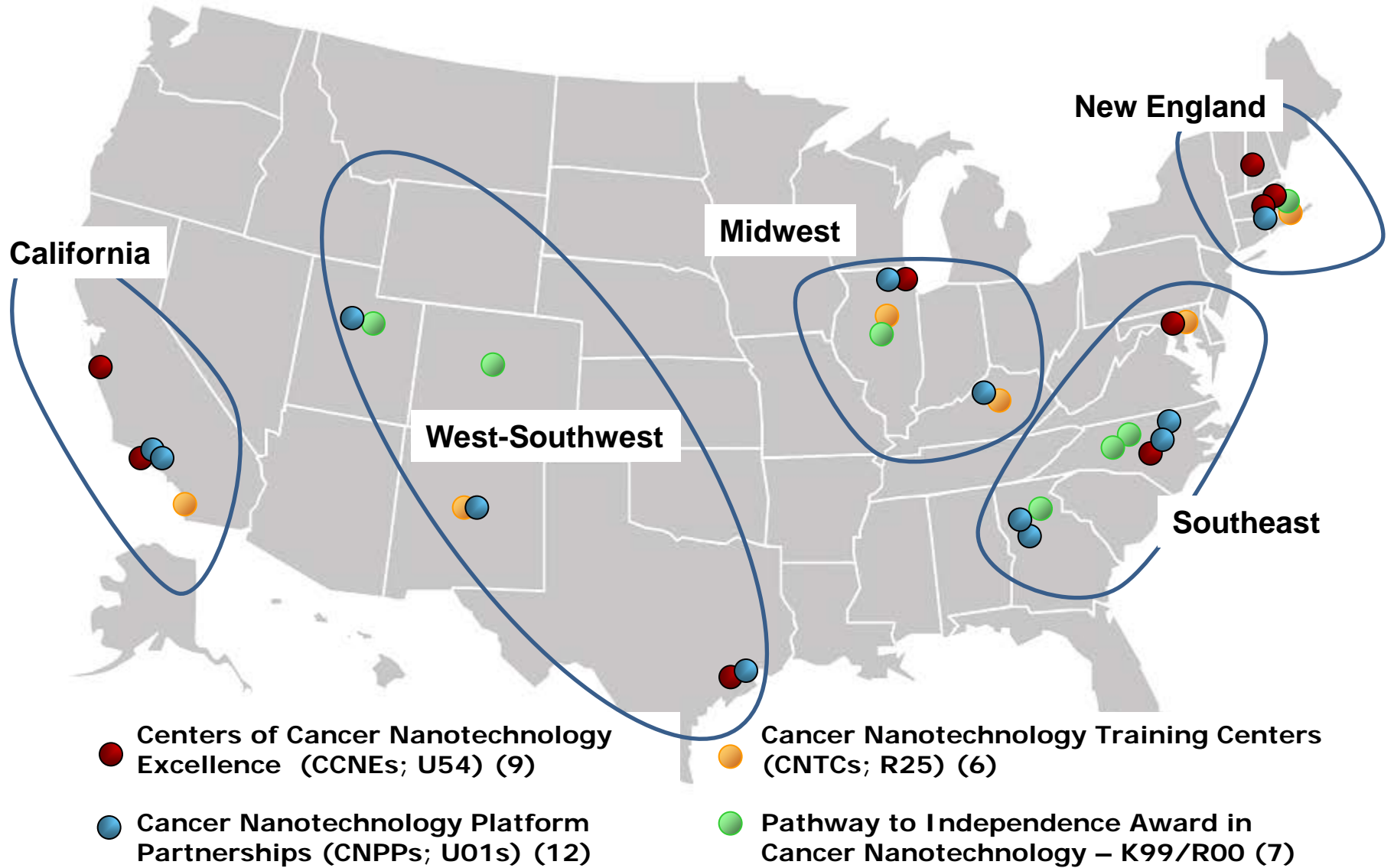**Alliance Clinical Committee (ACC)**

Other NCI Programs

- Phase I: 2005 – 2010
- Phase II: 2010 – 2015
- Phase III: 2015-2020

- Alliance's development model—most promising strategies handed off to for-profit partners for effective translation and commercialization

- Focus on cancers characterized by low survival rates: pancreatic, ovarian, brain, lung
- Focus on improving diagnostic detection and therapeutic index; overcoming biological barriers

NCI **Alliance**
Nanotech
in Cancer

Phase II Alliance Distribution

New England

Midwest

California

West-Southwest

Southeast

Centers of Cancer Nanotechnology Excellence (CCNEs; U54) (9)

Cancer Nanotechnology Training Centers (CNTCs; R25) (6)

Cancer Nanotechnology Platform Partnerships (CNPPs; U01s) (12)

Pathway to Independence Award in Cancer Nanotechnology – K99/R00 (7)

NCI **Alliance** for
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National Cancer Institute

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Office of Cancer Nanotechnology Research: Interactions

- Alliance members also have opportunities to work together through topic-specific working groups (animal models, biotargeting) and Challenge Projects (Phase II)

- OCNR also facilitates interactions between Alliance investigators and other NCI/NIH programs, nanotechnology institutions, and organizations

- Significant role in promoting nanotechnology applications to biomedicine by interacting with these programs, other federal agencies (e.g., through NNI) and the wider research community—e.g., Nano Startup Challenge in Cancer

| Translating Genomic Targets in Cancer Therapeutics Using Nanotechnology	PAR-16-044: Image-guided Drug Delivery in Cancer (R01)	US-China Symposium on Nanobiology and Nanomedicine
• Connecting investigators in Alliance with investigators in other NCI programs--CTD^2 Network • Exchanging resources, meeting reciprocal needs	• Developing funding opportunities with other Institutes—NCI and NIBIB • Advance aspects of image-guided interventions	• Collaboration between NCI, other NIH Institutes, and the NCNST of China • Explore collaborative opportunities and facilitate discussions on medical nanotechnologies

NCI Alliance for Nanotechnology in Cancer

Translational Support

Nanotechnology Characterization Laboratory (NCL)

http://ncl.cancer.gov –applications due next on March 1, 2016

- Pre-clinical characterization of nanomedicines
- Three way agreement of NCI, FDA, and NIST
- Supports extramural community
- Assisted with characterization leading to six IND or IDE filings with FDA
- Launching NCL 2.0—transnational collaborations, extending to indications outside of cancer—e.g., EHS

Nanoparticle Biocompatibility

NCI **Allian** **Nanotechnology** in Cancer

Translation of Nanotechnology in Cancer Consortium (TONIC)

- Public–private partnership
- Corporate membership--14 industry members (e.g. Janssen, AstraZeneca, Onyx Pharma, Teva), three patient advocacy group members (e.g., American Brain Tumor Association)
- Discussion forum for opportunities in nanotechnologies and strategies to accelerate translation to clinic
  - Workshops
  - Showcasing of technologies
  - Joint, pre-competitive projects
  - Nanodrug Clinical Working Group— Developing protocols to enable study of drug delivery in patients by imaging
- Companies also either involved or partially funding (MedImmune) Nano Startup Challenge in Cancer-- http://www.nscsquared.org/
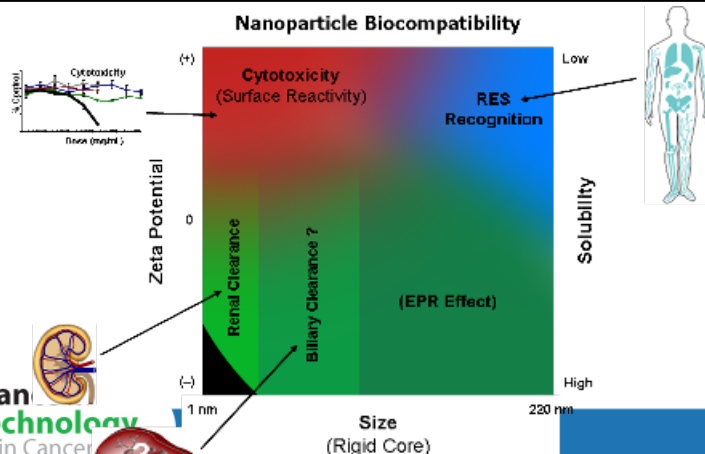
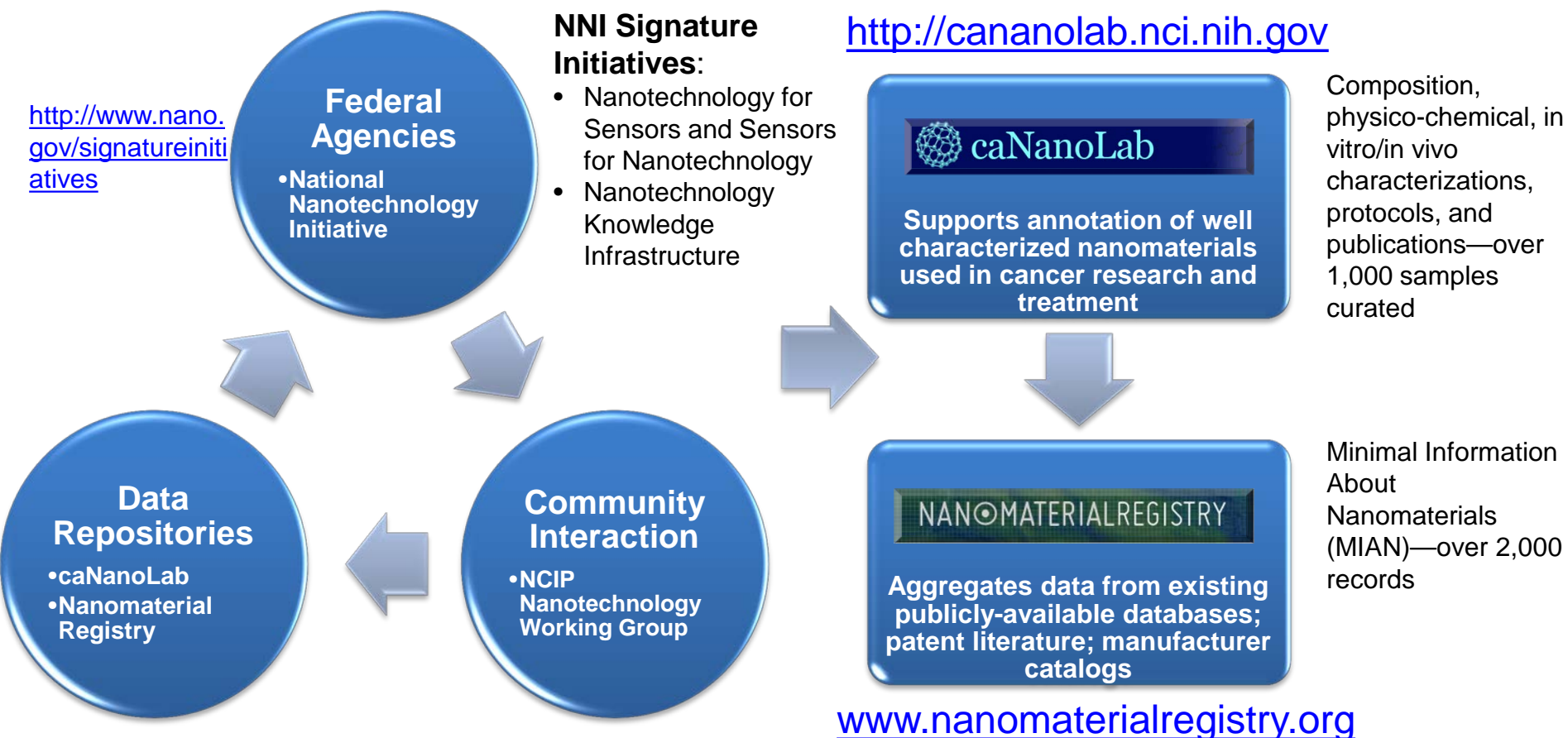# Nano Startup Challenge in Cancer

- Joint effort between NCI and the Center for Advancing Innovation (CAI; http://www.thecenterforadvancinginnovation.org)
- Purpose is to launch of startups centered around commercially viable cancer nanotech inventions
- Participants form teams and develop business plans around cancer nanotech inventions that either originate from the intramural NIH program or are brought forward by the team
- Teams are advised and evaluated by experienced researchers, industry leaders, and investors brought together by CAI
- Previous Challenges: The Breast Cancer Startup Challenge, The Neuro Startup Challenge
- Can learn more at http://www.nscsquared.org/
- First step, Phase 0, is letter of intent—upcoming deadline **March 1, 2016**!!

Resources for Nanomaterial Data Sharing and Standards Development

- Realize importance of data sharing and re-use to enable knowledge discovery and improve the rational design of nanomaterials –access to datasets and protocols

http://www.nano.gov/signatureinitiatives

Federal Agencies
- National Nanotechnology Initiative

NNI Signature Initiatives:
- Nanotechnology for Sensors and Sensors for Nanotechnology
- Nanotechnology Knowledge Infrastructure

http://cananolab.nci.nih.gov

caNanoLab

Supports annotation of well characterized nanomaterials used in cancer research and treatment

Composition, physico-chemical, in vitro/in vivo characterizations, protocols, and publications—over 1,000 samples curated

Data Repositories
- caNanoLab
- Nanomaterial Registry

Community Interaction
- NCIP Nanotechnology Working Group

NANO MATERIAL REGISTRY

Aggregates data from existing publicly-available databases; patent literature; manufacturer catalogs

Minimal Information About Nanomaterials (MIAN)—over 2,000 records

www.nanomaterialregistry.org

NCI **Alliance** for **Nanotechnology** in Cancer

cancer Nanotechnology Laboratory (caNanoLab) Data Portal

Home Page

http://cananolab.nci.nih.gov

- Facilitates data sharing to expedite and validate use of nanomaterials in biomedicine

- Provides access to characterization data, protocols, and publications

- In house curator; data submission directly by users (access to data private or public)

- Making strong efforts to curate from the broader international community
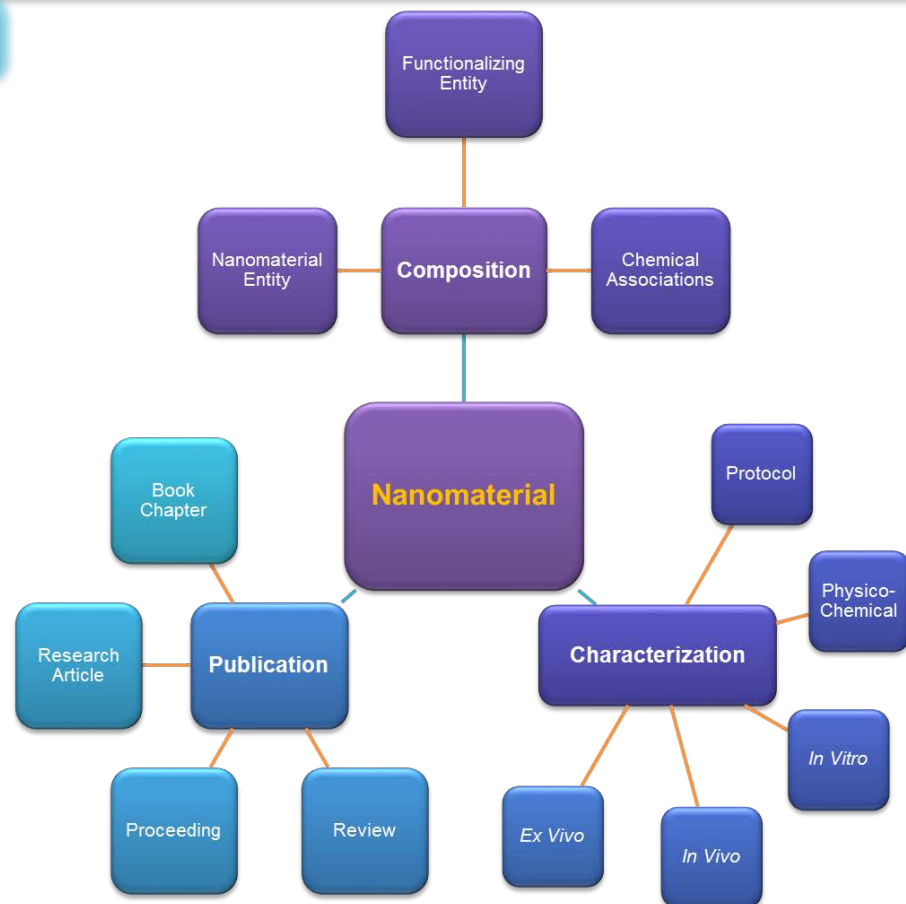
Supported by NCI Office of Cancer Nanotechnology Research and NCI Center for Biomedical Informatics and Information Technology

Gaheen et al., 2013, *Comput Sci Discov;* Morris et al., 2015, *Beilstein J Nanotechnol*

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Nanomaterial Registry

- Archives research data on nanomaterials and their biological and environmental implications
    - Aggregated data from existing publicly-available databases, patent literature, manufacturer catalogs, individual labs
    - Tools to evaluate content—compliance levels, comparison tools, data visualization dashboard; Minimal information about a nanoparticle (MIAN)

- Integrated modeling and simulation tools for Registry data analysis (nanoHUB; https://nanohub.org/groups/nanomaterialregistry)

- Provides export function to allow easy data download from site and working on data submission page/template; boilerplate text for NSF/NIH data management plans

- caNanoLab feeds into Registry--835 records, and several in queue

https://www.nanomaterialregistry.org/

Supported by NIBIB   NIH NATIONAL CANCER INSTITUTE

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NCI Alliance Program - Achievements

- **Scientific Output**
  - More than 25 distinct nanomaterial delivery vehicles at various stages of maturity and numerous innovative technologies reported in the literature since 2011
  - Close to 1500 papers and 300 patent filings and disclosures since program start
  - Over 300 different nanoparticle formulations evaluated by the NCI's Nanotechnology Characterization Laboratory (NCL)

- **Clinical Translation**
  - over 75 companies in the space of diagnostics and therapy are associated with the program. Majority of them are start-ups.
  - More than17 on-going clinical trials are associated with program projects
  - Several companies are in IND or pre-IND discussions with U.S. FDA

- **Community Resources**
  - Support for clinical translation—NCL and TONIC consortium
  - Centralized databases of nanomaterial characterization information—caNanoLab and Nanomaterial Registry web portals

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Program Renewal and Next Phase
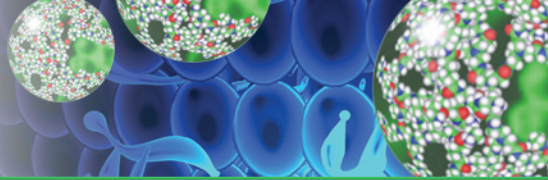
NCI Alliance Phase II		NCI Alliance Phase III	
Centers of Cancer Nanotechnology Excellence (CCNE) U54 Cooperative Agreement	→	**Centers of Cancer Nanotechnology Excellence (CCNE) U54 Cooperative Agreement**	**Six CCNEs**
Cancer Nanotechnology Platform Partnerships U01 Cooperative Agreement	→	**Innovative Research in Cancer Nanotechnology (IRCN) Awards U01 Cooperative Agreement**	**Seven IRCNs so far**
Multi-disciplinary Training K99/R00 Awards, R25 Awards	→	**T32 Cancer Nanotechnology Training Programs**	**Five CNTCs so far**
Nanotechnology Characterization Laboratory	→	**Nanotechnology Characterization Laboratory**	

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Alliance Program Phase III:
CCNEs and IRCNs

- NCI intends to continue support for research in three broad areas of nanotechnology-based cancer care applications:

  - early diagnosis using *in vitro* assays and devices or *in vivo* imaging techniques

  - multifunctional nano-therapeutics, including nanoparticle-driven immunotherapies

  - devices and techniques for cancer prevention and control

NEW!!

- **Tumor Types:** should be rationally selected, where "tumor type" refers to either tumors of a specific tissue of origin or tumors with critical abnormalities in a particular molecular pathway(s) shared in cancers arising from a variety of tissues.

- **Milestones:** applicants need to provide a set of discrete benchmarks that will allow unequivocal determination of the progress made towards the goals of the project.

NEW!!

- **Data Sharing Plan:** Sharing of nanomaterial data needs to occur through appropriate publically accessible databases: NCI's cancer Nanotechnology Laboratory (caNanoLab) data portal (https://cananolab.nci.nih.gov/caNanoLab/)

  - At least one scientifically qualified person needs to be designated as the nanomaterial data sharing coordinator after an award has been made

NCI **Alliance** for
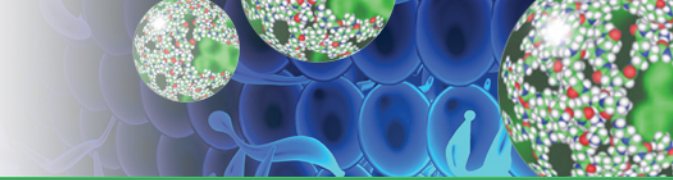**Nanotechnology**
in Cancer

CCNE Characteristics

- Overall goal of CCNEs-- rapid advance of novel cancer care applications based on nanotechnology

  - Funding work up to preclinical stage;expected to seek other sources of funding that would allow for clinical trials, as early as during award period

  - must be strongly committed to and capable of further translation and commercialization; can be via partnership with for-profit entities

- Each Center expected for on a 'scientific theme' associated with a nanotechnology-based solution to an overarching problem in cancer biology and/or oncology

- Research Projects expected to be synergistic; expected to be a mix of basic research/discovery projects and translational projects

- Example translational directions—Nanotechnology-enabled multiplex diagnostic devices; Nucleic acid-based nanotherapies

- Example basic research/discovery directions—Understanding of mechanisms of nanoparticle delivery to cancer cells and tissues in vivo (e.g., nanoparticle endosomal escape); Development of new tissue and animal model systems for the screening of nanotechnology compounds

Phase III CCNEs

- Center of Cancer Nanotechnology Excellence for Translational Diagnostics—Stanford University

- Center for Multiple Myeloma Nanotherapy—Washington University

- MSKCC-Cornell Center for Translation of Cancer Nanomedicine—Memorial Sloan Kettering and Cornell University

- Nano Approaches to Modulate Host Cell Response for Cancer Therapy—University of North Carolina-Chapel Hill

- Nanosystems Biology Cancer Center (NSBCC)—California Institute of Technology and University of California, Los Angeles

- Nucleic Acid-Based Nanoconstructs for the Treatment of Cancer—Northwestern University

- For more info go to http://nano.cancer.gov/action/programs/ccne.asp

IRCN Characteristics

IRCN projects expected to address major barriers in cancer biology and/or oncology using nanotechnology and should emphasize fundamental understanding of nanomaterial and nanodevice interactions with biological systems.

- Fundamental understanding of the processes pertinent to the use of nanotechnology in cancer (e.g.):
    - nanomaterial and/or nanodevice interactions with biological systems
    - mechanisms of delivery of nanoparticles and/or nanodevices to desired and intended cancer targets *in vivo*
    - characterization of *in vitro* detection and diagnostic devices

- Clinical translation is not an objective of IRCN projects

- Example research directions--Detailed studies and understanding of delivery mechanisms; Development of improved multi-biomarker detection and/or diagnostic devices (e.g., fundamental studies of nanomaterial properties that affect sensitivity and specificity)

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IRCN FOA Still Open

Open to International Applicants!

Innovative Research in Cancer Nanotechnology (IRCN) Awards U01 Cooperative Agreement

No set-aside funds; Not percentiled

PAR-14-285; **Next applications due April 14, 2016**

$450K/yr/award
Two receipts/yr until 2017:
October 13, 2016; April 14, 2017

- Projects should be designed to enable multi-disciplinary research and transformative discoveries in cancer biology and/or oncology through the use of nanotechnology

- Funded projects become part of NCI Alliance for Nanotechnology in Cancer network. The network will provide opportunities for collaborations with other Alliance members and enhanced interactions with NCI programs

- If appropriate, work should aid in clinical translation, *but clinical translation is not the ultimate goal of these awards*

Phase III IRCNs So Far

- Nanoscale Metal-organic Frameworks for Light Triggered and X-ray Induced Photodynamic Therapy of Head and Neck Cancers—University of Chicago

- Stroma Breaking Theranostic Nanoparticles for Targeted Pancreatic Cancer Therapy—Emory University

- Targeted Core Shell Nanogels for Triple Negative Breast Cancer—University of North Carolina-Chapel Hill

- The rodent eye as a non-invasive window for understanding cancer nanotherapeutics—University of California, Davis

- Thermoresponsive NanoVelcro CTC Purification System for Prostate Cancer Profiling—University of California, Los Angeles and Cedars-Sinai Medical Center

- Treatment of Glioblastoma Using Chain-Like Nanoparticles—Case Western Reserve University

- UCLA Multifunctional Mesoporous Silica Nanoparticle Platform for Treatment of Pancreas Cancer—University of California, Los Angeles

- For more info go to http://nano.cancer.gov/action/programs/nanotech_platforms.asp

NCI Alliance for Nanotechnology in Cancer

T32 Training Program Call for CNTCs

T32 Cancer Nanotechnology Training Programs

Proposals received through Parent T32 PA, PA-14-015
Awards held by NCI's Center for Cancer Training

Next applications due May 25, 2016

Notice of NCI interest in Cancer Nano T32s—NOT-CA-14-035

- Carolina Cancer Nanotechnology Training Program—University of North Carolina-Chapel Hill
- Cancer Nanotechnology Training Program—Northwestern University
- Cancer-Translational Nanotechnology Training Program—Stanford University
- Interdisciplinary Translational Pre/Postdoctoral Program in Cancer Nanotechnology—University of Texas at MD Anderson Cancer Center
- Predoctoral and Postdoctoral Training Program in Nanotechnology for Cancer Research—Johns Hopkins University

Sharing Data Through caNanoLab

- Data deposition requirement for CCNE and IRCN Alliance program participants, (CNTCs also encouraged to do so)—noted in funding opportunity announcements (RFA-CA-14-013, PAR-14-285)

- In the past encouraged to do so, but deposition is now a Term and Condition of Award

- caNanoLab inclusion in data sharing plan and the naming of a designated nanomaterial data sharing coordinator is required once an award has been made

https://wiki.nci.nih.gov/display/caNanoLab/caNanoLab+FAQ

caNanoLab Enhancements to Support User Search and Submission

- **caNanoLab 2.1 is latest release (Nov 2015) and expands on caNanoLab 2.0 features (Dec 2014)**

  - <u>Usability enhancements</u> from feedback obtained via the caNanoLab survey

  - <u>myWorkspace feature</u> to allow users to view submitted samples, protocols, and publications and their submission status

  - <u>myFavorites feature</u> to allow user to save samples, protocols, and publications for easy access

  - <u>Integration with a publication vendors</u> to retrieve samples by publication

  - Support for <u>Advanced and Google-like Search</u> capabilities

- Future plans include support for ISA-TAB-Nano and other usability enhancements

MyWorkspace

☑ Samples ☑ Protocols ☑ Publications

My Samples

Actions	Sample Name	Sample Submission Status	Created Date	Sample Access
View Edit	Dendrimer-Demo	In Draft	12/17/10	(Owner, Shared by: Curator, Demo University)
View Edit	Liposome-Demo	In Draft	12/9/11	(Owner, Shared by: Curator)
View Edit	Carbon_Nanotube-Demo	In Draft	2/29/12	(Owner, Shared by: Carbon Tube Group, Curator)
View Edit	Metal_Particle-Demo	In Draft	4/24/12	(Owner, Shared by: Curator)

My Protocols

Actions	Protocol Name	Protocol Submission Status	Created Date	Protocol Access
View Edit	NIST - NCL Joint Assay Protocol, PCC-6	Retracted	12/8/10	(Owner, Shared by: Curator, Public)
View Edit	NIST - NCL Joint Assay Protocol, PCC-7	Approved	12/8/10	(Owner, Shared by: Curator, Public)
View Edit	NIST - NCL Joint Assay Protocol, PCC-10	Approved	12/8/10	(Owner, Shared by: Curator, Public)
View Edit	NIST - NCL Joint Assay Protocol, PCC-8	Approved	12/8/10	(Owner, Shared by: Curator, Public)
View Edit	NIST - NCL Joint Assay Protocol, PCC-9	Approved	12/8/10	(Owner, Shared by: Curator, Public)
View Edit	NIST - NCL Joint Assay Protocol, PCC-11	Retracted	12/8/10	(Owner, Shared by: Curator, Public)
View Edit	NIST - NCL Joint Assay Protocol, PCC-14	Approved	12/8/10	(Owner, Shared by: Curator, Public)
View Edit	NIST - NCL Joint Assay Protocol, PCC-12	Approved		

PubMed-Based Query

Sample Information by Publication

Publication REF	Authors	Title	Sample Composition	Sample Characterization	Journal	Year	Vol(Iss)Pg
PubMed ID: 16876898	Niidome, T, Yamagata, M, Okamoto, Y, Akiyama, Y, Takahashi, H, Kawano, T, Katayama, Y, Niidome, Y	PEG-modified gold nanorods with a stealth character for in vivo applications.	Samples curated in caNanoLab: KU_JSTC-TNiidomeJCR2006-01 KU_JSTC-TNiidomeJCR2006-02	Samples curated in caNanoLab: KU_JSTC-TNiidomeJCR2006-01 KU_JSTC-TNiidomeJCR2006-02	Journal of controlled release : official journal of the Controlled Release Society	2006	114:343-347

Gold nanorods prepared in hexadecyltrimethylammonium bromide (CTAB) solution are expected to provide novel materials for photothermal therapy and photo-controlled drug delivery systems. Since gold nanorods stabilized with CTAB show strong cytotoxicity, we developed a technique to modify these with polyethyleneglycol (PEG) for medical applications. PEG-modification was achieved by adding mPEG-SH in the CTAB solution, then, excess CTAB was removed by dialysis. PEG-modified gold nanoparticles showed a nearly neutral surface, and had little cytotoxicity in vitro. Following intravenous injection into mice, 54% of injected PEG modified gold nanoparticles were found in blood at 0.5 h after intravenous injection, whereas most of gold was detected in

Advanced Search

Advanced Sample Search

Sample Criteria

[-- Please Select -- ▼] [-- Please Select -- ▼] [_____]

[Add] [Reset]

Composition Criteria

nanomaterial entity   dendrimer   [Edit]

[-- Please Select -- ▼] [-- Please Select -- ▼] with chemical name [-- Please Select -- ▼] [_____]

[Add] [Reset]

Characterization Criteria

| physico-chemical characterization | size | size | > | 10 | nm | [Edit] |
| in vitro characterization | cytotoxicity | LC50 | > | 10 | mg/L | [Edit] |

[-- Please Select -- ▼] [-- Please Select -- ▼] [-- Please Select -- ▼]

Sharing Data through caNanoLab
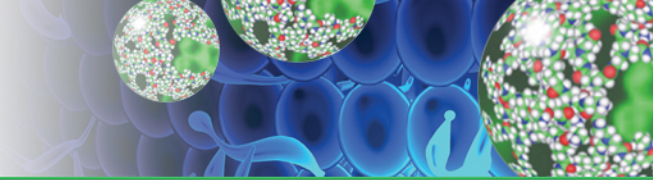
- Encourage submission directly by users—Alliance or otherwise; specifically submission while research in progress and not just after publications (caNanoLab feature—public or private mode)

- Held hands-on caNanoLab demo session for data coordinators during Alliance Kick-Off Meeting in November 2015—led by Sharon Gaheen

- Received helpful feedback:

  – User interface and process seem pretty straightforward

  – Interest in submitting image data—how can this be done in caNanoLab?

  – Interest in use of local instances of caNanoLab to maintain samples until ready to make public

NCI **Alliance** for **Nanotechnology** in Cancer

Linking caNanoLab to The Cancer Imaging Archive (TCIA)
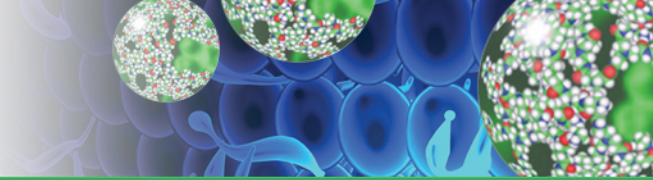
Collections of freely accessible DICOM images and supplementary data to foster re-use and reproducibility within the cancer imaging research community

- Supports public and NCI's Cancer Imaging Program
- Created and originally hosted by Wash U. and now at University of Arkansas for Medical Sciences—PI is Fred Prior, also caNanoLab data coordinator for Wash U. CCNE

Unique Features of TCIA

- Highly curated problem-focused sets of DICOM standard clinical patient imaging data—can be extended to support preclinical images and data

- Documentation of linked research initiatives and associated metadata

- Can assign Digital Object Identifiers (DOIs) to TCIA collections for ease of retrieval

- Programmable Interface connects TCIA data directly to other applications

- *First step approach for linking—link caNanoLab and TCIA via DOIs; can be entered into URL fields in caNanoLab*

Linking caNanoLab Instances
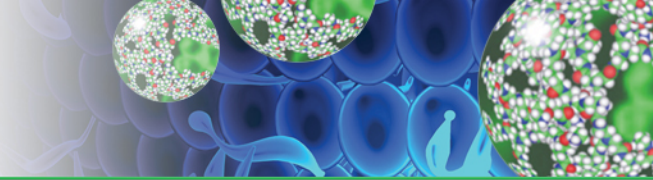
NCI Instance

Want to be able to query across nodes

Looking into options; web services
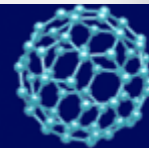
Wash U. Instance

Northwestern Instance

? Instance

Resources

- caNanoLab Portal
  - Production: https://cananolab.nci.nih.gov
- caNanoLab Wiki
  - https://wiki.nci.nih.gov/display/caNanoLab/caNanoLab+Wiki+Home+Page
- caNanoLab Usability Group
  - https://nciphub.org/groups/cananolab_usability/
- caNanoLab ListServ
  - CANANOLAB-USERS-L-request@LIST.NIH.GOV

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Office of Cancer Nanotechnology Research

Consultants
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Sima Pandya – Leidos/FNLCR
Michal Lijowski – Essential Software
Mervi Heiskanen – NCI/CBIIT
Juli Klemm – NCI/CBITT

Dorothy Farrell   Nicholas Panaro   Stephanie Morris
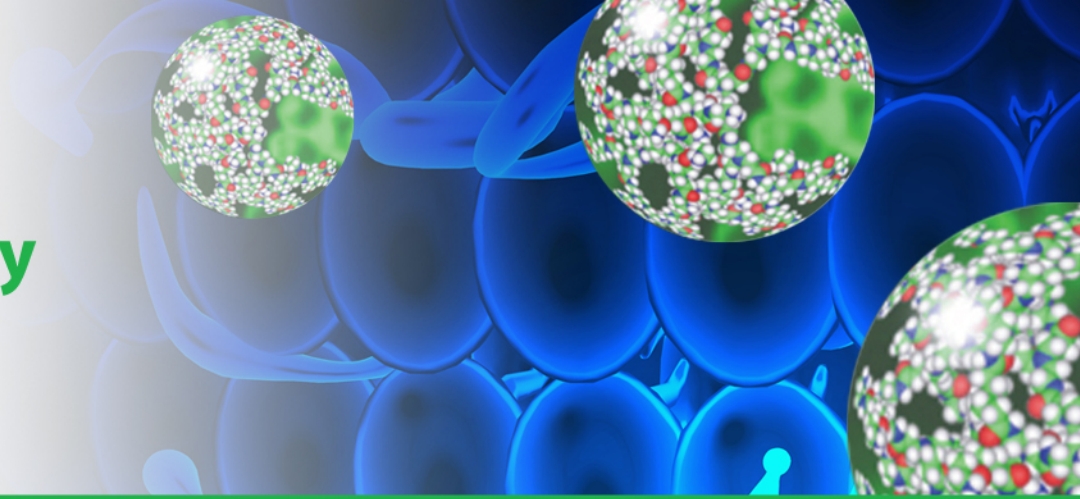
Christopher Hartshorn   Natalie Abrams   Christina Liu

http://www.nano.cancer.gov/
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Questions?

Thank you!

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