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# CANCER NANOTECHNOLOGY PLAN 2015



# Cancer Nanotechnology Plan 2015

Office of Cancer Nanotechnology Research

Center for Strategic Scientific Initiatives

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## Current State of the Field

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Nanotechnology offers the capability to unlock new avenues in the patient specific prevention, early diagnosis, control and treatment of cancer. As such, nanotechnology is expected to offer a significant improvement as compared to the current standard of care in oncology. To capitalize on its potential, the U.S. National Cancer Institute (NCI) in 2004 launched the NCI Alliance for Nanotechnology in Cancer. The Alliance is a large multidisciplinary effort involving researchers and clinicians, who have been working tirelessly in developing new nanotechnological approaches to develop new, and improve upon existing, therapeutic modalities, and similarly for diagnostic and detection techniques. The collective focus has remained on one thing; *a decrease in societal cancer-related morbidity/mortality of multiple tumor types via nanotechnology*. In as much, the Alliance has made very significant progress over the last 10 years producing many scientific discoveries and forming multiple companies, which are commercializing the technologies developed in academia.

Since the beginning of the program, the field of cancer nanotechnology has continually evolved and matured. Recognizing this constant evolution, we publish the *Cancer Nanotechnology Plan (CaNanoPlan)* to acknowledge these changes and to attempt charting the path forward for this dynamic field. The authors of this book include clinicians and researchers from the academic, industrial and government sectors. Of importance to notice, is that the number of covered topics has grown substantially since the last edition of CaNanoPlan published in 2010—this is a direct result of the ever-expanding number of areas in the cancer research space that nanotechnology solutions are being effectively used for. Our hope is to deliver to you, the reader, a *current and future state of the cancer nanotechnology field*, without bias, and, more importantly, to impart the numerous areas in which nanotechnological discoveries will impact the future of medical approaches to cancer care.

## **Nanomedicines: Are they a platform for drug delivery common to many cancer types or a new approach to design drugs for specific tumor types?**

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Simply stated, nanomedicines are both. The NCI Alliance for Nanotechnology in Cancer is now entering the third phase of its existence (Phase I and II funding from 2005-2010 and 2011-2015, respectively), and it is an appropriate time to assess where nanomedicines have been and where they are going. Nanomedicine is the medical application of nanotechnology<sup>1</sup> (specifically for cancer see Chow and Ho<sup>2</sup>), so I consider nanomedicines to be nanoparticle-based therapeutics for the treatment of human disease. At this time, the term nanomedicine is used more liberally in that it is employed to categorize nanoparticle-based, therapeutic entities whether or not they are used for the treatment of humans. Petros and DeSimone<sup>3</sup> provide an excellent historical timeline for the development of nanoparticle-based therapeutic entities, while Davis et al.<sup>4</sup> describe how nanoparticle-based, experimental therapeutics distinguish themselves from previous anticancer therapies. Here, I will address the title question by discussing the transition from the “so called” first generation of nanoparticles (Petros and DeSimone, 2008) to the current application of nanoparticle-based, investigational therapeutics for the treatment of cancer.

First generation nanomedicines such as Doxil® (~ 100 nm nanoparticle - liposome encapsulated doxorubicin; approved in 1995) and Abraxane® (albumin-based nanoparticle formulation (~ 120 nm) containing paclitaxel; approved in 2005) are the most referenced nanomedicines that currently are being used to treat cancer patients. These commercial products have provided benefits to patients. For example, Doxil® greatly assists in mitigating the heart damage that can occur with doxorubicin, and Abraxane® does not have the classic hypersensitivity issues due to the cremophor component of paclitaxel formulations. However, these products do have properties that are undesirable. For example, nanoparticle formulations have the potential to create new toxicities that are not observed with the naked drug molecules,

and this phenomenon is observed with Doxil® (causes a form of skin toxicity that is due to the liposomal formulation, while free doxorubicin does not reveal this side effect). Additionally, Doxil® shows changes in pharmacokinetics (PK) upon multiple-cycle dosing in patients<sup>5</sup>. Abraxane® does not function as a true nanoparticle, and should be called a nanoparticle formulation because it dissolves upon administration due to contact with the blood<sup>6</sup>. As such, the control over drug properties, such as release rates, is not possible with these formulations. While Doxil®, Abraxane®<sup>7,8</sup> and other first generation nanomedicines have certain features that modern nanoparticles strive to eliminate or improve upon, these pioneering therapeutics have provided the field of nanomedicines a legitimate starting point. Additionally, they have generated a baseline of human therapeutic data to learn from and for which modern nanomedicines must strive to exceed<sup>9</sup>.

### ***Nanomedicines are evolving platforms for continually improving drug delivery that is common to many cancer types***

Nanomedicines can be used to deliver drugs to many cancer types. As the field of nanomedicine has progressed, due in part do to increased knowledge of nanoparticle synthesis (better homogeneity is important<sup>10</sup>) and nanoparticle properties (though improved measurement techniques and methodologies), better understanding of how nanoparticles behave in animals<sup>11,12</sup> and humans<sup>13,14</sup> is occurring. This information is enabling nanomedicines to evolve to the point of providing increased functionality that improves the delivery of drug molecules to cancer patients. Nanomedicines seek to improve PK properties (enhanced solubility of the drug, tunable circulation times, tunable release of the drug, even at the site of active in the tumor) and alter biodistribution; in order to have low amounts of drug in non-target tissues and increased drug in tumors for greatly diminished side effect profiles (and most importantly, no new side effects due to the nanoparticle) in patients. These properties can: (i) enable drug combinations formerly inhibited by toxicity limits, (ii) enable new classes of drug delivery (for example, siRNA), and (iii) provide cell specific targeting within a tumor (all illustrated below).

Liposomal formulations such as those used with products like Doxil® have been improved upon, and now can provide new types of nanomedicines. For example, CPX-351 (Celator Pharmaceuticals) is a liposomal formulation of cytarabine and daunorubin in a 5:1 ratio for the treatment of high-risk AML patients. In

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**...CRLX101 has  
now been shown in  
clinical trials to be  
combinable with  
other drugs as well  
as radiation therapy.**

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this case, the liposome acts to maintain the two drugs in a ratio that creates a synergistic efficacy of the target cancer. This product showed enhanced efficacy in Phase II clinical trials, and is currently being tested in a Phase III trial (NCT01696084). In addition to delivering drug molecules, lipid-based nanoparticles are now used to deliver small interfering RNA (siRNA)<sup>15,16</sup> and

other nucleic acids<sup>17</sup>. Tabernero et al.<sup>15</sup> have published the first-in-human clinical results for simultaneously delivering siRNAs against two different gene targets to cancer patients.

Polymer containing nanoparticles are also being developed as nanomedicines for cancer, and they are showing new and interesting behaviors in animal studies and human clinical trials. For example, Schluep et al.<sup>18</sup> showed that a polymeric nanoparticle containing the tubulysin peptide can be an effective antitumor agent while the tubulysin alone is so toxic that there is no therapeutic window for it, even in mice. These types of data show how nanomedicines can

open new opportunities with compounds that are not viable on their own (due to toxicity and/or other issues). Polymeric nanoparticles have also been used to deliver siRNA, and in fact, were the first example of siRNA delivery to cancer patients<sup>19</sup>. Additionally, there are situations where the therapeutic agent need not be delivered to the cancer cells, but rather to other cell types within the tumor (like macrophages or stromal tissue). Ortega et al. recently showed how a polymeric nanoparticle could deliver siRNA to tumor-associated macrophages<sup>20</sup>.

Polymer containing nanoparticles are progressing in clinical studies. Examples of this type of nanomedicine are the polymeric micelles Genexol-PM (approved in South Korea) and NK105<sup>21</sup>, and the homogeneous polymeric nanoparticles CRLX101<sup>13</sup> and BIND-014<sup>22</sup>. NK105 is currently in Phase III clinical testing (NCT01644890), and both of the polymeric nanoparticles are currently in Phase II clinical studies. Of importance to the field of nanomedicine, CRLX101 has now been shown in clinical trials to be combinable with other drugs as well as radiation therapy. This is an important point, as nanomedicines should produce an efficacious therapy with low side effects that they can be used in typical combination therapy regimens. As it is well understood, that combinations of therapeutic agents are ultimately the desired goal in treating cancer patients, in order to provide efficacy and suppress resistance mechanisms from emerging. Pham et al.<sup>23</sup> recently described how CRLX101 (containing the drug molecule, camptothecin) could be used in combination with bevacizumab in ovarian

(both animal and human results) and kidney (human results) tumors. In refractory, metastatic renal cell carcinoma, the combination therapy significantly outperformed a monotherapy of bevacizumab or topotecan (FDA approved analog of camptothecin). A key point is that in the human clinical trials, the doses of CRLX101 or bevacizumab when used in combination did not have to be lowered from the amounts administered when they are used as monotherapies.

Overall, current investigational nanomedicines are showing interesting behavior in animal and human studies. They are providing new properties that have not previously been available (for example, CRLX101 can provide durable inhibition of HIF-1alpha that can be used in combination with anti-angiogenesis therapeutics<sup>23</sup>), and are enabling new types of therapeutic entities like siRNA.

### ***Nanomedicines are a new approach to design drugs for specific tumor types***

In essence, nanomedicines are small chemical systems, so they can consist of several components that are designed to provide multiple functions, such as the targeting of specific tumor types. A clear example of this approach is in the delivery of siRNA. Since siRNA can be used to inhibit essentially any gene, and multiple targets can be simultaneously inhibited, specific tumor types can be targeted and treated using this approach. Recently, Yuan et al. showed that four different siRNAs could be delivered to tumor xenografts using a nanoparticle delivery system<sup>24</sup>. Additionally, improved therapeutic efficacy was observed when simultaneously delivering siRNAs against KRAS and PIK3CA/B. This study nicely demonstrates the power of siRNA therapeutics for cancer by showing that multiple gene targets can be simultaneously inhibited (without increased toxicity like would be the case with combining other therapeutic molecules) to produce greater anti-tumor efficacy. This is the goal for the clinical application of siRNA treatments of cancer, and if achievable, could be a “game changing” way to treat cancer. Information from three finished Phase I trials with siRNA are available to guide future studies<sup>14–16,19</sup>. At this time, all of the clinical trials that have employed siRNA do not attack a specific tumor type. However, it is expected that this approach will be used to treat cancer patients with specific cancer types in the near future.

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**...four different siRNAs could be delivered to tumor xenografts using a nanoparticle delivery system.**

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**Within the next 5 years it is most likely that a number of new nanomedicines will become FDA approved.**

Another approach for creating specific tumor targeting nanomedicines involves the inclusion of a so-called “targeting agent” to the nanoparticle to provide for “active targeting”<sup>25</sup>. These targeting agents engage cell surface receptors to not only provide for active targeting, but also to enable a number of other biological functions. CALAA-01 contains the human transferrin protein (Tf) on its surface to engage transferrin receptors (TfR) that are upregulated on the surface of many cancer cell types<sup>26</sup>. The Tf enhances the amount and rate of nanoparticle uptake into the cancer cells. Thus, in this case and others that target the TfR<sup>27</sup>, these nanoparticles are appropriate for treating the limited number of cancer cell types that have upregulated TfR. The targeting agents can have biological functions in addition to providing cancer cell uptake, e.g., antibodies and antibody fragments can block signaling effects. An example of

this type of nanoparticle, that has been tested in a Phase I clinical trial, is a liposome encapsulating doxorubicin and containing the Fab’ fragment of the antibody cetuximab (binds to EGFR)<sup>28</sup>. This nanoparticle is appropriate for treating cancers with overexpressed EGFR. The inclusion of targeting agents adds complexity to the nanoparticles, and the costs versus benefits of these agents have been discussed<sup>29</sup>. However, this type of additional functionality in nanoparticles can clearly be used to create nanoparticles that are designed to treat specific cancer types, e.g., those with upregulated surface proteins like Her2, EGFR, etc. Historically, it has been difficult to achieve functions from the targeting agents. Although recently, investigators have learned how to construct nanoparticles that can have multiple functions, including those of a

targeting agent, where the functions work at the appropriate time and place along the delivery process rather than annihilating each other like in the past<sup>30</sup>.

### ***What does the future hold for cancer nanomedicine?***

Within the next 5 years it is most likely that a number of new nanomedicines will become FDA approved. The cancer nanomedicines that are nearing final clinical testing and approval are those carrying small molecule drugs. Additionally, within this time, there should be the first of several approved siRNA-based nanomedicines. These nanomedicines will not be to treat cancer, but rather for the treatment of liver diseases. However, they will lead the way for siRNA-based nanomedicines to be approved for cancer at a latter time (say within 10 years).

Because of the safety of nanomedicines, once they are approved, it is expected that they will be combined with numerous other therapeutics (including new immunotherapeutics) to provide more individualized and potent therapies to cancer patients. Thus, nanomedicines will be utilized in combination therapies to treat a broad spectrum of cancer types AND to treat specific tumor types, where the mode of deployment of the nanomedicine will depend only upon their specific designs and chemical configuration.

## Mission of the NCI Alliance for Nanotechnology in Cancer Program

Nanotechnology is the application of materials, functionalized structures, devices, or systems at the atomic, molecular, or macromolecular scales. At these length scales, approximately the *1-100 nanometer range* as defined by the [U.S. National Nanotechnology Initiative](#) (NNI), unique and specific physical properties of matter exist, which can be readily manipulated for a desired application or effect. Furthermore, nanoscale structures can be used as individual entities or integrated into larger material components, systems, and architectures. Nanotechnology-based structures and devices are already enabling a large number of novel applications in various fields – including medicine.

Currently, scientists are limited in their ability to turn promising molecular discoveries into cancer patient benefits. Nanotechnology can provide technical control and tools to enable the development of new diagnostics, therapeutics, and preventions that keep pace with today's explosion in knowledge.

The [Office of Cancer Nanotechnology Research](#) (OCNR) within the [Center for](#)



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[Strategic Scientific Initiatives](#) (CSSI) at the [National Cancer Institute](#) (NCI) of the [National Institutes of Health](#) (NIH), develops and implements programs with and for the extramural research community related to the use of nanotechnology in medicine and cancer. The overarching goal of these initiatives is to discover and develop innovative nanotechnologies for application(s), ranging from discovery through to clinical translation phases, for the delivery of innovative clinically relevant technologies aimed at cancer prevention, diagnosis, control, and treatment. These initiatives include a programmatic effort known, collectively, as the [NCI Alliance for Nanotechnology in Cancer](#), which aligns to several key areas of the National Cancer Institute's existing priority areas as displayed in **Figure 1**.

The OCNR's *NCI Alliance for Nanotechnology in Cancer* was designed to develop research capabilities for multidisciplinary team research, with the goal of advancing basic science, prevention, diagnostic, and/or treatment efforts from the research discovery to preclinical and early clinical development stages. The Alliance's development model calls for the most promising strategies discovered

and developed by its grantees to be handed off to potential for-profit partners for effective clinical translation and commercial development. Furthermore, to expedite translation into the clinical setting, it calls for the technologies to be characterized by the Nanotechnology Characterization Laboratory (NCL) in Frederick, MD.

The *Alliance for Nanotechnology in Cancer* is engaged in efforts to harness the power of nanotechnology to radically change the way we diagnose, treat and prevent cancer. As such, the *NCI Alliance for Nanotechnology in Cancer* is a comprehensive, systematized and multidisciplinary initiative encompassing the public and private sectors, designed to accelerate the application of the best capabilities of nanotechnological developments into the realm of contemporary oncology<sup>31</sup>.

## Purpose of Cancer Nanotechnology Plan 2015

The primary purpose of the *Cancer Nanotechnology Plan 2015* is to serve as a strategic document to the *NCI Alliance for Nanotechnology in Cancer* as well as a guiding document to the cancer nanotechnology and oncology fields, as a whole. Now in its third incarnation, this **CaNanoPlan 2015** has increased in scope, mostly, due to the fact that the field has significantly matured and expanded over the last decade. It includes contributions from researchers, clinicians, policy makers, and industrial experts in order to give a broad perspective on where the field is now and where it is heading in the future.



**Figure 1.** Graphical depiction of NCI Alliance for Nanotechnology in Cancer research areas (colored only) relative to the overall NCI priority areas.

# CURRENT STATE OF THE PROGRAM

In its first round (*Phase I, 2005-2010*), the Alliance focused on translational research (e.g., clinically worthy technologies) and developmental efforts to set the framework for the future. During this period, the program focused on multifunctional therapeutics, *in vivo* molecular imaging (imaging systems and contrast agents), and reporters of efficacy as well as on the areas of early detection, prevention, and control. The research covered a broad spectrum of cancer-specific targets<sup>32</sup>. The awards made during this period included, **eight** U54 (formally called **Centers of Cancer Nanotechnology Excellence** or **CCNE**) and **twelve** R01 (formally called **Cancer Nanotechnology Platform Partnerships** or **CNPP**) grants. The Alliance was overseen by the Coordination and Governance Committee (CGC), which consisted of its principle investigators and the National Cancer Institute program staff. Near the conclusion of the first round, strategies were re-assessed from lessons learned by the NCI, CGC, and the extramural communities to determine the best path forward for the next round<sup>33,34</sup>.

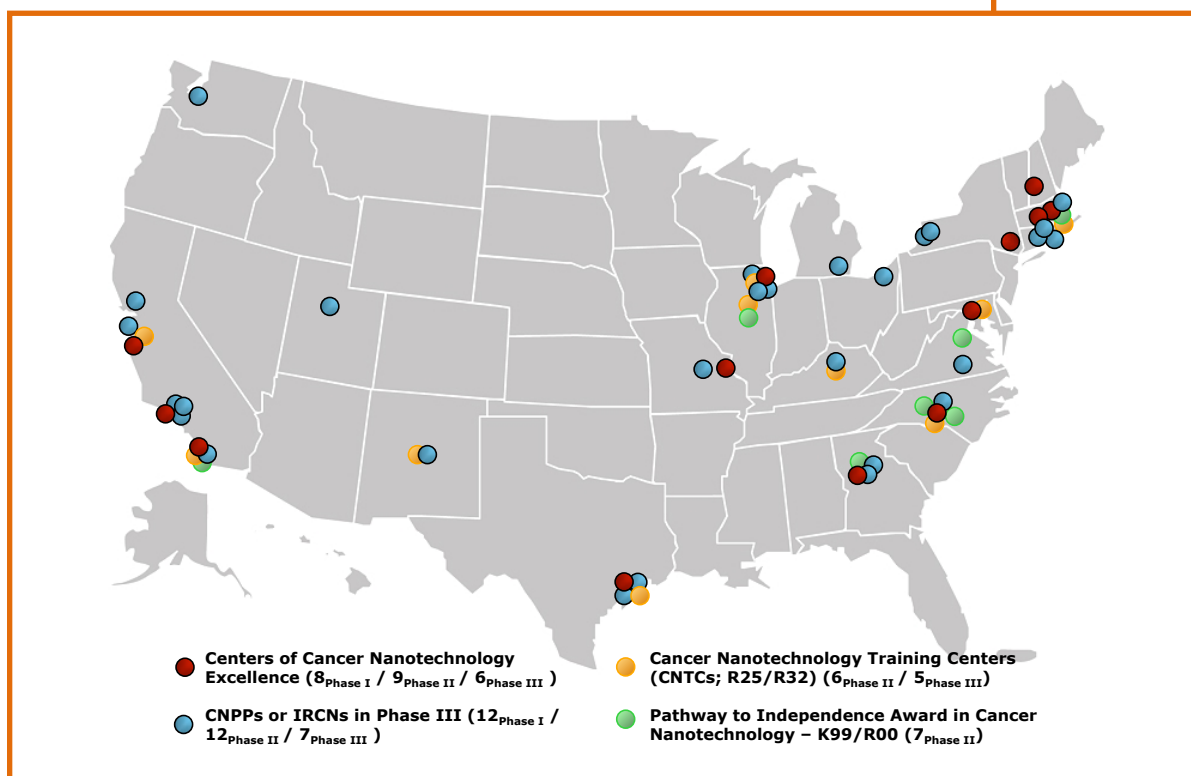


In its second round (*Phase II, 2010-2015*), the Alliance re-balanced itself while maintaining translational research for its CCNEs with more basic research for its CNPPs. Also, the training and developmental efforts to proliferate the preparation of the next generation of multidisciplinary researchers in the field of cancer nanotechnology were expanded. This training component was viewed as an increasingly critical element to developing the multi- and trans-disciplinary scientists necessary to the future implementation of nano-enabled interventions in the practice of

clinical oncology. In an attempt to emphasize cancers with the poorest survival rates and explore successful use of nanotechnology in therapies and diagnostics for them, Phase II of the program focused on brain, lung, pancreatic, and ovarian cancers. The awards made during this period included, **nine** U54 (**CCNEs**), **twelve**

U01 (CNPPs), **six** R25 (formally called **Cancer Nanotechnology Training Center** or **CNTC**), and **seven** K99/R00 *Pathway to Independence Award* grants. Nearing the expiration of this second phase in 2013, again a reevaluation was performed in order to formulate a path forward for the program, guided by similar principles as before<sup>35,36</sup>.

To date, the communal output from the Alliance members has been substantial. Beginning with the output of robust science, the Alliance has published over 2,750 peer-reviewed journal articles that have been collectively cited over 83,500 times across the scientific literature spectrum generating an average impact factor of 7.7. From the perspective of clinical translation, the Alliance researchers have filed over 220 patents/disclosures, filed many applications to the FDA with over 18 clinical trials approved, and formed over 85 companies that have collectively commercialized multiple products. This collective



**Figure 2.** Map of United States as a geographical depiction of the locations of the NCI funded institutions (past and present, all represented) within the Alliance as of Fall 2015. CCNEs (red dots), CNPPs/IRCNs (blue dots), CNTCs (orange dots) and Pathway to Independence (green dots) all displayed circa their actual location in U.S.

output has come by way of NCI funding of over 1250 individual researchers and trainees. All of these statistics are direct results from work completed on Alliance-specific funded projects during only the 10-year period of the first two phases and are compiled in the **Infographic**.

Presently, the *NCI Alliance for Nanotechnology in Cancer* program is beginning its third round (i.e., Phase III), which began Fall 2015. The academic institutions that have been awarded grants during all three rounds to date are displayed, geographically, on the map in **Figure 2**. Although, this third round is similar overall to the previous, there are still several key differences. In this third phase, **six** U54 (CCNEs) have been awarded and the U01 granting mechanism has been altered from an RFA to a PAR for recurrent acceptance of applications including two application receipt dates per year through 2017. U01 grants are now formally termed [Innovative Research in Cancer Nanotechnology](#) (IRCNs) under this FOA, which reflects a shift in program focus towards addressing major barriers in cancer biology and/or oncology using nanotechnology and with an emphasis on fundamental understanding of nanomaterial interactions with biological systems and/or mechanisms of their *in vivo* delivery. CNTCs have also been transitioned to continual submission and are now funded via a [T32 granting mechanism](#) albeit through recurrent receipt dates. Although, the focus on training the next generation cancer nanotechnology experts has remained effectively unchanged. As of Fall 2015, **seven** U01 (IRCN) and **five** (CNTC) awards have been funded, although it is anticipated that more could be made over the course of next several years as more applications come in for the upcoming submission dates.

## Nanotechnology Characterization Laboratory



In an effort to help advance the clinical translation of novel nanomedicines designed to improve therapeutic outcomes and enhance diagnostic capabilities, the National Cancer Institute, in concert with the [Food and Drug Administration](#) (FDA) and the [National Institute of Standards and Technology](#) (NIST), created the [Nanotechnology Characterization Laboratory](#) (NCL). The NCL has been pursuing preclinical characterization and development of these oncology-directed therapies and diagnostics for more than ten years now. In this time, NCL's multi-disciplinary team has worked with more than 100 of the world's foremost nanotechnology research organizations and evaluated

more than 300 different nanomaterials. Nearly a dozen NCL collaborators are now in human clinical trials with novel treatment strategies afforded through nanotechnology. NCL's unique setup has afforded an extraordinary opportunity to explore the biocompatibility trends and advantages and disadvantages of a vast array of nanoplateforms, cytotoxics, and targeting strategies in a relatively limited time span. Through sustained research and extensive educational outreach, the NCL strives to continually improve the pursuit of these much needed therapies, speeding their progression to clinical trials.

## caNanoLab



The [cancer Nanotechnology Laboratory](#) (caNanoLab) is a web-based portal and data repository that allows researchers to submit and retrieve information on

well-characterized nanomaterials including their composition, function, physical properties, and *in vitro* / *in vivo* experimental characterizations. Furthermore, information on the protocols used for these characterizations and links to any related publications may be similarly accessed. Initiated in 2006 by the National Cancer Institute as a collaborative effort between the NCI Center for Biomedical Informatics and Information Technology (CBIIT) and the NCI OCNr, caNanoLab serves as an established resource with an infrastructure supporting the structured collection of nanotechnology data to address the needs of the cancer biomedical and nanotechnology communities. While the majority of caNanoLab data has been entered through an in-house curator, individual users can submit data via web-based forms and an established, simple workflow. Submitters can customize the visibility of their data which ranges from private, sharable within a collaboration group, to open for public consumption. caNanoLab can also be used for discovery purposes by searching the results of all the publicly available data, protocols, and information about publications using webform-based queries. These results can be downloaded in spreadsheet-based reports for re-use and additional analyses. caNanoLab software is open source and available for download for local installation. Currently, the NCI instance of caNanoLab has information on 1,090 curated nanomaterial samples, 46 protocols, and 1,901 publications. Users are primarily from the U.S., but have grown to include users from several other countries such as Great Britain, Germany, China, the Netherlands, Spain, and Japan. In 2014, the number of unique portal visitors numbered over 3,000.



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## TONIC Consortium

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The Alliance for Nanotechnology in Cancer established the [Translation Of Nanotechnology In Cancer](#) (TONIC) consortium in October 2011 to bring together public, private, and academic sectors interested in nanomedicine drug development, with the mission of accelerating the translation and development of nanotechnology solutions for the early detection, diagnosis, and treatment of cancer. TONIC members organized to combine their expertise to identify and evaluate the most promising technology candidates to develop a robust translational roadmap for the development of nanotechnology-based cancer products. The main goals of this partnership model include providing Alliance researchers insight into industry needs in technology platforms and drug targets, promoting collaborations between Alliance investigators and industry partners on promising pre-competitive and late-stage programs, and serving as a sustained forum for nanotechnology idea exchange. The partnership further provides TONIC members the opportunity to interact with regulatory authorities and the Nanotechnology Characterization Laboratory to promote the qualification, development, and regulatory acceptance of nanotechnologies in cancer. TONIC also encourages the sharing of consortium project results with the scientific community and independent verification opportunities to ensure data reproducibility and robustness.

Membership to the TONIC consortium remains free of charge, and for companies is limited to those that (1) have a successful track record of translating diagnostics and drug formulations and reaching their regulatory approval and, (2) are engaged in the development of nanotechnology-based formulations with application to imaging, diagnostics and therapy. In addition, these companies are expected to have a corporate structure with centralized operations and the capability and resources to effectively move along translational efforts. Currently, membership includes 14 corporate partners, and three patient advocacy groups, with participation by NCL and the FDA.

TONIC has organized several meetings and presentations at various venues over the past three years to educate Pharma and enhance awareness of nanotechnology platform opportunities in developing cancer solutions. It continues to participate in the annual Alliance principal investigators' meetings to promote networking and collaborations between industry and academic groups, and encourages the evaluation of external opportunities and platforms. The consortium has been credited with facilitating interactions

with NCL for TEVA and Astra Zeneca, two TONIC members. TEVA and NCL signed an agreement to initiate a collaborative study. Cytimmune credits TONIC for facilitating a research agreement with AstraZeneca to create a new nanomedicine using an AstraZeneca proprietary drug mounted on Cytimmune's PEGylated TNF gold nanoparticle platform. Moving forward, TONIC continues to take advantage of new opportunities to accelerate the consortium's mission of translating nanotechnologies to the clinic, and enhance academic-industrial partnerships.

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