NCL
Nanotechnology
Characterization
Laboratory

Annual Report 2024

Nanotechnology Characterization Laboratory
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Celebrating 20 Years

> On behalf of the entire lab, we would like to extend a heartfelt thank you to all NCL's collaborators, former team members, and colleagues who helped shape the lab into the powerhouse it is today. Your contributions, nanoparticle submissions, insightful discussions, and demand for a deeper understanding of nanoparticle properties and characteristics have, and continue, to make a difference in the field of cancer.
>
> **Marina A. Dobrovolskaia & Stephan T. Stern**
> Laboratory Co-Directors

NCL MARKS 20 YEARS

In 2024, the NCL observed the 20th anniversary of the lab's founding. To mark the momentous occasion, the Frederick National Laboratory for Cancer Research (FNL) hosted a symposium featuring a full day of presentations from some of world's leading nanomedicine developers, a poster session, a vendor show, laboratory tours, and an evening reception with networking opportunities.

"***Advancing Medical Applications of Cancer Nanotechnology: Celebrating Two Successful Decades of the NCI's Nanotechnology Characterization Laboratory Service to the Research Community***," kicked off with opening remarks from NCI's Dr. Piotr Grodzinski, FNL's Drs. Dwight Nissley and Leonard Freeman, and NCL's co-directors, Drs. Marina Dobrovolskaia and Stephan Stern. This was followed up with three impactful keynote presentations from Dr. Branden Brough, Director of the National Nanotechnology Coordination Office, describing national priorities for the field, Dr. Mauro Ferrari, Professor at the University of Washington, offering his perspective on the interdisciplinary nature of nanomedicine, and Dr. Pieter Cullis, Professor at the University of British Columbia, presenting the evolution of lipid nanoparticles and their impact on the future of nanomedicine.

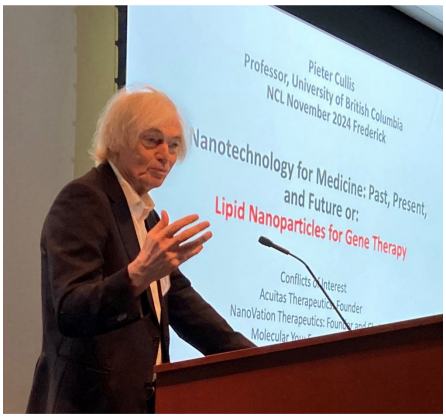
Participants next heard from current and former NCL collaborators describe the novel developments they've made in cancer nanomedicine research. Dr. Yechezkel Barenholz, Hebrew University of Jerusalem, talked about Doxil and the evolution of liposome technology. Dr. Matthieu Germain, Nanobiotix, described the company's Nanoprimer technology, a non-drug loaded liposome intended to boost the efficacy of nanomedicine formulations. Dr. Nicole Steinmetz, University of California San Diego, presented a novel plant virus technology being developed as an immunotherapy against cancer. Dr. Neil Desai, Aanastra, Inc., talked about his work developing albumin-based formulations such as Abraxane and Fyarro. Dr. Len Pagliaro, Sona Nanotech, detailed his company's work developing gold nanorods for targeted hyperthermia treatment of tumors. And, finally, Dr. Glen Kwon, University of Wisconsin, described his group's development of a novel polymeric paclitaxel formulation and the manufacturing advances made to eliminate harmful organic solvents.

Several dozen posters were also on display. Labs from NCI presented posters describing a CRISPR-Cas9 lipid nanoparticle formulation, as well as a stealth lipid nanoparticle for higher payload incorporation. Dr. Jeff Bulte's team at Johns Hopkins University showcased albumin, bismuth sulfide, and superparamagnetic iron oxide nanoparticles being developed as a theranostic. Dr. Jill Smith, physician-scientist from Georgetown University, presented work on a biodegradable polyplex formulation able to detect and treat early precancerous pancreatic intraepithelial neoplasia (PanIN) lesions. Dozens of other posters highlighted a breadth of formulations and technologies being developed to further advance nanomedicine for the prevention, detection, and treatment of cancer.

Vendors from various organizations were also on-site to showcase their latest technologies. Anatom Technology, representing Horiba and MicroFluidics, offered information on the latest microfluidic technologies for formulation development. Associates of Cape Cod, Inc. representatives were available to describe solutions for endotoxin testing. SPARTA Biodiscovery provided an introduction to new technology they are developing for single particle analysis using Raman spectroscopy. Other participating vendors included Aldevron, Beckman Coulter, GenScript, STEMCELL Technologies, Waters Corporation, and Fisher Scientific.

Branden Brough, PhD

Mauro Ferrari, PhD



Pieter Cullis, PhD

EVOLUTION OF CANCER NANOTECHNOLOGY RESEARCH

Twenty years of collaborations with cancer nanotechnology researchers around the globe has allowed the NCL to witness the evolution of the field—the shift in prevalence of various nanoparticle platforms, the adoption of immunotherapies and nucleic acid cargos from traditional cytotoxic treatments, and the broadening of cancer indications being studied.

Cancer Indications

In the early years, researchers primarily focused on a handful of cancer indications, with breast, ovarian, brain, and pancreatic comprising over 70% of all concepts seen. The remaining studied lung, prostate, cervical, and skin cancers. Not surprising, this coincided with the most prevalent cancers—breast, prostate, and lung—as well as some of the most difficult to detect and treat cancers—ovarian, pancreatic, brain (glioma), and skin (melanoma).

As the field continued to grow, so did the expansion into other cancer indications, brain, breast, lung, ovarian, and pancreatic cancers continued to be among the most studied, but many others began to receive attention as well. Rare cancers such as perivascular epithelioid cell tumor (PEComa)—estimated to affect fewer than 300 people in the US annually—saw the market approval of its first treatment option in 2021, Fyarro, a nab-sirolimus formulation. Personalized treatments saw expanded exploration in the preclinical space. Researchers also began to focus specifically on treating metastases (e.g., brain metastases from breast cancer, intraperitoneal metastases from ovarian cancer). Metastatic lesions are the primary cause of most cancer-related deaths, but current therapies are largely designed to treat the primary tumor. If researchers can successfully develop therapies to specifically target metastases, this could provide an enormous survival benefit for thousands of patients.

Nanoparticle Platforms

The first FDA-approved nanomedicine was Doxil, a PEGylated liposome encapsulating doxorubicin, approved in 1995. Today, liposomes are still a dominate technology in both the commercial and preclinical spaces and are used in both oncology and non-oncology fields. Metal-based formulations were also early players in nanomedicine due in large part to the imaging capabilities of metals such as iron oxide and gadolinium. Together, liposomes and metal/metal oxide formulations comprised nearly 50% of the platforms submitted to the NCL in the first years.

As technologies for nanomaterial characterization have advanced, so have the formulations. Liposomes and metal-based formulations comprised <20% of NCL submissions in the last five years. More prominent have become polymeric-based formulations, including the use of prodrug formulations designed to provide drug release at the tumor site for an improved therapeutic efficacy. A variety of other technologies are also being explored including hydrogel formulations designed to provide sustained release at the implant site, exosomes, therapeutic nucleic acids, and lipid nanoparticle and polyplex formulations for improved delivery of nucleic acid cargo.

Therapeutic APIs

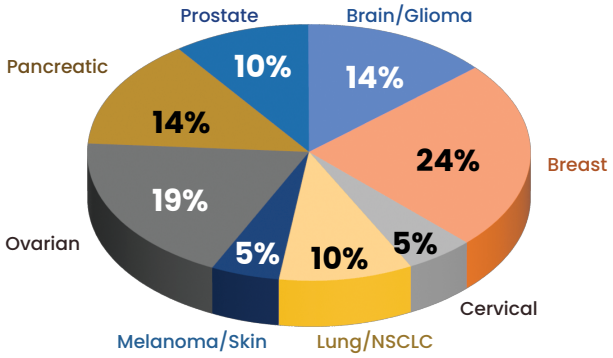
Chemotherapy has been a mainstay treatment option for cancer for decades, using cytotoxic agents such as doxorubicin, paclitaxel, docetaxel, and cisplatin, among others. Liposome technology afforded an alternative to traditional doxorubicin treatment with Doxil, which decreased the dose-limiting cardiotoxicity of the drug. Later, a nanoalbumin formulation of paclitaxel (Abraxane) provided an alternative to Taxol treatment which reduced anaphylactoid hypersensitivity reactions, also known as complement activation related pseudoallergy (CARPA) syndrome. Liposomes have also been used for formulations of irinotecan (Onivyde) and the combination of daunorubicin and cytarabine (Vyxeos). Similarly, many early nanotechnology submissions to the NCL program focused on developing nanotechnology solutions to improve existing chemotherapies.

Immunotherapies, vaccines, personalized medicines, and improved technologies for delivering nucleic acids have broadened the landscape of therapeutic cargo. A broad range of antibodies, proteins, and peptides are being used to trigger immune responses to help fight cancer, often in combination with traditional chemotherapeutic agents in complex, multifunctional nanoparticles. The broad applicability of immunotherapies such as Keytruda (pembrolizumab) have sparked interest in anti-PD-1 and PD-L1 formulations. Similarly, with the approval of the COVID vaccines and lipid nanoparticles, this technology is now being used for a plethora of nucleic acid-based targeted treatments. Small molecule inhibitors, such as proteasome, microtubule, kinase, and TOPK inhibitors have also become a common active pharmaceutical ingredient being explored as alternatives to traditional high-toxicity cytotoxic agents.

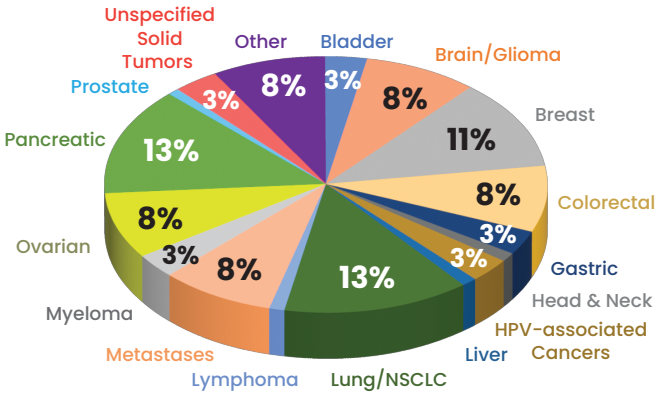
EVOLUTION OF CANCER NANOTECHNOLOGY: CONCEPTS SEEN BY THE NCL

Cancer Indications

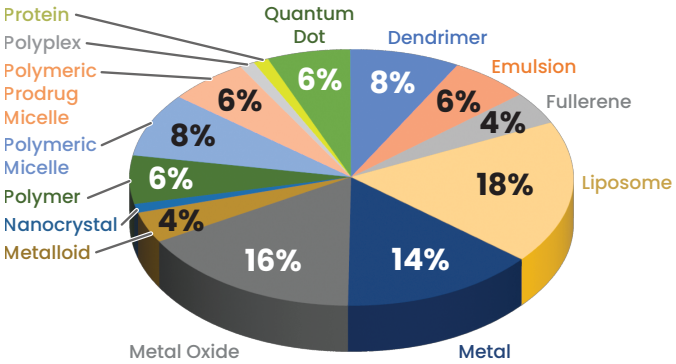
2005–2009

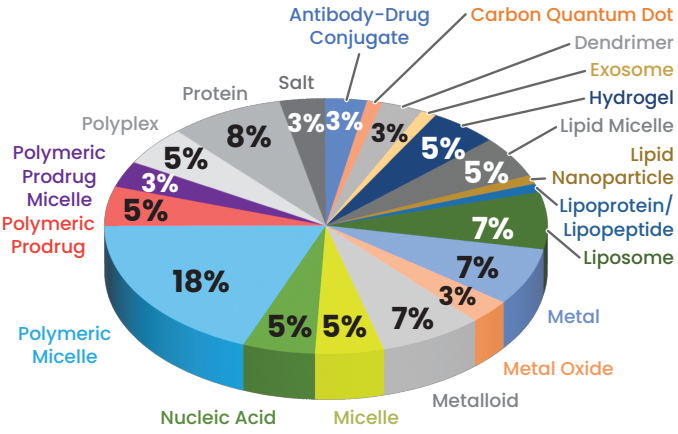


2020–2024

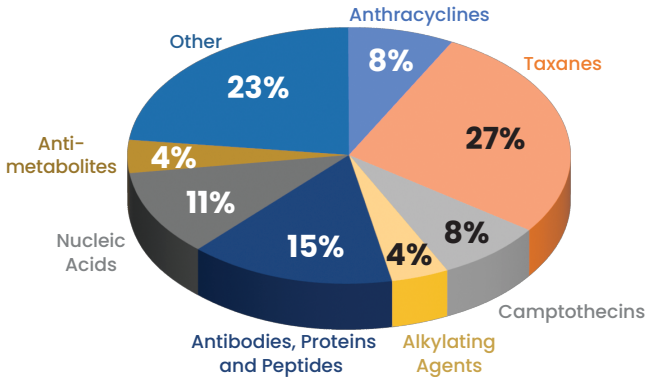


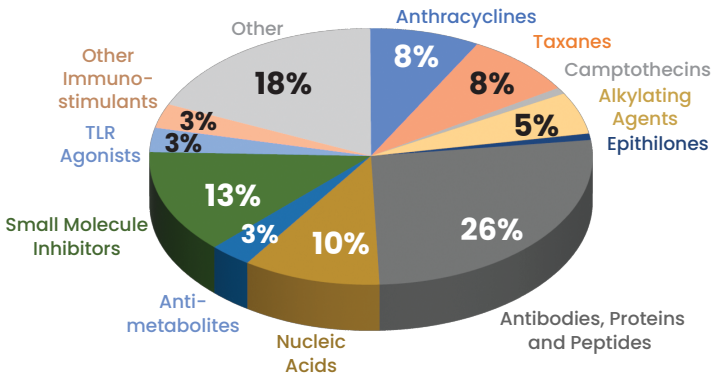
Nanoparticle Platforms





Therapeutic APIs





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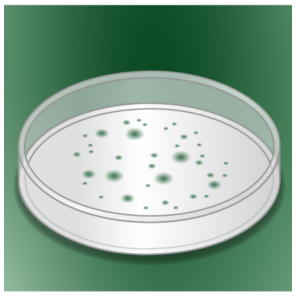
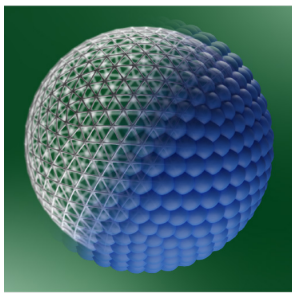
THE ASSAY CASCADE CHARACTERIZATION PROGRAM

The 2024 year saw record- or near-record-highs in metrics across the board, showing the Assay Cascade service is gaining popularity and growing momentum—even after 20 years. Researchers have expressed an increased demand for the unique capabilities and expertise the NCL team has to offer as they continue to push the boundaries of novel nanotech formulation and drug development.



Many laboratories still struggle with sterility aspects of synthesis, such as microbial, endotoxin, and β-glucan contamination, or simply don't understand the importance of these innate immune response modulating impurities and how they can drastically affect data interpretation, especially the influence it can have on the efficacy of immunotherapies. NCL's expertise in understanding the unique intricacies of endotoxin detection, quantification, removal, and inhibition and enhancement often seen with nanoparticles is a highly sought after resource. The NCL has helped countless investigators overcome these challenges and routinely provides hands-on training to researchers in learning appropriate techniques to properly evaluate their nanoformulations.



The vast state-of-the-art instrumentation in NCL's physicochemical characterization section is another sought-after feature of the program. The NCL effectively offers researchers access to the most current techniques and instruments on the market, providing them a wealth of information on their concepts. With the limitations in resources that many academic and start-up companies face, the breadth of data generated within NCL's physicochemical characterization section can significantly speed the development and optimization process.

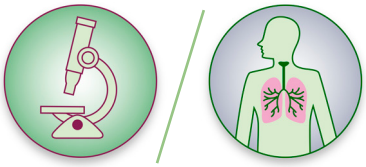
Immunotoxicity is one of the leading causes of failure for drug candidates in clinical trials. Helping to identify and mitigate these toxicities can save years of research and millions of dollars, potentially salvaging the concept with appropriate corrective actions. NCL's immunology program has developed dozens of in vitro and in vivo immunotoxicity assays to assist in this regard. Moreover, all in vitro assays are conducted in a human matrix to as closely mimic what might occur in the clinic. And with the experience gained from more than five hundred concepts that have gone through the Assay Cascade, NCL can help to identify the most likely toxicities a formulation might induce based on the composition and physicochemical properties.

Understanding the pharmacokinetics and toxicology of complex formulations and developing suitable bioanalytical techniques can be a significant hurdle for many. NCL has designed, conducted, and analyzed hundreds of animal studies, cementing the program among the top providers in nanomedicine pharmacology and toxicology. NCL's in vivo program is one of the lab's most requested resources, focusing on pharmacokinetic studies, such as bioequivalence, bioavailability and biodistribution, but also including toxicity and efficacy studies, as well as array of imaging techniques. The ability to provide investigators in depth in vivo characterization data can propel research, oftentimes being used directly in IND filings, as well as to support grant and venture capital proposals to fund necessary regulatory GMP/GLP studies.

2024: A Year of Highs

Active Projects	Unique Nanoparticle Submissions	Total Nanoparticle Batches Characterized	Assay Cascade Reports
50	**43**	**77**	**26**
Yearly Average: 20	*Yearly Average: 29*	*Yearly Average: 61*	*Yearly Average: 8*

APPLICATIONS SUPPORT LEAD FORMULATION CHARACTERIZATION, SAR STUDIES, TECHNOLOGY ADVANCEMENT AND METHOD DEVELOPMENT



With the expansion of the Assay Cascade program in 2023, the NCL sought to offer expertise, characterization, and capabilities to an even broader group. By offering limited scope studies for earlier stage concepts, the NCL hopes to provide researchers with answers that can help them more quickly and efficiently optimize their cancer nanomedicine concepts.

In this short time, the new application types have become quite popular, comprising over 30% of the total applications received for the program in 2024. Because these are limited-scope projects, the NCL can stretch resources to support more of these earlier concepts, as evidenced by the very high acceptance rate—50% for 2024.

Researchers are encouraged to utilize the data from these studies to complete optimization and efficacy testing of the formulations, after which they can re-apply to the NCL's Assay Cascade program for full characterization of their lead nanomedicine concept.

Two Application Options

Lead Cancer Nanomedicine Characterization

Objective: To provide characterization of a candidate cancer nanomedicine formulation, whereby the lead formulation for translation has been selected and pre-tested. The most appropriate assays from NCL's Assay Cascade are selected to further inform the translational development, customized for each concept.

Cost for the Service: $0; available by application only

Application Deadlines:

March 3, 2025
September 2, 2025

Application & Evaluation Criteria

https://www.cancer.gov/nano/research/ncl/assay-cascade/application-process#characteristics-of-proposed-therapeutic-vaccine-and-diagnostic-concepts-to-be-addressed-in-your-white-paper-submission

Structure-Activity Relationship Studies · Technology Advancement · Method Development

Objective: To aid in the down-selection of a lead candidate by providing a limited structure-activity relationship study; to further inform the technology development by providing limited scope analyses; to provide support in the development of analytical/bioanalytical assays for formulations with unique requirements.

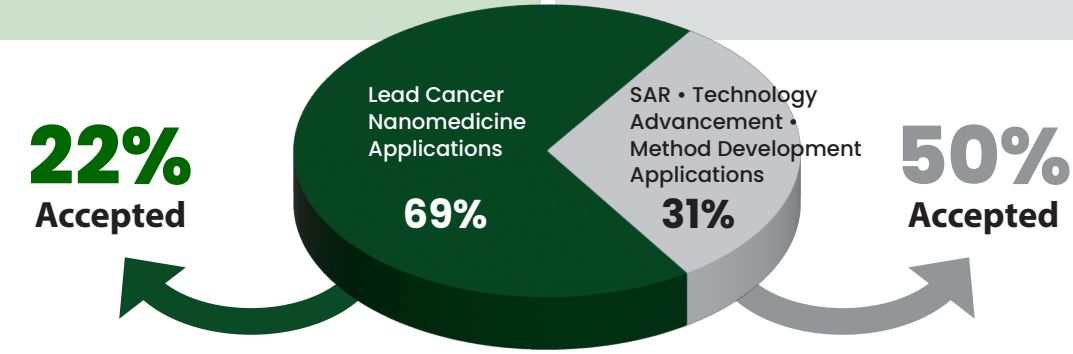
Cost for the Service: $0; available by application only

Application Deadlines:

March 3, 2025
September 2, 2025

Application & Evaluation Criteria

https://www.cancer.gov/nano/research/ncl/assay-cascade/application-process#characteristics-of-proposed-sar-studies-technology-advancements-and-method-development-efforts-to-be-addressed-in-white-paper-submission



PUBLICATION OF METHODS

During the first year after launching NCL characterization services to the public, the Assay Cascade—a collection of analytical, in vitro and in vivo protocols comprising physicochemical, immunology, pharmacology and toxicology—contained only about a dozen fully validated protocols. Over the last 20 years, the Assay Cascade has expanded and evolved to nearly 90 protocols and characterization guides.

To ensure the broadest access to these protocols, they are made available to the research community via a variety of platforms. As they are developed and applied, many protocols are published as part of peer-reviewed manuscripts. The complete portfolio of the most current versions of the protocols are maintained on the NCL's website; here, researchers can freely download the step-by-step protocols and detailed characterization guides for adaptation in their own laboratories. Additionally, since 2024, the protocols are featured in the National Library of Medicine's Bookshelf; this collection, cross-referenced in PubMed, also contains downloadable citations for incorporation into various reference manager softwares. The NCL also deposits protocols in NCI's caNanoLab database; this public resource contains both current and (select) previous versions of protocols from NCL and other laboratories, in addition to cancer nanomedicine characterization data and publications.

The collection has also been featured in the Methods in Molecular Biology series published by Springer Publishing Group. In 2024, the third edition of this series was published, Characterization of Nanoparticles Intended for Drug Delivery (third edition), editors J.D. Clogston, R.M. Crist, M.A. Dobrovolskaia, and S.T. Stern. This third edition features 28 chapters, with new and revised protocols in physicochemical characterization (e.g., asymmetric-flow field-flow fractionation, single particle inductively coupled plasma mass spectrometry, ion quantitation in liposomal products using charged aerosol detection, and headspace gas chromatography for quantitation of residual organic solvent impurities), immunology (e.g., intracellular complement activation, autoimmunity, anti-PEG antibodies, delayed-type hypersensitivity reactions, and immunophenotyping), and pharmacology (temperature-dependent drug release and immunohistochemistry to evaluate tissue distribution).

Combined with the first (2011, S.M. McNeil, editor) and second (2018, S.M. McNeil, editor) editions, the series has 75 chapters describing various protocols in addition to overview chapters on the advancements in technology, discussion of characterization challenges, and regulatory considerations. The collection continues to grow in popularity, with roughly 350,000 accesses from the Springer website, and more than 1,000 citations of the individual chapters.

Resources for NCL Protocols

NCL Website

https://www.cancer.gov/nano/research/ncl/protocols-capabilities

National Library of Medicine & PubMed

https://www.ncbi.nlm.nih.gov/books/NBK604273

caNanoLab

https://cananolab.cancer.gov

Methods in Molecular Biology

https://link.springer.com/book/10.1007/978-1-0716-3786-9

COLLABORATIVE PUBLICATIONS FROM ASSAY CASCADE PROJECTS

Data generated from Assay Cascade collaborations can be used by the Principal Investigator/ Company for any purpose. Often, investigators wish to publish these research findings in peer-reviewed journals. At the completion of an Assay Cascade collaboration, the submitting investigator will receive a comprehensive report detailing the methods, results, and data analysis suitable for inclusion in most manuscripts. Depending on the breadth and scope of NCL's contribution to the overall manuscript, NCL staff are often invited as co-authors. Below are two such examples, concepts that completed the NCL's Assay Cascade characterization program, and the PI-initiated collaborative publications that resulted.

The laboratory of Prof. Nicole Steinmetz, University of California San Diego, is developing plant viruses as immunotherapy treatment for cancer, specifically, cowpea mosaic virus (CPMV). During the course of collaboration, the NCL has conducted physicochemical characterization, extensive in vitro immunotoxicity analyses, and an in vivo multi-dose toxicity study. Additionally, the NCL provided extensive training to Prof. Steinmetz's students as part of the FNL's Guest Researcher program.

Results from some of these analyses were recently published in two 2024 manuscripts. The first (A. Simms, et al.) describes extensive stability studies, evaluating the physicochemical properties and in vitro and in vivo activity of the CPMV therapy under a variety of storage conditions, where NCL provided in vitro cytokine analysis of fresh versus aged CPMV samples. The second (A.O. Omole, et al.) more broadly describes the overall properties of the prospective therapy, using NCL physicochemical characterization data such as cryo-electron microscopy and asymmetric-flow field-flow fractionation and in vitro immunotoxicity data such as chemotaxis, phagocytosis, lymphocyte activation, leukocyte procoagulant activity, and hemocompatibility studies.

Cowpea mosaic virus intratumoral immunotherapy maintains stability and efficacy after long-term storage.

A. Simms, Z. Zhao, E. Cedrone, M.A. Dobrovolskaia, N.F. Steinmetz
Bioeng Transl Med. 2024, 9(6), e10693. PMID: 39545091.

Cellular fate of a plant virus immunotherapy candidate.

A.O. Omole, J.F. Affonso de Oliveira, L. Sutorus, S. Karan, Z. Zhao, B.W. Neun, E. Cedrone, J.D. Clogston, J. Xu, M. Sierk, Q. Chen, D. Meerzaman, M.A. Dobrovolskaia, N.F. Steinmetz
Commun Biol. 2024, 7(1), 1382. PMID: 39443610.

Prof. Yechezkel Barenholz, The Hebrew University of Jerusalem, submitted a novel mupirocin liposomal formulation being developed to target tumor microbiota—without altering the gut microbiota—to improve the efficacy of administered chemotherapeutic agents. For this work, NCL conducted a thorough physicochemical characterization, extensive in vitro immunotoxicity studies, and an in vivo pharmacokinetic analysis. During the PK analysis, ex vivo sample processing exaggerated release of mupirocin from the liposome; therefore, a unique method was developed to instead monitor the major metabolite of mupirocin, monic acid A.

Nano-mupirocin as tumor-targeted antibiotic: Physicochemical, immunotoxicological and pharmacokinetic characterization, and effect on gut microbiome.

A. Cern, S.L. Skoczen, K.S. Snapp, A. Hod, D. Zilbersheid, Y. Bavli, T. Alon-Maimon, G. Bachrach, X. Wei, B. Berman, M. Yassour, E. Cedrone, B.W. Neun, M.A. Dobrovolskaia, J.D. Clogston, S.T. Stern, Y. Barenholz
J Control Release. 2024, 373, 713-726. PMID: 39038544.

SUCCESS OF NCL COLLABORATORS' REGULATORY PURSUIT

For each concept that is accepted into the NCL's Assay Cascade characterization program, the team carefully develops an individualized research plan, considering the nanoparticle platform, active pharmaceutical ingredient, excipients in the formulation, cancer indication, expected clinical dose, and intended route of administration. Our previous experience with hundreds of unique technologies helps us to identify key assays that should be considered for testing the physical and chemical properties as well as the safety profile of the formulation.

The ultimate goal of these collaborations is to help developers think about the translational potential of their formulations, whether that is advancing their concept to clinical trials or informing the reformulation of the concept to develop a more promising clinical candidate. While the data can be used for any number of purposes, many use the data to support regulatory filings, often supplementing their filings with NCL's data packages. Additionally, NCL staff often attend regulatory meetings (at the request of the PI/company), e.g., pre-IND or pre-IDE meetings with the FDA, to address questions on any NCL-generated data included in their package.

Most recently, NCL staff attended a regulatory meeting for collaborator Sona Nanotech, for their gold nanorod technology being developed for intratumoral hyperthermia treatment of tumors. NCL first began working with this technology in 2016, when it was originally developed by Siva Therapeutics. NCL provided studies such as sterility, endotoxin, and β-glucan testing; physicochemical analyses such as electron microscopy and compositional analysis to quantitate gold, PEG, and surfactants used in the formulation process; in vitro cytotoxicity and cell uptake studies in several cell lines; in vitro hematocompatibility testing; and in vivo pharmacokinetic and tissue distribution studies including an ICP-MS mass balance of gold in the blood and organs of the animals.

Siva Therapeutics was acquired by Sona Nanotech in 2023 as part of a multi-million-dollar deal. This acquisition helped to spur the further translational development of the formulation wherein they re-engaged the NCL to help confirm properties of the formulation remained unchanged as they improved the manufacturing process. NCL repeated several of the earlier studies on new batches of the material, and the data were incorporated into Sona Nanotech's portfolio for the FDA. In Q1 2024, Sona invited the NCL senior staff to participate in the pre-submission meeting, lending their expertise to discussion of NCL's incorporated datasets.

Sona Nanotech continues to make progress in the development of their novel technology and in addressing regulatory questions with the goal of initiating first-in-human trials in the near future.

Read more about Sona Nanotech's gold nanorod technology in this recent publication:

Targeted intra-tumoral hyperthermia using uniquely biocompatible gold nanorods induces strong immunogenic cell death in two immunogenically 'cold' tumor models. Fonts in Immunol. 2025;15. DOI: 10.3389/fimmu.2024.1512543

NCL Presentation to Regulatory Professionals

In addition to attending regulatory meetings with collaborators, NCL staff also routinely present to regulatory authorities in various internal workshops and meetings. NCL staff share the latest trends and developments seen through Assay Cascade submissions as well as get feedback on the most pressing questions from a regulatory perspective—helping us to better tailor our research to address these concerns.

In 2024, NCL presented the latest findings from the NCL Assay Cascade and common trends observed with the most utilized nanotechnology platforms to the FDA's National Center for Toxicological Research.

If you are interested in having an NCL staff member present to your group, please reach out and let us know which topics are of most interest. NCL can be contacted by email at ncl@mail.nih.gov.

NANOTECH FORMULATION

Though not part of the NCL's free Assay Cascade characterization service, the NCL also provides nanotech formulation services for DCTD-approved projects. Formulation support is also available to the extramural community through Cooperative Research and Development Agreements (CRADA); these projects incur a cost for the initiating party and require approval from NCI's Division of Cancer Treatment and Diagnosis.

The NCL can support several formulation projects each year. Our expertise is centered around polymeric and lipid-based formulations, such as polymeric prodrug development, polyplex formulations, liposomes, and lipid nanoparticles. In addition to the development of the formulation, NCL provides stability and characterization of the newly developed concepts to meet the individual needs of each requestor. Formulations developed at the NCL are also eligible for characterization in the NCL Assay Cascade following the White Paper application process and review, according to the acceptance criteria linked on page 5 of this report.

2024 Highlights

This past year, the NCL's Formulation section collaborated with Helix Biotech to evaluate use of the Nova impinging jet mixer for scaling of nanotechnology formulations optimized by microfluidics. These formulations included liposomes, lipid nanoparticles, and polymeric nanoparticles. We were able to model the device settings and physicochemical properties to allow for comparable attributes between the two instruments. This work will be presented in a joint manuscript currently in preparation.

NCL Formulation also continued collaboration with Dr. Jason Marshall (Scientific Manager, Cancer Immunoprevention Laboratory (CIPL), NCI Vaccine, Immunity and Cancer Directorate) to evaluate peptide polyplex and mRNA lipid nanoparticle (LNP) therapeutic vaccines for KRAS mutant cancers and a novel antigen presenting cell-targeted mRNA-LNP vaccine developed at NCL. As part of this collaboration, NCL trained CIPL staff in mRNA LNP formulation. We also collaborated with Dr. John Tisdale, Principal Investigator, Cellular and Molecular Therapeutics Branch, NHLBI. In this collaboration we trained Dr. Tisdale's group in development of hematopoietic stem cell (HSC)-targeted CRISPR-LNP for treatment of sickle cell disease. These HSC-targeted LNP constructs are currently being evaluated in both in vitro and in vivo models of sickle cell. Some of these findings were recently presented in poster format.

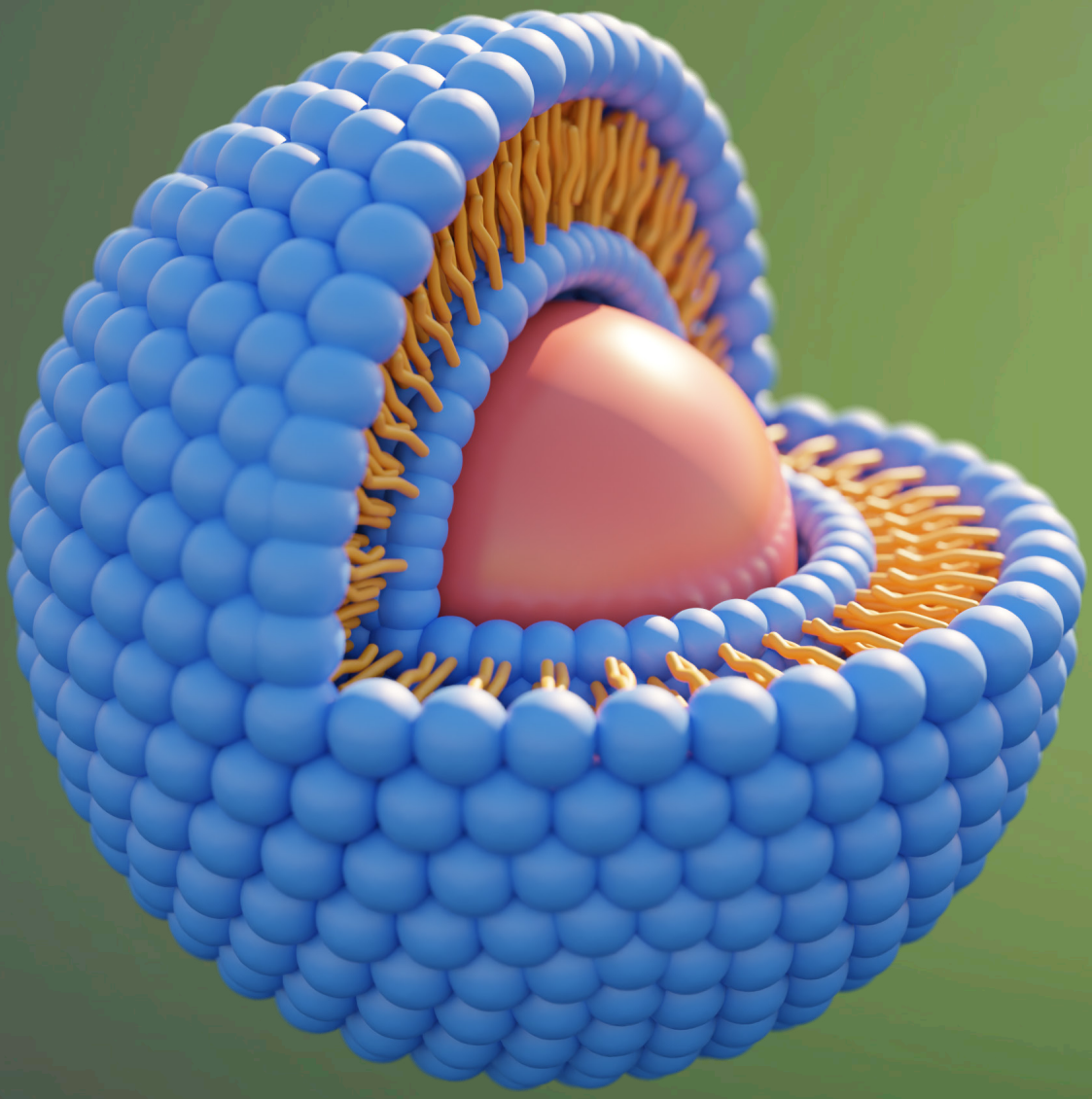
NCL Formulation also continued collaboration with Dr. Jay Berzofsky (Branch Chief, NCI Vaccine Branch), Dr. Terabe (Head of the Basic Immunology Research Program, NCI Neuro-Oncology Branch), and Dr. Jack Hoopes (Professor, Dartmouth Medical School) for development and in vivo characterization of a targeted polymeric glycolipid iNKT adjuvant prodrug for cancer immunotherapy. We are currently in the process of evaluating the glycolipid prodrug in mouse pancreatic, osteosarcoma, and gliobastoma models, as well as actual canine sarcoma and feline mast cell tumor patients. This work is the subject of a national stage patent, as well as several manuscripts submitted and in preparation.

Lastly, NCL Formulation continued collaboration with Dr. Jill Smith (Professor of Medicine, Georgetown School of Medicine) for development of a CCK-B-targeted KrasG12D/gastrin siRNA polyplex delivery system for treatment of pre-cancerous pancreatic intraductal neoplasia (PanIN) and development of a CCK-B-targeted gastrin locked nucleic acid (LNA) gapmer. A joint NIH-Georgetown patent application was submitted for the LNA gapmer technology, as well as a manuscript detailing the work.

Interested in learning more about NCL's formulation capabilities?

Please reach out to us to schedule a discussion, ncl@mail.nih.gov.

Frederick
National Laboratory
for Cancer Research



The NCL is part of the Frederick National Laboratory for Cancer Research (FNLCR). FNLCR is operated by Leidos Biomedical Research, Inc., for the National Cancer Institute, under contract 75N91019D00024.