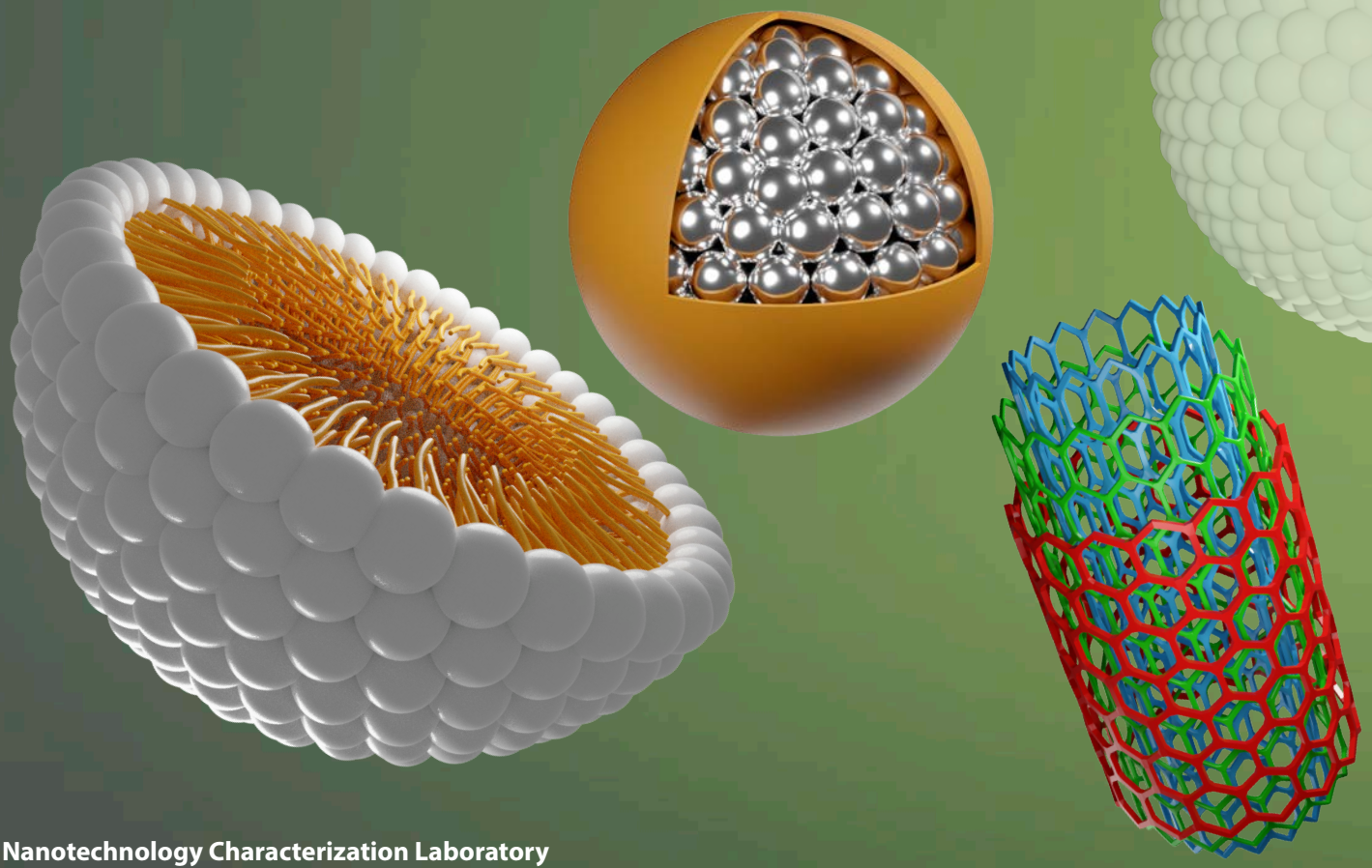
NCL
Nanotechnology
Characterization
Laboratory

Nanomedicine

Characterization, Formulation, Testing, Research and more



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ABOUT US

Who We Are

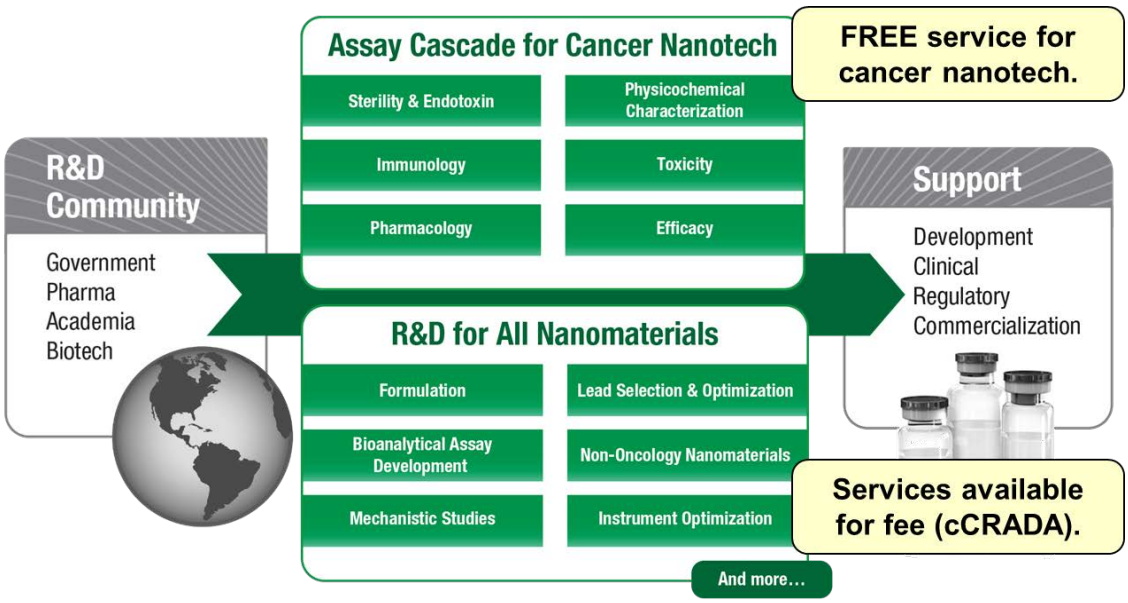
The Nanotechnology Characterization Lab (NCL) is a multidisciplinary team of scientists dedicated to advancing the science and testing of nanomedicines. Founded in 2004 as a collaboration among the National Cancer Institute (NCI), the Food and Drug Administration (FDA) and the National Institute for Standards and Technology (NIST), the NCL has an in-depth knowledge of the multitude of platforms and active pharmaceutical ingredients used in nanomedicine research.

What We Offer

We have several mechanisms available for collaboration, which span simple consultation to a rigorous testing of your nanoformulation:

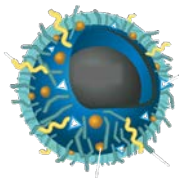
- **Assay Cascade Characterization Service**: FREE testing of your cancer-related nanoformulation in NCL's three-tiered Assay Cascade. Available via application.
- **cCRADA and IAA**: Fee-based research and development specifically tailored to your research needs.
- **TSA**: Fee-for-service assays to assess the in vitro and in vivo pharmacokinetic properties of your nanoformulation. No application or pre-requirements.
- **PAR 20-116**: NCL provides characterization support for applications accepted through NCI's PAR 20-116 grant mechanism.
- **Consultation**: FREE email and/or teleconference consultation on relevant testing applicable to your nanoformulation.

Additional details on each service are described throughout the brochure.



ASSAY CASCADE CHARACTERIZATION SERVICE

NCL's Assay Cascade is a tiered approach to fully assessing the physical, chemical and biological properties of a nanomaterial. NCL evaluates nanomaterials in three primary areas: physicochemical properties, immunology, and pharmacology/toxicology. The types of assays routinely conducted as part of NCL's Assay Cascade characterization service are outlined on our website, https://ncl.cancer.gov/resources/assay-cascade-protocols. For accepted formulations, ***all characterization is conducted free of charge for the submitting investigator***.



Physicochemical Characterization

In Vitro and In Vivo Immunology

In Vitro and In Vivo Pharmacology and Toxicology

Gaining Access

Access to NCL's Assay Cascade characterization service is granted through an application process. Applications are accepted four times every year, with deadlines the first business days of March, June, September and December.

To be considered for the service, the nanotechnology must have a cancer indication (e.g., therapeutic, imaging, diagnostic), and the applicant must have prior proof of concept efficacy data.

The application process is 2-steps. Step 1 is completion of a written White Paper application, due on the above-mentioned dates. Select applications will be invited to present their concept to the review committee as Step 2 of the process.

You can find additional details about the application process as well as the full evaluation criteria on our website: https://ncl.cancer.gov/working-ncl/ncl-assay-cascade-application-process.

What to Expect

Once applications are accepted, the NCL Section Leaders will work with you to develop a research plan specifically tailored to your formulation.

Characterization will be conducted in stages, with go/no-go criteria at each stage.

Following each stage, the data will be shared with you and the next assays will be mutually agreed upon.

Upon completion of all studies, you will be provided a comprehensive written report detailing all experiments conducted, methods utilized, and analysis of the accumulated data.

You are free to use all NCL generated data for publications, grants, securing venture capital, regulatory filings, etc.

The average collaboration spans 6-18 months, dependent upon the research plan for each project.

More Information

We encourage you to visit our website for more details, including answers to many frequently asked questions: https://ncl.cancer.gov/resources/frequently-asked-questions-faqs

Want to discuss your specific concept? Send us an email (ncl@mail.nih.gov) and we'll be glad to arrange a conference call.

COOPERATIVE RESEARCH AND DEVELOPMENT AND INTER-AGENCY AGREEMENTS

Contractor Cooperative Research and Development Agreements (cCRADA) (for non-Government organizations) and Inter-Agency Agreements (IAA) (for US Government organizations) are collaborative research projects specifically tailored to meet your research and development needs. There are no application requirements such as prior proof of concept data or that the formulation be used for cancer. Select examples of cCRADA and IAA projects are outlined below, including formulation services, method development, mechanistic studies and more.

Importantly, cCRADA and IAA projects are required to be fully-funded by the submitting investigator and can only be accepted where NCL has the resources available to meet your needs.

Nanotech Formulation

- Reformulation of both traditional and novel APIs.
- Incorporation of active targeting ligands.
- Address previously disqualifying toxicity or missed metric.
- Concurrent in vitro and/or in vivo testing for toxicity, efficacy, PK.

NCL has unique expertise for matching APIs with nanotech-based formulations.

Non-oncology Nanomaterials

- Characterization of nanomedicines for non-oncology applications, nanoparticles for environmental, health and safety risks, etc.
- Evaluate nanomedicines for immune modulation, other indications.
- Generate predictive toxicity profiles based on the physicochemical properties of nanomaterials.

Knowledge/Assays for cancer nanomedicines address similar gaps for non-oncology.

Method Development

- Development and validation of assays for lot release, biological activity, and more.
- Methods for evaluating nanomedicines in biological matrix, assessing polydispersity, etc.
- Collaborations with instrument manufacturers to improve nanotech bioanalytical tools.
- Methods to support clinical trials and bioequivalence studies.
- Collaborate on protocol standardization.

Methodologies to inform/contribute to translation and regulatory approval.

Safety and Mechanistic Studies

Exploring common reasons for preclinical and early clinical failure of nanoformulated drugs:

- Endotoxin contamination
- Cytokine storm
- Hypersensitivity reactions
- Complement activation
- Thrombogenicity (disseminated intravascular coagulation; DIC)
- Exaggeration of API immunotoxicity by NP carrier

Ensuring nanotech keeps pace with the improved understanding of cancer biology.

Interested in Learning More?

Please visit our website to read more about potential cCRADA and IAA projects, https://ncl.cancer.gov/working-ncl/ccrada-application-process

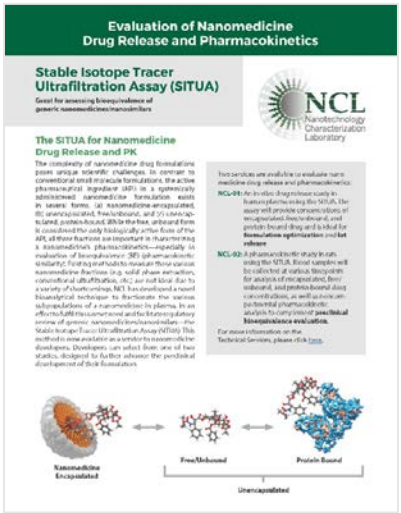
If you would like to discuss a possible cCRADA or IAA project, reach out to us at ncl@mail.nih.gov to schedule a conference call.

TECHNICAL SERVICE AGREEMENTS

Technical service agreements (TSA) are fee-for-service contracts to purchase select assays. There are no requirements such as an application process, prior proof-of-concept data, or that the formulation have a cancer indication.

The NCL currently has two technical services available for purchase, an in vitro drug release assay in human plasma (NCL-01) and an in vivo pharmacokinetic study (NCL-02). Both services utilize a stable isotope tracer ultrafiltration assay (SITUA); download the information at the link below to learn more.

https://ncl.cancer.gov/working-ncl/technical-services


Evaluation of Nanomedicine Drug Release and Pharmacokinetics

Stable Isotope Tracer Ultrafiltration Assay (SITUA)

NCL Nanotechnology Characterization Laboratory

The SITUA for Nanomedicine Drug Release and PK

Nanomedicine Encapsulated

Free/Unbound

Protein Bound

Unencapsulated

Click image to download this brochure for additional details and FAQs on the SITUA and the services NCL offers.

Nanomedicine In Vitro Drug Release (NCL-01)

In vitro drug release study in human plasma using the stable isotope tracer ultrafiltration assay (SITUA) to provide concentrations of:

- Encapsulated drug
- Free/unbound drug
- Protein-bound drug

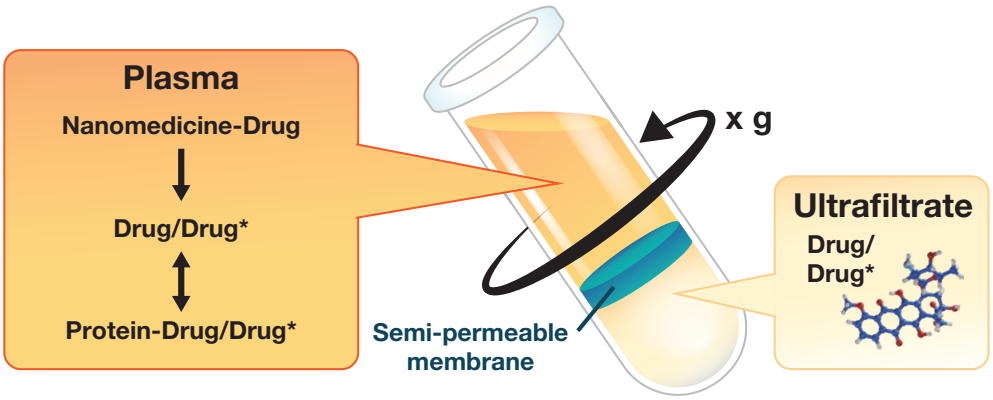
Ideal for formulation optimization, lot release, and estimation of in vivo PK.

Nanomedicine Pharmacokinetic Studies (NCL-02)

Nanomedicine PK study in rats using the SITUA. Blood samples collected at various timepoints for analysis of:

- Encapsulated drug
- Free/unbound drug
- Protein-bound drug
- Noncompartmental pharmacokinetic parameters for all drug species

Complements preclinical bioequivalence evaluation.



Stable Isotope Tracer Ultrafiltration Assay (SITUA). NCL developed a novel drug fractionation method to evaluate drug release in physiological matrix. (Reproduced with permission from *ACS Pharmacol Transl Sci*, **2020**, 3(3), 547–558.)

Relevant NCL Publications

Read more about the SITUA and its applicability to nanomedicine pharmacokinetics and bioequivalence studies in these publications:

Skoczen et al, *ACS Pharmacol Transl Sci*, **2020**, 3(3), 547-588. PMID: 32566919
Skoczen and Stern, *Methods in Molecular Biology*, Vol. 1628, **2018**, 223-239. PMID: 29039106
Stern et al, *Drug Metab Dispos*, **2016**, 44(12), 1934-1939. PMID: 27670412
Skoczen et al, *J Control Release*, **2015**, 220(PtA), 169-174. PMID: 26596375

PAR 20-116

Toward Translation of Nanotechnology Cancer Interventions (TTNCI)

NIH NATIONAL CANCER INSTITUTE

The National Cancer Institute has issued a call for proposals under PAR 20-116. This funding opportunity is aimed at enabling the translation of nanotechnology-based cancer interventions. The awarded technologies are expected to progress in development such that, following the award period, they can continue with other NCI translational programs such as the NCI Experimental Therapeutics (NExT) program.

Key Details:

- Application Due Dates: May 20, 2021; November 18, 2021
- More Info: https://grants.nih.gov/grants/guide/pa-files/par-20-116.html

PAR 20-284

Innovative Research in Cancer Nanotechnology (IRCN, PAR 20-284)

The National Cancer Institute has a call for proposals under PAR 20-284. Proposed projects should address major barriers in cancer biology and/or oncology using nanotechnology and should focus on mechanistic studies to expand the fundamental understanding of nanomaterial and/or nano-device interactions with biological systems.

Key Details:

- Application Due Dates: May 6, 2021; November 4, 2021
- More Info: https://grants.nih.gov/grants/guide/pa-files/PAR-20-284.html.

Where NCL Fits In

Projects selected by the NCI for funding under PAR 20-116 are automatically accepted for characterization in the NCL Assay Cascade. All awardees are expected to provide their nanoformulation for characterization at the NCL, and should do so early on in the award cycle.

Projects selected by the NCI for funding under PAR 20-284 are also eligible for NCL characterization. Awardees are encouraged, but not required, to provide their nanoformulation for characterization at the NCL.

A minimum set of characterization will be conducted for every nanoparticle submission to the NCL (both PAR 20-116 & 20-284), including assessment of sterility and endotoxin levels, nanoparticle size, zeta potential, and drug loading. Additional experiments may also be conducted and will be decided on a case-by-case basis with input from awardees and NCI.

All studies performed at the NCL will be provided at no-cost to the awardee (both PAR 20-116 and PAR 20-284) and will not be deducted from awarded funds. Likewise, no funds need to be allocated for NCL testing in the grant proposal's budget.

What to Expect

Shortly after receiving your PAR funding, the NCL will reach out to you to request additional information, as well as to discuss the timeline for submission of your nanoparticle formulation to NCL for testing.

All formulations submitted to NCL will undergo the same preliminary screening as outlined in the box to the left. Additional studies may be conducted throughout the course of your funding period.

Data generated will be shared with both you and NCI. You are free to use NCL-generated data for publications, other grant proposals, securing venture capital for spin-off companies, regulatory filings, etc.

More Information

Please visit our website to learn more about NCL testing for PAR 20-116 and PAR 20-284 funded projects: https://ncl.cancer.gov/working-ncl/par-20-116-par-20-284.

Feel free to contact us (ncl@mail.nih.gov) for questions or to discuss testing of your formulation.

RESOURCES

Consultation

Not ready to apply but need advice on next steps? The NCL panel of scientists have a broad range of expertise, and experience with a multitude of nanoformulations, and are ready to share this insight with you. The team is happy to provide consultation on testing relevant to your concept as you continue development in preparation for NCL application, regulatory filings, etc.

Reach out via email, ncl@mail.nih.gov, to schedule your call.

Protocols

The NCL has more than 70 protocols for nanomaterial characterization in the areas of physicochemical characterization, sterility, endotoxin testing, in vitro cytotoxicity, in vitro hematotoxicity, in vitro immunotoxicity, pharmacology and more.

All protocols are freely available for download: https://ncl.cancer.gov/resources/assay-cascade-protocols

These protocols have been tested with more than 400 different nanomaterials, spanning a variety of platform types and APIs. If you have questions regarding testing of your materials using any NCL protocol, please reach out to us. Our experts are happy to help guide you through the protocol. NCL can also assist developers in transferring protocols to GLP-compliant CMO/CROs.

Contract Manufacturing and Research Organizations

The NCL primarily conducts work at the preclinical stage of development, with the goal of assisting developers further advance their concept towards clinical translational. In addition to aiding in the transfer of protocols to GLP-compliant CMO/CROs, the NCL also maintains a list of CMO/CROs developers can engage for these next steps. You can access the list here: https://ncl.cancer.gov/sites/default/files/Nano%20CMO%20CRO%20list.pdf

If you have other recommendations for the list, please let us know. Our goal is to provide developers with information on available resources for the next steps in their developmental path.

Bibliography

With more than 15 years experience in nanomedicine characterization, the NCL has more than 200 publications in the field. Publications are conveniently organized into several sub-topics for quick reference to your area of interest.

Browse NCL publications in:

- Sterility, Endotoxin and Beta-Glucans
- Physicochemical Characterization
- Safety, Efficacy and Imaging
- Pharmacology and Toxicology
- Immunology
- Autophagy
- General Nanomedicine/Preclinical Characterization
- Reviews and Perspectives

https://ncl.cancer.gov/resources/ncl-scientific-bibliography

Want to Learn More?

Please reach out to us via phone (301-846-6939) or email (ncl@mail.nih.gov). Our team will be happy to discuss collaboration opportunities in more detail as they pertain to your specific concept.

All conversations can be conducted under CDA if required.

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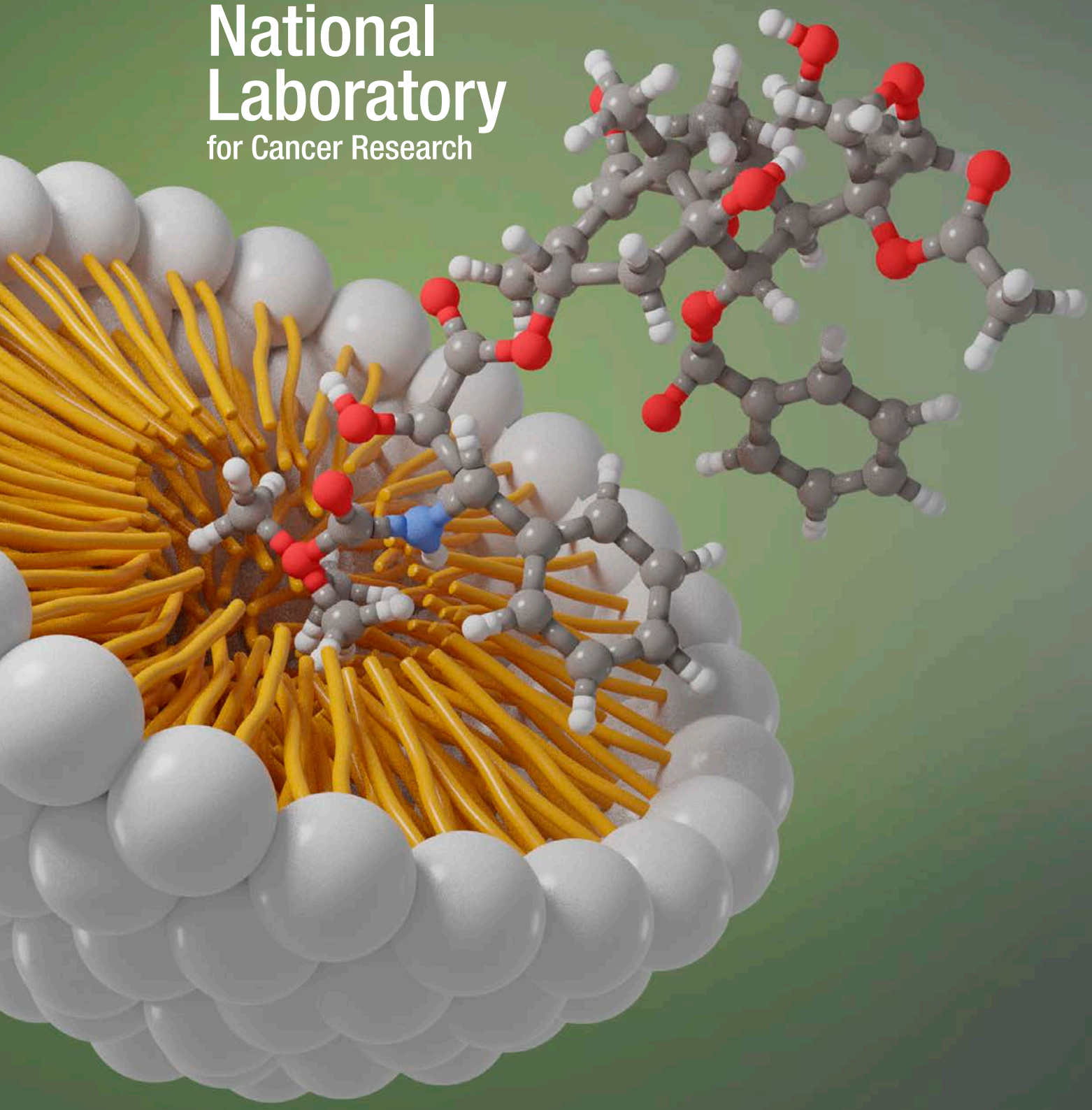

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