U.S. Department of Health and Human Services
Public Health Service
National Institutes of Health
National Cancer Institute

14th Virtual Meeting
Frederick National Laboratory Advisory Committee

Summary of Meeting
19 October 2023

National Cancer Institute
National Institutes of Health
Bethesda, Maryland

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The Frederick National Laboratory Advisory Committee (FNLAC) convened for its 14th Virtual Meeting on 19 October 2023. The meeting was open to the public from 1:00 to 3:38 p.m. EDT. The FNLAC Chairperson, Dr. Candace S. Johnson, President and CEO, M&T Bank Presidential Chair in Leadership, Roswell Park Comprehensive Cancer Center, presided.

FNLAC Members
Dr. Candace S. Johnson (Chair)
Dr. Carol J. Bult
Dr. John H. Bushweller
Dr. Timothy A. Chan
Dr. Lisa M. Coussens (absent)
Dr. Blossom A. Damania
Ms. Julie Papanek Grant
Dr. Angela M. Gronenborn
Dr. Mary J.C. Hendrix
Dr. Rodney J.Y. Ho
Dr. Allison Hubel
Dr. Dineo Khabele
Dr. Anant Madabhushi
Dr. Nilsa C. Ramirez Milan
Dr. Patrick Nana-Sinkam
Dr. Erle S. Robertson
Dr. Linda F. van Dyk

NCI Senior Leadership
Dr. James H. Doroshow
Dr. Anthony Kerlavage
Dr. Kristin L. Komschlies
Dr. Douglas R. Lowy
Ms. Anne Lubenow
Dr. Dinah S. Singer

Executive Secretary
Dr. Christopher D. Kane

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I. OPENING REMARKS—DR. CANDACE S. JOHNSON

Dr. Candace S. Johnson, Chair, called to order the 14th Virtual Meeting of the Frederick National Laboratory Advisory Committee (FNLAC) and welcomed the Committee members, National Cancer Institute (NCI) staff, and guests. Dr. Johnson reminded members of the conflict-of-interest guidelines and confidentiality requirements. Members of the public were welcomed and invited to submit to Dr. Christopher D. Kane, Executive Secretary, in writing and within 10 days, any comments regarding items discussed during the meeting.

Motion. A motion to accept the minutes of the 10 July 2023 meeting was approved unanimously.

Dr. Johnson called Committee members' attention to the future meeting dates listed on the agenda. She noted that the 29 February 2024 meeting is planned to be held virtually, and the 9–10 July and 22–23 October 2024 meetings are planned to be held in person.

II. NCI PRINCIPAL DEPUTY DIRECTOR'S REPORT—DR. DOUGLAS R. LOWY

Dr. Douglas R. Lowy, Principal Deputy Director, NCI, also welcomed the FNLAC members and attendees to the meeting. He stated that Dr. Monica M. Bertagnolli, Director, NCI, has been nominated as the next NIH Director, and her Senate committee hearing was held on 18 October 2023. Dr. Lowy also welcomed two new FNLAC Ex Officio members: **Dr. Blossom A. Damania,** Vice Dean for Research, School of Medicine, Director, Programs in Virology and Global Oncology, Lineberger Cancer Center, The University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, and **Ms. Julie Papanek Grant,** General Partner, Canaan, Menlo Park, California. Dr. Lowy reviewed the agenda and provided updates on recent NCI news and updates, Cancer Moonshot℠ activities, and the NCI budget outlook.

Cancer Mortality Trends. Dr. Lowy presented cancer mortality trends for both men and women by race and ethnicity from 2000 to 2019. He explained that the disparity between Black and White men has decreased during this period, which is partly attributable to decreases in the rate of lung cancer mortality in these groups. In contrast, these disparities have persisted for American Indian and Alaska Native men. Disparities between Black and White women have persisted to a greater degree than in men, which is partly attributable to breast cancer rates in Black women; recent U.S. Food and Drug Agency (FDA) approvals for breast cancer treatment might help decrease this disparity in the future.

NCI Program and Research Updates. Dr. Lowy highlighted several NCI programs and research activities. An NCI-led clinical trial resulted in the approval of atezolizumab, a treatment for advanced alveolar soft part sarcoma, a rare cancer that primarily affects adolescents and young adults. Dr. Lowy noted that Dr. James H. Doroshow, Deputy Director, Clinical and Translational Research, and Director, Division of Cancer Treatment and Diagnosis (DCTD), NCI, was the senior investigator for this study. Additionally, the My Pediatric and Adult Rare Tumor (MyPART) Network is engaging patients, family members, advocates, clinicians, and scientists as partners in research. Dr. Lowy also highlighted recent work enabled by the NCI Patient-Derived Models Repository; the pediatric low-grade glioma cell line has been fully characterized and is publicly available.

Frederick National Laboratory for Cancer Research (FNCLR) Updates. The FNLCR released a novel anti-COVID-19 monoclonal antibody, which has the potential to overcome prior resistance to earlier monoclonals. Dr. Lowy explained that the antibody will be used in clinical trials for cases in immunosuppressed individuals. Additionally, the RAS Initiative team discovered that neurofibromin (NF1) exists as a high-affinity dimer, and a subset of mutant forms bind to the wild-type monomer, leading to the degradation of both the mutant and wild-type proteins and a more severe

phenotype. This work provides insight into genotype–phenotype correlations for patient counseling, disease management, and treatment.

Cancer Moonshot. Dr. Lowy reminded the FNLAC members of the goals of the reignited Cancer Moonshot: Reduce the U.S. cancer death rate by 50 percent in the next 25 years, overcome cancer disparities, and end cancer as we know it for all. Dr. Lowy emphasized that these goals are challenging and encouraged the FNLAC members to consider how the NCI can ensure that the goals become feasible. A Cancer Cabinet meeting was held on 13 September 2023 to advance the goals of the Cancer Moonshot using an all-of-government approach. Dr. Lowy explained that this meeting highlighted NCI's collaborations with other government agencies and departments. Discussions included such topics as multi-cancer detection tests and a new collaboration with the U.S. Department of Veterans Affairs. Dr. Lowy also noted that a Cancer Survivorship Summit was held on 16 October 2023 and focused on gaps in survivorship care, policy proposals, and community-based resources and support services.

National Cancer Plan (NCP). Dr. Lowy reminded FNLAC members of the NCP, which is complementary to the Cancer Moonshot. The NCP outlines eight goals: prevent cancer, detect cancers early, develop effective treatments, eliminate inequities, deliver optimal care, engage every person, maximize data utility, and optimize the workforce. Additionally, the President's Cancer Panel convened a community meeting on 7 September 2023 to identify common themes and priority areas, including the cancer research and care workforce, accessibility of care, data sharing and interoperability, and social determinants of health.

NCI Budget. Dr. Lowy provided updates on the NCI budget. He explained that NCI's appropriations and paylines have risen since fiscal year (FY) 2016, but its purchasing power has decreased. Additionally, the percentage of modular awards has decreased progressively during the past decade. Dr. Lowy briefly outlined NCI's FY 2025 Professional Judgment Budget Proposal, which highlights such scientific opportunities as improving patients' lives through symptom science research, revolutionizing cancer clinical trials, clarifying the impact of the environment on cancer risk, harnessing the power of cancer data, and unraveling the complexity of cancer metastasis. He emphasized that sustained increases in funding are needed to meet NCI's goals and narrow gaps in cancer research and care.

Challenges related to a flat FY 2024 budget include Cancer Moonshot funding, maintenance of current paylines, funding for noncompeting awards, and increased mandatory expenses. Dr. Lowy emphasized that the NCI budget reflects multiple interconnected components, including research funding, training and workforce development, improved health outcomes, NCI-Designated Cancer Centers (Cancer Centers) and clinical trials, and operating expenses. A flat budget would affect the research project grant (RPG) pool, Cancer Center support grants, cancer training awards, Specialized Programs of Research Excellence (SPORE) grants, and the Intramural Research Program.

Dr. Lowy concluded by sharing the following key messages: The need to advance scientific discovery and technology is now being matched by opportunities for meaningful advances, but the anticipated resources for FY 2024 might not match these opportunities. The NCI must work together to steward its resources in partnership with the cancer research community to make progress against cancer as rapidly as possible.

In the discussion, the following points were made:

- Advances in lung cancer research have helped reduce racial disparities in overall cancer mortality for men, and advances in breast cancer research have the potential to help reduce racial disparities in overall cancer mortality for women. More work is needed to further reduce these disparities.

Important considerations for Black women include biological factors (e.g., susceptibility to certain forms of breast cancer that previously have been understudied) and access to care.

- The NCI might consider preparing a breakdown of cancer mortality data on response rates to NCI-sponsored trials across populations and disease types. These metrics could provide insight into the effects of access, screening, and biological factors. This question has been explored previously within the peer-reviewed scientific literature.

- Moving forward, training and stewardship will be essential in ensuring that new investigators are recruited and retained within the cancer research workforce.

III. FREDERICK NATIONAL LABORATORY FOR CANCER RESEARCH (FNLCR) AND THE NCI'S NEW PRECISION MEDICINE INITIATIVES—DRS. JAMES H. DOROSHOW, P. "MICKEY" WILLIAMS, HELEN CHEN, LYNDSAY HARRIS, AND RICHARD F. LITTLE

Dr. Doroshow provided an overview of FNLCR's new Precision Medicine Initiatives. He emphasized that the initiatives resulted from a coordinated effort across the NCI, FNLCR, and extramural research community. He recognized the FNLCR for its role in producing data, developing assays, and providing oversight across the national network of laboratories.

Clinical Laboratory Support of NCI's Precision Medicine Trials. Dr. P. "Mickey" Williams, Director, Molecular Characterization Laboratory, FNLCR, presented on NCI-MATCH (Molecular Analysis for Therapy Choice), a multi-treatment arm trial that made use of next-generation sequencing to detect actionable somatic mutations with evidence of predicting treatment response. NCI-MATCH opened its enrollment in November 2015, when the use of next-generation sequencing as a clinical assay was relatively new. The team developed a clinical laboratory network and a standardized assay to ensure consistent real-time tumor-screening results. A Designated Laboratory Network (DLN) of 11 vetted laboratories was established in 2017. Dr. Williams noted that DLN assays are performed prior to trial enrollment, as a part of routine patient management.

Building on this success, the NCI established the Molecular Diagnostics Network (MDNet), which supports NCI's Precision Medicine Trials Initiatives. MDNet uses the DLN for standard-of-care assays and maintains subcontracts with the FNLCR and external laboratories for novel assays. Dr. Williams briefly highlighted current assay support for iMATCH (immunotherapy), ComboMATCH (combination therapy), and MyeloMATCH (myeloid malignancies). He explained that FNLCR staff work with the NCI and trial investigators to identify predictive biomarkers and appropriate assays; topics of consideration include clinical reports, documentation of performance of protocols, specific biomarkers and thresholds, specimen pre-analytics, and required turnaround time for results.

Dr. Williams explained that the laboratories are vetted and continually assessed for assay performance. ComboMATCH currently seeks to expand its network to additional laboratories and is coordinating closely with the FDA. Subcontracts are established for highly subjective and novel assays. Reference and quality control materials also are an area of interest, and efforts are ongoing. He emphasized that the team is building on its success from NCI-MATCH and has incorporated additional laboratories and expertise to continue support of MDNet. The program remains focused on providing accurate, "fit-for-intended-use," and well-documented assays to ensure that the data generated are reproducible and available in the public domain.

iMATCH. Dr. Helen Chen, Investigational Drug Branch, Cancer Therapy Evaluation Program (CTEP), DCTD, NCI, explained that a major impediment to further development of

immunotherapy is lack of patient selection markers for combination regimens designed to overcome the complex mechanisms of resistance. iMATCH represents a stepwise approach toward this goal. The team is building on current knowledge and developing a strategy to improve current approaches. iMATCH is exploring prospective use of tumor mutation burden and inflammation markers for biological stratification of enrichment in signal-seeking trials. The future goal is to develop true precision biomarkers for specific regimens and combinations.

The iMATCH concept is to enhance the clinical evaluation of novel immuno-oncology agents or combinations by providing a central assay platform for both prospective and retrospective molecular characterizations. iMATCH will represent a cross–National Clinical Trials Network (NCTN) effort, with all groups developing subprotocols based on a central assay protocol. Dr. Chen presented a schema for the iMATCH concept. Using a recent biopsy, testing would be performed to generate integral markers for therapeutic protocols to define subgroups for enrichment or stratification. She explained that unlike in other trials through the Precision Medicine Initiatives, integral markers are biology-based rather than target-based. Cutoffs are predefined based on the best available data and can be adjusted as needed. Regimens can be tested in all subgroups, but each group must have a predefined sample size.

The iMATCH pilot trial is being performed to assess feasibility and preliminary efficacy. Interim analyses will be performed after stage 1 for assay turnaround time and subgroup distribution, and predetermined cutoffs will be adjusted in stage 2 as needed. To date, 30 patients have been tested and treated, and more will be enrolled over time. In the future, trials will be conducted as standalone studies that use the same central testing platform and are in a specified clinical setting. Depending on the clinical setting and testing regime, integral markers could be used up front or during stage 2 of the trial.

Overall, iMATCH is intended to ensure adequate representation of potentially relevant biology and adequate sample size with biomarkers for meaningful retrospective analysis. A robust and reliable biomarker infrastructure is essential to realizing iMATCH's vision; this infrastructure includes complex assay platforms and analytic pipelines, rapid turnaround to enable up-front patient enrichment and to inform interim analysis and adaptive designs, and flexibility and capacity to add or develop new markers. Dr. Chen remarked that the FNLCR provides a unique resource with the experience and expertise necessary for developing such complex platforms as iMATCH.

ComboMATCH. Dr. Lyndsay Harris, Cancer Diagnosis Program, DCTD, NCI, explained that the premise of ComboMATCH is that drug combinations are more likely to provide clinical benefit than single agents in most situations. The team hypothesized that preclinical data from *in vivo* models of combinations demonstrating drug synergy and prolonged tumor regressions can predict clinical benefit in defined patient groups. ComboMATCH will use both single-arm studies and Phase II randomized trials in both histology-agnostic and histology-specific patient cohorts. This effort requires initial algorithms for interpreting commercial next-generation sequencing testing for eligibility, as well as circulating tumor DNA assessments before, during, and after treatment.

The ComboMATCH protocol organization includes a screening study for registration, followed by cassettes of studies conducted through the cooperative groups. Patients undergo standard-of-care genomic testing and are enrolled with relevant clinical information. MATCHBox, an NCI-designed computational platform, uses genomic and clinical data for trial assignment. Dr. Harris noted that 40 patients have been registered, and 21 have been enrolled in treatment sub-studies to date. As patients progress, they are provided the opportunity to enroll in other appropriate MATCHBox studies.

ComboMATCH leadership decided on the creation of a Steering Committee, Agents and Genes Working Group, Protocol Logistics Working Group, Molecular Biomarker and Specimen Management Working Group, and Precision Medicine Analysis and Coordination Center. Dr. Harris explained that these entities are involved in protocol reviews (i.e., concept, protocol, and amendment). Additionally, she

explained that the DLN is used to refer patients to the ComboMATCH trial and is composed of vetted academic and commercial laboratories performing next-generation sequencing as part of standard of care. She briefly listed current academic and commercial laboratories within the network. She also highlighted MDNet, which performs whole-exome sequencing, RNA sequencing, immunohistochemistry assays, tissue processing, and biobanking.

MyeloMATCH. Dr. Richard F. Little, Clinical Investigations Branch, CTEP, DCTD, NCI, shared that MyeloMATCH aims to (1) create a portfolio of rationally designed treatment sub-studies onto which patients sequentially enroll over their entire treatment journey, (2) create an efficient operational model attractive to industry partners and NCTN sites to accelerate therapeutic advances for myeloid malignancies, and (3) develop the careers of young investigators by promoting leadership throughout the clinical trial portfolio and laboratory program. Dr. Little explained that as an increasingly lower remaining tumor burden is achieved, the focus will be to target residual disease more effectively.

MyeloMATCH is composed of a Senior Scientific Council that includes an Agents and Genes Committee and a Laboratory Committee. Five clinical basket working groups have been formed in the following areas: older acute myeloid leukemia (AML), younger AML, myelodysplastic syndromes (MDS), transplant cell-based therapy, and next-generation sequencing–directed treatment. Dr. Little emphasized that MyeloMATCH provides support for young investigators through the working groups.

The structure of MyeloMATCH includes four tiers. The first tier is focused on Genexus, cytogenetics, and fluorescence *in situ* hybridization for targeted treatments or risk-based assessments. The second tier is focused on flow cytometry, and the third tier is focused on transplant cellular therapy. The fourth tier is focused on error-corrected next-generation sequencing, and patients are assessed for potential relapse. Dr. Little briefly outlined the master screening and reassessment protocol. He also outlined the first-generation studies in the older, younger, MDS, and transplant/immuno/cellular therapy baskets. He noted that most of the studies are randomized Phase II trials focused on identifying early signals of drug activity that would overcome resistance, compared to the control arm.

Dr. Little concluded by emphasizing that MyeloMATCH is DCTD's largest and most complex trial in a single disease area, treating patients through sequential treatment sub-studies from initial diagnosis until progression or death. The assay data will promote rapid treatment assignment and inform clonal evolution and provide insights into treatment sensitivity and resistance. Additionally, this work could provide insights toward changing AML and MDS treatment paradigms. He reflected that the trial would not be feasible without the infrastructure provided through the DCTD and FNLCR.

In the discussion, the following points were made:

- The iMATCH treatment regimen was determined in discussion with extramural investigators. The decision was made based on activity in other tumor types and in combination with immunotherapy.

- The NCI-MATCH pathology slides have been digitized and are being used in relevant studies. ComboMATCH is pursuing similar digitization efforts of samples that are submitted for further analysis.

- Lists of genes for screening will be updated as needed, based on the current data. The lists are based on guidance from international consensus groups, but harmonization remains an ongoing challenge. The study is focused on predictive, not prognostic, findings.

- The MyeloMATCH flow cytometry measurements are being performed onsite and shipped for analysis, and a standardized process is in place. Other analyses can be performed on the same sets of specimens. This approach can provide insight into potential variations.

IV. CRYO-EM STUDY OF THE SARS-COV-2 POLYPROTEIN CLEAVAGE BY THE MAIN PROTEASE M^{PRO}—DR. KATSUHIKO MURAKAMI

Dr. Katsuhiko Murakami, Professor of Biochemistry and Molecular Biology, Eberly College of Science, The Pennsylvania State University, discussed his work on SARS-CoV-2 polyprotein cleavage, which was enabled through support by the NCI and the National Cryogenic Electron Microscopy (Cryo-EM) Facility (NCEF). Dr. Murakami's laboratory is focused on macromolecular changes that occur during transcription in bacteria and archaea. Dr. Murakami explained that FNLCR's resources helped the team members access the instrumentation needed for their experiments until the institution acquired its own instrument with suitable capabilities.

During the COVID-19 pandemic, the team applied its expertise in structural biology to better understand the SARS-CoV-2 virus. Researchers examined how mRNA is translated to polyprotein and processed to enable new infections. The main protease (M^{pro}) forms a homodimer, and mutations of the active site—at the catalytic dyad His41 and Cys14—disrupt enzyme activity. This protease is a potential target for antiviral drug development. When the team began its work on M^{pro}, an X-ray crystallography structure was available. Researchers were interested in how the active sites are recognized in catalytic reactions. Another group published a defined order for cleavage reactions, but more structural work was needed to understand how the M^{pro} interacts with polyproteins. Dr. Murakami explained that cryo-EM provides a valuable method to study these interactions.

The team prepared an M^{pro}-C145A derivative, nsp7-19 polyprotein, and M^{pro}/polyprotein complex. Dr. Murakami explained that the complex is relatively stable and has a molecular weight of about 100 kD, which is a challenge for cryo-EM measurements. The parameters were adjusted to maximize the quality of the microscopic imaging. The researchers achieved 2.5 Å resolution with C2 symmetries. They visualized binding to the active site, which corresponded to the polyproteins. From this work, they concluded that the M^{pro}–polyprotein interaction occurs exclusively within the recognition peptide, with no external interactions occurring. The team also determined the structure of wild-type M^{pro}. Dr. Murakami shared images generated using cryo-EM.

Building on its findings, the team proposed polyprotein-driven and M^{pro}-driven models. Under the first model, they hypothesized that a limited number of recognition sites are exposed on the surface of the polyprotein for recruiting M^{pro}. Releasing the protein exposes additional recognition sites for continued processing. Under the second model, recognition sites are already exposed on the surface of the polyprotein, and M^{pro} selects a preferred cleavage site based on the site's affinity to M^{pro}.

In conclusion, this work led to the first high-resolution cryo-EM structures of M^{pro} and its complex with polyprotein. Limited interaction was observed between M^{pro} and polyprotein around the recognition sequence. The structure, conformation, and dynamics of the polyproteins might determine the sequence of polyprotein cleavage by M^{pro}. Future directions include determining the complete polyprotein structure and investigating allosteric regulation of two active sites within the M^{pro} dimer during polyprotein processing.

In the discussion, the following points were made:

- Generally, the active site binds to a 10-residue peptide. The active site cavity can recognize about 10 amino acid residues, which might provide insight into the preferred recognition sequence for

cleavage. No such differences in the sequences were observed, however. Thus, the team has proposed that the polyprotein produces only one recognition sequence in this process.

V. NATIONAL CRYO-EM PROGRAM (NCEP) UPDATE—DR. DWIGHT NISSLEY

Dr. Dwight Nissley, Director, Cancer Research and Technology Program (CRTP), FNLCR, presented an update on the National Cryo-EM Program (NCEP). He remarked that FNLCR's operational model includes national missions (e.g., RAS Initiative, NCEP, NCI–U.S. Department of Energy Collaboration), extramural support (e.g., Nanotechnology Characterization Laboratory, Antibody Characterization Laboratory), and technology for the NIH and NCI (e.g., microscopy, protein expression and characterization, genomics and proteomics).

The National Cryo-EM Facility (NCEF) was established in 2017 to support the extramural community, and the facility was intended to expand as technologies continue to develop. The Cryo-EM Research and Development program was created in 2019 to explore new platforms and to support methods and technology development for the cryo-EM field. The NCEP supports three user groups: (1) research groups with experience in cryo-EM technology, (2) structural biologists from adjacent disciplines (e.g., X-ray, nuclear magnetic resonance), and (3) biologists focused on important biomedical problems who are interested in adding cryo-EM methods to their toolkit.

Dr. Nissley provided a brief outline of the NCEF organization and operational metrics. The user base includes 145 investigators from more than 50 institutions. A total of 1,050 imaging sessions have been conducted during the past 6.5 years, with an average of 15.6 imaging sessions per month during the previous year. This work has yielded 106 publications, with 26 publications during the past year, many of which are in high-impact journals. Additionally, more than 210 structures have been deposited. He presented several case examples of user success resulting from the NCEF. Their findings related to tRNA maturation, immune responses in tumor environments, tumorigenesis and aging, and cold sensation.

The NCEF includes two Titan Krios microscopes, each of which is equipped with a Gatan K3 direct detector and a BioQuantum energy filter. Currently, general imaging is performed at 180 images per hour. Both instruments have been updated to increase throughput, and efforts to further increase the input through new software and workflows are ongoing. The team also is testing a VitroJet for automated grid preparation, which would help increase reproducibility and throughput. Under this approach, users will be able to send samples that are then frozen once the platform is validated. They are developing a reporting framework to provide users feedback to continue their experiments, with a focus on users who lack sufficient cryo-EM infrastructure at their home institutions.

The Advanced Cryo-EM Technology Team is focused on using lower energy electron microscopes to generate high-resolution structures to decrease space requirements and cost. Dr. Nissley presented representative data from this effort. The team has established a contractor Cooperative Research and Development Agreement (cCRADA) with Gatan, Inc., with a focus on feature and performance testing of Latitude-S, a software platform for automated cryo-EM collection. The goals of this effort are to increase software efficiency, optimize the data acquisition process, explore data collection efficiency, and evaluate a new version of Gatan cameras.

Dr. Nissley noted that Ewald spheres remain an ongoing area of concern in the field, and the team is focused on exploring this topic further. The NCEP also is collaborating with the RAS Initiative to visualize NF1 complexes in the RAS–mitogen-activated protein kinase signaling pathway. He shared representative images from recent cryo-EM efforts (e.g., lactate dehydrogenase, human serum albumin). Future directions include an improved single-particle cryo-EM platform and *in situ* tomography. The team is interested in developing a cost-effective microscope with minimized chromatic aberration for

ultra-high-resolution single-particle cryo-EM imaging. The researchers also are interested in enabling the visualization of molecules within the cellular context, providing deeper biological insights.

The next Cryo-EM Training Program session is anticipated to take place in summer 2024 and will be held in person at FNLCR's Advanced Technology Research Facility. The event will feature guest lecturers who will provide classroom instruction on such topics as sample preparation, grid screening, data collection and processing, structure determination, and model building and validation.

In the discussion, the following points were made:

- Increased capacities for high-resolution measurements provide opportunities for small-molecule drug discovery. The NCEP is interested in exploring this area further in the future, but potential applications depend on the molecule of interest.

- The NCEP has considered conducting training for support staff and facility managers, which could help with the operation of other facilities. Training of young investigators also is critical.

- Advances in tomography would expand capabilities for users. The NCEP is interested in establishing the platform, and the effort will constitute a multiyear process.

VI. CLOSING REMARKS—DR. CANDACE S. JOHNSON

Dr. Johnson expressed appreciation to the Committee members and other participants for attending. Members were reminded to submit potential agenda topics for future FNLAC meetings to Dr. Kane.

VII. ADJOURNMENT—DR. CANDACE S. JOHNSON

There being no further business, Dr. Johnson adjourned the 14th Virtual Meeting of the FNLAC at 3:38 p.m. EDT on Thursday, 19 October 2023.

March 14, 2024 — /s/
Date — Candace S. Johnson, Ph.D., Chair

March 15, 2024 — /s/
Date — Christopher D. Kane, Ph.D., Executive Secretary