

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH
NATIONAL CANCER INSTITUTE
AD HOC TRANSLATIONAL RESEARCH STRATEGY SUBCOMMITTEE
(TRSS) MEETING**

**Summary of Meeting
January 14, 2021**

Webinar

**CLINICAL TRIALS AND TRANSLATIONAL RESEARCH ADVISORY COMMITTEE
AD HOC TRANSLATIONAL RESEARCH STRATEGY SUBCOMMITTEE**

Summary of Meeting

January 14, 2021

A meeting of the ad hoc Translational Research Strategy Subcommittee (TRSS) of the Clinical Trials and Translational Research Advisory Committee (CTAC) of the National Cancer Institute (NCI) was held by webinar on Thursday, January 14, 2021, at 11:01 a.m. The TRSS chairs, Dr. Davidson and Dr. Dang, presided.¹ The meeting was adjourned at 12:01 p.m.

Co-Chairs

Chi V. Dang
Nancy E. Davidson

Ex Officio Members

James H. Doroshow, NCI

TRSS Members

Francis Ali-Osman
Walter J. Curran, Jr.
David A. Mankoff
Lynn M. Matrisian
Roman Perez-Soler
Kevin M. Shannon
David A. Tuveson
Kevin P. White
Max S. Wicha

Executive Secretary

Peter Ujhazy, NCI

Presenters

Chi V. Dang, MD, PhD, Scientific Director, Ludwig Institute for Cancer Research; Professor, The Wistar Institute
Nancy E. Davidson, MD, Senior Vice President, Director and Full Member, Clinical Research Division, Fred Hutchinson Cancer Research Center

¹A roster of TRSS members and their affiliations is included as an appendix.

TABLE OF CONTENTS
Thursday, January 14, 2021

I.	Welcome and Opening Statement.....	1
II.	Discussion of Revised Charge to TRSS.....	1
III.	Discussion of Opportunities and Gaps in Translational Research.....	2
IV.	Wrap-Up & Adjournment.....	5
V.	Adjourn.....	5
	Appendix.....	6

I. Welcome and Opening Statement

Chi V. Dang, MD, PhD

Nancy E. Davidson, MD

Dr. Davidson reviewed the confidentiality and conflict-of-interest practices required of TRSS members during their deliberations. She invited members of the public to send written comments on issues discussed during the meeting to Dr. Ujhazy within 10 days of the meeting. Dr. Dang then reviewed the meeting agenda.

II. Discussion of Revised Charge to TRSS

Chi V. Dang, MD, PhD

Nancy E. Davidson, MD

Dr. Dang explained that he had prepared a draft charge statement for TRSS using the description of a TRSS-like group in a 2016 Specialized Program of Research Excellence (SPORE) working group report. Dr. Dang asked TRSS members to comment on this document.

Focus on R01 Investigators. Dr. Matrisian asked why the third task listed in the statement calls for identifying translational knowledge gaps that might be addressed by R01 investigators and not by investigators from larger research programs, such as P01 program awards and SPOREs. Translational research requires input from investigators with different areas of expertise and different capabilities; Dr. Matrisian therefore suggested broadening this task to include investigators from P01, SPORE, and other large programs.

Dr. Dang explained that incentives are available for P01 and SPORE programs to conduct translational research, but not for R01 investigators. This aspect of TRSS's work focuses on incentives for investigators to submit R01 applications for studies that can feed the translational research pipeline. For example, a program announcement might call for R01 applications for basic research (e.g., on the molecular mechanisms of fibrosis) that could support translational research on pancreatic cancer. Such advances would not require large teams and could, instead, be made by many different research teams that explore the same topic. Some P01 and SPORE programs already conduct this type of research.

Dr. Shannon pointed out that the fourth task, to identify and suggest research opportunities for concept development by NCI, can pertain to other types of awards. The Board of Scientific Advisors (BSA) and National Cancer Advisory Board are concerned about the R01 pool, and support is needed for this type of funding. NCI funding for larger programs tends to go to institutions that already have many NCI awards, and the concern is that talented R01 investigators at other institutions are not obtaining NCI funding. Dr. Dang agreed that the fourth task captures research programs under the oversight of BSA and the National Cancer Advisory Board.

Other Suggested Modifications of the Charge. Dr. Mankoff noted that he had a conflict of interest because he is a member of a study section that is about to review an application for the mechanism he was about to describe. NCI has an award for partnerships between academic researchers and companies through which the academic partner can conduct laboratory research that the industry partner can translate into the clinic. Dr. Mankoff suggested that the TRSS charge statement mention this opportunity as an option for translating research findings into the clinic.

Dr. White commented that R01 research to address translational gaps is likely to be based on data produced by large program grants and consortia. Dr. White asked how TRSS can help NCI shape R01 announcements calling for research that takes advantage of NCI's investments in larger research programs. Dr. Dang said that TRSS needs to discuss how best to accomplish this goal with NCI.

Dr. Curran approved of the proposed tasks in the draft TRSS charge statement. He suggested that TRSS also identify ways to optimize opportunities for translational investigators to use the tissue banks and data collected and stored by large research programs, including the NCI Cooperative Groups and NCI-Designated Cancer Centers.

Dr. Chi asked TRSS members to send additional edits to the TRSS charge document to Dr. Ujhazy.

III. Discussion of Opportunities and Gaps in Translational Research

Gastroesophageal Cancer as a TRSS Topic. Dr. Dang explained that Dr. Ujhazy had asked TRSS to consider whether gastroesophageal cancer might be an appropriate topic. A working group could be formed to develop recommendations on this topic in the same way that previous TRSS working groups have produced recommendations on glioblastoma multiforme and radiation oncology. Dr. Dang asked TRSS to send Dr. Ujhazy ideas for this working group to address.

Dr. Shannon suggested that TRSS emphasize the importance of selecting working group members with diverse areas of expertise. The Radiation Oncology Working Group, for example, included only radiation oncologists, and it might have benefited from input from medical oncologists or others to address the relationship between radiation oncology and other fields of medicine. The gastroesophageal cancer working group should include experts in other types of cancer and in organoids. Dr. Dang added that this working group should include individuals with clinical expertise to identify unmet needs that could be addressed by research.

Dr. Tuveson said that the Board of Scientific Advisors (BSA) has discussed gastroesophageal cancer, and NCI proposed developing a U01 funding mechanism on this cancer. However, when Dr. Tuveson pointed out to NCI that this field does not have enough investigators for a U01 program, NCI decided to fund an R01 program instead. Similar problems exist in many other areas of cancer.

Dr. Dang wondered whether TRSS should address gastroesophageal cancer if BSA is already addressing this topic. Dr. Tuveson explained that BSA had discussed a recommendation for NCI to issue R01 awards that would help attract and retain new gastroesophageal cancer researchers. TRSS should not address the same topics as BSA. Dr. Shannon said that gastroesophageal cancer is an understudied area, and TRSS could discuss barriers to entry into this field.

Dr. Davidson explained that the task of TRSS is to identify topics for BSA to determine how to address. Dr. Dang added that TRSS is supposed to identify gaps in translational research, and BSA will decide whether to recommend research to answer these questions.

Dr. Ujhazy explained that the program/RFA approved by the BSA is focusing on basic research, whereas TRSS is discussing the needs for translational research on gastroesophageal cancer. The two efforts are complementary rather than overlapping. Dr. Doroshov agreed.

TRSS Process. Dr. Ujhazy had also asked TRSS to identify other potential topics to address, and several members had sent in suggestions. Dr. Dang and Dr. Davidson proposed that TRSS meet quarterly. Before each meeting, TRSS members would submit topics for prioritization at the meeting. Ideally, TRSS will discuss two topics at each meeting and develop recommendations for NCI. NCI will then examine its portfolio to determine whether it is already addressing any of these recommendations; it will then consider whether to address the other recommendations and, if so, how.

Dr. Perez-Soler pointed out that TRSS is made up of very senior investigators, and he suggested that NCI consider forming a similar group of promising early-career investigators who have funding for translational research. This group would have a different perspective than TRSS on research gaps. Dr. Dang agreed that early-career investigators are an important group to consult about research gaps, but he thought that NCI does not need to form a group of such individuals. Instead, NCI could ask them to contribute suggestions to a portal. Dr. Davidson added that NCI could reach early-career investigators through professional societies, which have major efforts to organize these individuals.

Dr. Davidson suggested that TRSS ask individuals who are not TRSS members to submit potential TRSS topics, which TRSS could prioritize to determine which ones are most suitable to discuss. Dr. Dang suggested that NCI issue a request for information asking for topics, just as the Cancer Moonshot Blue Ribbon Panel did.

Dr. Davidson wondered whether such an approach is within the TRSS scope. Dr. Doroshov replied that collecting a wide range of ideas would be useful. NCI has done this in the past, including for the Cancer Moonshot and for the restructuring of the NCI clinical trials system. NCI could set up a portal to collect suggestions, but the challenge will be to ensure that a broad range of users interacts with the portal on an ongoing basis.

Dr. Dang suggested asking American Society of Clinical Oncology members to submit ideas. Dr. Davidson agreed and suggested that NCI also request ideas from other societies, such as the American Association for Cancer Research and subspecialty societies (e.g., American Society for Radiation Oncology). Dr. Shannon added the American Society of Hematology to the list of societies to engage, as well as SPORE principal investigators, cancer center directors, and Cooperative Group investigators. Dr. Davidson said that instead of asking society members to interact with a portal on an ongoing basis, NCI could simply issue an e-mail blast asking for ideas. Such a message would generate many suggestions and might therefore be sufficient. If NCI needs additional ideas, it could repeat the process in the future.

Dr. Matrisian identified three areas for TRSS to consider when prioritizing topics: scientific merit, clinical need, and feasibility.

Research Models. A topic proposed by Dr. Shannon is the need for better animal models (e.g., xenograft and genetically engineered animal models vs. organoids), which are fundamental to translational research. Dr. Dang proposed that TRSS choose animal models as its first topic to ensure that the discoveries from animal model studies can be translated to the clinic.

Dr. Davidson agreed that the issue of models is an important one to address and would be a good starting point for TRSS. Dr. Dang said that TRSS can probably address no more than two ideas at a time, but he agreed that models is a suitable initial topic and one that involves imaging, therapy, and genetics. Dr. Shannon commented that the reason he had suggested this topic was that much of the progress in pancreatic cancer research has resulted from the development of a knock-in mouse strain. He listed other reasons to develop recommendations for animal models:

- Lack of evidence to support the common assumption that patient-derived xenograft models are superior to others
- Potential of improved imaging to improve the use of models
- Lack of good models as a barrier to progress in some areas, such as gastroesophageal cancer
- Need for a next-generation series of models that will enable the identification of immuno-oncology agents and drug combinations as well as mechanisms of resistance
- Need for more rigorous studies that compare models to determine which ones are predictive and to test drugs known to be effective

Dr. Matrisian stated that the challenge with models is determining which are most predictive of clinical success, which might vary by cancer type. This type of research could be transformational.

Other Topics. Dr. Ali-Osman said that the traditional way to address topics like those mentioned is to identify critical questions and then use R01 awards. This approach could be broadened by using other funding mechanisms. TRSS needs to identify areas that NCI can address in a focused fashion. He hoped that TRSS will consider other cancers as well as topics that do not focus on a specific type of cancer and that require this type of focused approach. A request for applications is one way to draw attention to a problem.

Dr. Doroshov reported that when he arrived at NCI 16 years earlier, every NCI division was asked to fund all pancreatic cancer applications with a score near the payline because of the dearth of research on this topic. Increasing the number of pancreatic cancer investigators to the numbers needed to create a research field took several years, but this process was catalyzed by the pancreatic cancer report. Even though NCI did not have the funding to issue a request for applications for pancreatic cancer research, this effort was successful. Similarly, a program announcement led to some very strong applications and the development of an effective consortium to address small-cell lung cancer. Although this research has not led to a cure, it has been very productive and has resulted in true translational advances because of the spotlight on the area. NCI needs to cast a wide net for input on a wide range of potential topics that could benefit from this type of effort.

Dr. Wicha reported that organ-specific topics have led to clear successes, but TRSS should not be limited to such topics. Many of the most important breakthroughs in one tumor type apply to others, and many areas of scientific inquiry are ripe for exploitation across tumor types. Dr. Doroshov agreed.

Dr. Dang identified three domains of research gaps for TRSS to address:

- Cross-cutting topics that are relevant to several types of cancer
- Human resource infrastructure and technology gaps
- Disease-specific knowledge gaps

Dr. Doroshov said that identifying cross-cutting research gaps can be challenging. However, TRSS is poised to consider these types of topics, and its efforts could lead to ideas that NCI would not have otherwise considered.

Dr. Mankoff suggested integrated diagnostics as a cross-cutting topic to consider. There is an opportunity to bring various modalities (such as imaging and genomic and other assays) together and use data science to determine how to interpret them and guide the discovery of treatments. Dr. Dang agreed that this is an important topic and noted that the imaging research field needs more investigators.

Metrics of Success. Dr. Curran asked about metrics of success for TRSS, which might include whether translational research at NCI moved in the right direction between, for example, 2019 and 2022. Dr. Dang proposed that TRSS use a surrogate measure, such as whether TRSS suggestions are implemented in the form of requests for applications. Ideally, TRSS recommendations would lead to clinical trials that result in new approved treatments or new clinical practices, but this aim might be overambitious. The role of TRSS is to make recommendations for NCI to consider for funding.

Dr. Tuveson identified three challenges in cancer medicine: attracting investigators to study cancer, organizing investigators, and finishing research. Dr. Matrisian led a pancreatic cancer working group that was probably the catalyst for making investigators aware of the research needs in this area and

for increasing the number of investigators in the field. However, the challenge of organizing these investigators remains.

IV. Wrap-Up & Adjournment

Chi V. Dang, MD, PhD

Nancy E. Davidson, MD

Dr. Dang said that TRSS will meet again in the next quarter. He reminded TRSS members to send more feedback on ideas to Dr. Ujhazy for TRSS to consider as well as on the gastroesophageal cancer topic. Sheila Prindiville, MD, said that NCI will send information to TRSS members on mechanisms for gathering broad input on research gaps for TRSS to address.

V. Adjourn

There being no further business, the TRSS meeting was adjourned at 12:01 p.m.

Date	Chi V. Dang, MD, PhD, Co-Chair
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Date	Nancy E. Davidson, MD, Co-Chair
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Date	Peter Ujhazy, MD, PhD, Executive Secretary
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Appendix

**NATIONAL INSTITUTES OF HEALTH
National Cancer Institute
Clinical Trials and Translational Research Advisory Committee
Ad Hoc Translational Research Strategy Subcommittee**

CO-CHAIR

Chi V. Dang, MD, PhD

Scientific Director

Ludwig Institute for Cancer Research, New York

Professor, The Wistar Institute

Philadelphia, Pennsylvania

CO-CHAIR

Nancy E. Davidson, MD

Senior Vice President, Director and Full Member

Clinical Research Division

Fred Hutchinson Cancer Research Center

President & Executive Director

Seattle Cancer Care Alliance

Head, Division of Medical Oncology

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Distinguished Professor of

Neuro-Oncology Research

Professor of Surgery

Professor of Pathology

Department of Surgery and Pathology

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Gerd Muehllehner Professor of Radiology

Vice-Chair for Research

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Cold Spring Harbor, New York

Kevin P. White, PhD

President, Tempus Labs
James and Karen Frank Family Professor
Department of Human Genetics
Professor, Department of Ecology and Evolution
Director, Institute for Genomics and
Systems Biology
Knapp Center for Biomedical Discovery
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