Advancing Translational Cancer Research: A Vision for Transitioning into the Future

Report of the BSA/NCAB SPORE Evaluation Working Group

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NIH **NATIONAL CANCER INSTITUTE**

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Charge to the Working Group and key output

- Charge from former NCI Director Harold Varmus on December 3, 2014 and restated by Acting Director Douglas Lowy

- Recommend:

  - Best support for translational science in the future

  - How Specialized Programs of Research Excellence (SPORE) Program could enhance impactful translational research

- Many previous WGs' recommendations reviewed. The current WG recommends increased flexibility and:

  - development a more nimble, integrated oversight mechanism, termed Advance Cancer Translational Research Program (ACTRP) that spans multiple NCI extramural programs, and

  - development and implementation of a "SPORE Successor" Program, termed **T**ranslational **R**esearch **EX**cellence (TREX) program with flexibility as a central feature.

NCI Advanced
Cancer Translation Research Program (ACTRP)

BSA

NCI Translational Research Strategy (**NTRS**) Subcommittee

Portfolio Management DOC

Program Development

1) **disease-specific provocative questions**
2) **Set goals, milestones**

RO1　　P's, U's　　**TREX**　　NCTN

Intramural; NExT

Mechanism: Program announcements
RFA's; Precision Medicine initiative; Moonshot

Overall Broad Recommendations for Translational Cancer Research

- Ensure that the first priority for funding is to support the **highest quality science** (whether basic, translational, clinical or population).

- Maintain or **increase the current level of NCI funding** support for translational research at all stages.

- Develop incentives that will **encourage collaborations** with other academic institutions and industry.

- Increase **integration, leveraging, and interfacing of NCI currently funded translational programs** and with the biopharmaceutical industry, advocacy groups and other funding agencies to accelerate translation of scientific advances to the bedside.

SPORE Background & WG focus

- **SPORE Program launched in 1992 to provide an organ system based infrastructure for translational cancer research**

  - Translational research remains a top priority of NCI, and the SPORE program has been tremendously successful and paved our national commitment to taking science into the clinic.

  - Since it launched in 1992, our knowledge base and technological platforms have exploded since that time, requiring a re-examination of the SPORE program so that NCI can continue to accelerate translational research

  - While the SPORE program has been successful, increased flexibility in the SPORE program enabling the incorporation of more interdisciplinary research will further advance translation research

  - The WG have focused on and recommend key areas with increased flexibility that should result in more impact outcomes from investment in TREX (**TR**anslational **EX**cellence).

SPORE Background & WG focus

- **SPORE goals and requirements**

  - Focused on specific organ sites or common biological mechanism critical for promoting tumorigenesis and/or progression in organ sites

  - Requires four translational projects which must have a human endpoint

  - Each project includes a clinical and laboratory based PI

  - Supports Career Development and Developmental Research components and core services (tissue banks, biostatistics, etc.)

  - Flexibility to terminate projects early

  - Option for early detection, prevention, or population project

  - Requirement for collaborations with other SPOREs

- **Working Group focus**

  - Optimize flexibility to advance interdisciplinary translational research

SPORE Working Group Overview

- Recommendations seek to address the following needs:

  - Development and implementation of a "SPORE Successor" Program - TREX

  - Development of a more integrated translational research effort than spans multiple NCI extramural programs - ATCRP

TREX Program Specific Recommendations

- **Involvement of research advocates:** Effective involvement of research advocates with a collective patient perspective should continue to be an integral component of the TREX Program.

- **Encourage inter-institutional collaboration:** Strongly encourage impactful research projects that bring investigators from multiple institutions together. The Program should prioritize collaborative projects addressing both the most important questions within organ sites as well as "cross cancer" initiatives that focus on targeting commonly mutated genes or pathways. <u>Elimination of the requirement for a minimum number of projects</u> within each TREX will facilitate the development of both small focused projects and large scale team based projects.

TREX Program Specific Recommendations

- **Clinical investigator involvement:** Each individual research project should continue to include a clinical investigator and an investigator from another discipline.

- **Clinical endpoint:** At least one – but not all – translational research projects within the TREX program must incorporate a defined clinical endpoint.

- **TREX autonomy:** While the WG suggests enhanced coordination of the TREX Program with NCI-designated Cancer Centers, the WG recommends that the TREX Program PI retains full autonomy so as to fulfill the Program's stated goals.

TREX Program Specific Recommendations

- **Metadata consensus:** Development of and adoption of community consensus standards for clinical and biological metadata, including data security, should be key components of the TREX Program.

- **Data Management:** A TREX Program should encourage and value properly managed exchange of data between TREX Programs and with the larger cancer community and should encourage adoption of community data standards as they emerge.

- **Universal consent:** A TREX program should encourage development of a program-wide consent process that would inform patients about the: 1) risks and rewards of participating in a TREX program, and 2) possibility that some data may be made available to private sector collaborator that would enable use of individual patient information in research that is not envisioned at the time of consent.

TREX Program Specific Recommendations

- **Data commons:** A TREX program should contribute to the development of a functional data commons that will organize functional data being generated throughout the NCI research community in ways that will allow it to be readily accessed by research and clinical investigators in order to facilitate identification of causal relationships and that will contribute to the development of clinical decision support tools.

- **Laboratory models:** Informative laboratory models of important aspects of cancer should be encouraged and supported (i.e., collection of primary tumor specimens to generate patient derived xenografts (PDX) and organoids, paired germline samples, engineered tissues, etc.).

TREX Program Specific Recommendations

- **Translational cores:** The TREX Program should support translational cores to fill institutional infrastructural gaps, such as collection, archiving and distribution of tumor specimens or methodologies to support impactful research, and not overlap with existing institutional cores.

- **Career Development:** The Career Development component should be continued in the TREX Program to support the development of new translational investigators.

Recommendation: NCI Translational Research Strategy Subcommittee

Create a standing NCI Translational Research Strategy (NTRS) Subcommittee to guide the ATCRP

- Comprising extramural investigators, as well as representatives from pharmaceutical, biotechnology, computational and advocacy organization(s).

- Alignment with the NCI's Board of Scientific Advisors.

- To identify the most important opportunities to benefit patients, so as to serve as an integrated guide for NCI's translational investments.

Recommendation: NCI Translational Research Strategy Subcommittee

NTRS activities include:

- Identify the most provocative/impactful translational research questions

- Examine and identify the most important opportunities for application of new technologies to translational research

- Identify translational knowledge gaps that might be addressed by the research community

- New Funding Opportunity Announcement concepts for NCI and BSA consideration

- Provide broad advice to BSA and NCI leadership on broadening translational research portfolio; connects with the Cancer Moonshot Initiative

Conclusion

- The Working Group recognizes that translational research requires collaboration, flexibility and input from multiple stakeholders, including research advocates.

- The recommendations are intended to provide a framework that will allow increased flexibility for NCI to support translational research critical to patient outcomes, across all cancer sites.

- The Working Group realizes that these recommendations have many far-reaching implications and that translational research requires collaboration, flexibility and input from multiple stakeholders, including the advocacy community and industry.

- It is expected that a vigorous discussion in the extramural community to move forward will be required.

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