Dear ICI Community,

I am pleased to share a report on proceedings from ICI's 2019 Boston Summit as well as our plans for a new program resulting from our discussions. Development of this initiative would not have been possible without the guidance and insightful input provided by Summit participants.

Our new program will be called *ICI High Impact Collaborative Grants*. These grants will support collaborations involving multiple institutions that have high potential for near term clinical impact. A forthcoming request for proposals will explain the program in greater detail, but we wanted you to be the first to know about this new initiative.

During the Summit, participants recommended several other areas for ICI grants. These "Recommended Cancer Informatics Investment Areas" are being made available to the community for informational purposes. ICI will consider these recommendations if and when additional resources become available.

On behalf of my fellow ICI Advisors, thank you for participating in the Summit. Your efforts resulted in a new initiative that we anticipate will have a meaningful impact for cancer research and the patients we serve.

Chris Sander, PhD

Chair, ICI 2019 Summit

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2019 Summit Attendees

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Fund for Innovation In Cancer Informatics (ICI) 2019 Summit Consensus on ICI Investment Priorities

32 national leaders in cancer informatics generously chose to come together in Boston in early November of 2019 with the singular objective of helping ICI choose its first multi-year, multi-institutional collaborative investment. This effort was led by ICI Advisor, Chris Sander of Dana-Faber and a committee including ICI Advisors: Bob Grossman, Channing Paller and Niki Schultz , as well as outside advisors: Zak Kohane, Susanne Churchill, Meromit Singer and Søren Brunak.

The experts brought a wealth of innovative ideas, many of which are captured in a separate document listing potential projects. Examples: characterizing the chromatin state and 3D folding of rearranged cancer genomes, methods for analyzing and interpreting spatial molecular assays, organizing past and current metadata from "precision" or "targeted" clinical trials in a queryable form on the basis of drug target and genotypic / molecular entry, and large-scale, shared data depository of clinically generated data across both academic and community institutions.

In this document we illuminate elements of the core consensus that emerged with the ICI Summit:

ICI should target its larger investments in programs that will have near-term impact on survival and quality of life of cancer patients. The most promising area for such investment is enabling research-based decision support capabilities that will be actively used by clinicians as the direct result of ICI funded work.

Recommended investment area with potential for near term clinical impact:

Prioritize Clinical Decision Support. Improved decision support for medical oncologists, surgeons and radiation oncologists may be informed by cancer informatics initiatives directed toward the following goals shared by patients and physicians.

Goal 1: Improved / refined diagnosis, including via novel clinical assays, to give patients and physicians confidence that the selected treatment strategy is right for them and their disease.

Goal 2: Improved methods for assessment of success or failure of lines of therapy, especially reliable early indicators, so that decisions to change or continue current treatment can be made with confidence.

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A genitourinary clinician's perspective illuminates the value of these goals for patients:

With current diagnostic biomarkers, patients and physicians have limited tools to help them know whether the patient's disease is aggressive and whether it will respond to specific therapies. Early stage patients treated with active surveillance have improved quality of life and in many cases equal or greater long-term survival than those treated with surgery, radiation and/or androgen deprivation therapy. Understanding which prostate cancer patients have a cancer that may be so slow growing that they will die of other causes long before their prostate cancer becomes fatal, could help patients avoid the life-altering side effects of surgery and/or radiation. Current decision support techniques do not provide sufficient information to allow patients to make that decision confidently. Prostate biopsies also pose significant risk to patients; reliable analytics based on less invasive tools such as blood-based biomarkers or imaging may be helpful in stratifying patients to inform treatment decisions.

Further, metastatic patients may be treated with second line androgen deprivation and chemotherapy that have debilitating and potentially fatal side effects. Patients with particular mutations may benefit from more targeted approaches such as immunotherapy or PARP inhibitors.

With those goals in focus, the Summit participants identified requirements and potentially promising approaches:

Requirements for near-term clinical impact:

- Access to clinical data is essential for creation and assessment of decision support tools
- Partnerships with active clinicians with substantial patient caseloads is needed for both the initial determination of feasibility (can the needed data be gathered on patients?) and the longer-term demonstration of accuracy and utility through retrospective and prospective clinical trials.

Potentially promising clinical questions:

- How can methods for assessing "exceptional responders" in clinical trials be improved? Can cancer informatics enable genomic or multi-omic characterizations for comparisons of clinical trial patient sub-populations? In many "negative" phase II and III trials, a few patients may do very well on the experimental treatment (and are called "exceptional responders"), but the number of responders is too small to consider the drug worthy of further testing or of FDA approval. In this era of precision oncology, however, a new question is being asked: Do those "exceptional responders" have an "omic" profile that could be used as an inclusion criterion in a targeted clinical trial that would give patients with that profile or a closely related profile a promising new treatment option, through the continuing precision clinical trial and lead to a targeted therapy approved by the FDA?
- Can "omic" or imaging profiles of patients likely to respond to, or develop resistance to currently approved treatments be ascertained?
- Can the number of patients accrue to omic-targeted clinical trials be substantially increased thereby improving the chances of early approval of targeted treatments?
- How can the presentation of actionable -omic data to oncologists be improved sufficiently to substantially increase their use in treatment selection?
- Can improved risk assessment for specific cancer types from clinical records lead to substantial improvement in screening and prevention programs and early detection?

Research approaches that may be applied to answering those questions:

- Application of machine learning (ML/AI)
- Technical and semantic linking of different data types, such as genetic, molecular, image, disease state
- Multi-dimensional characterization of the definition of and transitions between disease states (resulting in actionable therapeutic biomarkers)
- Improved analytics to allow widespread use of non-invasive assays of circulating tumor DNA (liquid biopsies) for disease diagnosis and disease monitoring for disease state and response to treatment. Also for microbiome assays.
- Demonstrate methods to leverage heterogeneous omics, drug response and clinical data for deciphering regulatory pathways to study: (i) inter-patient population subtypes and intra-tumor heterogeneity, and (ii) mechanisms of drug resistance and response in cancer.
- Develop methods for single cell data analysis and single-cell precision modeling (including imaging data - multiplexed IHC) that have a direct impact on clinical trials for selection of combination therapies including immunotherapy.
- Reimagine data standardization within the scope of specific questions with clinical impact.
- Increase the available patient data by expanding direct patient participation and empower patients to share their genomic and clinical data through novel informatics techniques
- Develop methods of predicting progression of cancer from existing clinical data
- Incorporate mechanistic environment/exposures (by zip code) food desert, pollution, distance to pharmacy… to existing data sets.

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In evaluating proposals, the Summit attendees pointed out characteristics of proposals that should be prioritized:

- Direct and active participation of doctors in the development, implementation and use of the tools created through ICI funding. Oncologists are not using the tools that have been developed through past funding. Informatics proponents may claim potential clinical utility but ICI should require proof of that utility through participation of active clinical oncologists who will ask the right questions early and throughout the tool creation process.
- Partnerships with specific disease foundations that can increase the funding available to support proposed projects
- Collaboration with groups that have large databases that include clinical (EHR) data as well as omic data (Google, ASCO CancerLinQ, Veterans data, clinical trial data possibly through pharmaceutical companies)
- Support for standardized data formats (possibly through ICI grantee consensus)