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What is translational genomics? An expanded research agenda for improving individual and population health

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The mission of *Applied and Translational Genomics* is “to enhance the knowledge, clinical adoption and discussion of applied and translational genomics worldwide” [1]. But, it is still unclear what is meant by the term *translational genomics*. There are varying definitions of translational research [2] that have been applied to genomic medicine [3] and other areas (e.g., cancer survivorship research [4]).

Here, we briefly describe our view definition of translational research in genomics as spanning the whole spectrum of scientific activities going beyond the traditional “bench to bedside” model [1] to a more expanded continuum that includes improvement in healthcare and disease prevention [5]. We have previously described this framework (described as T0-T4 research) [6,7]. Currently, there is a great amount of genomic discovery research occurring that includes new genomic variants, biomarkers and other basic science discoveries (T0). Beyond the initial discovery, there are 4 overlapping phases of translational genomic research (Fig. 1): T1 research, which bridges discovery to candidate health applications, or “bench to beside”. T1 research encompasses the development of new diagnostic tests or interventions in the clinical setting but in a limited fashion. An example of T1 research would be evaluating gene–environment interactions or evaluating the function of genomic variants. T2 research evaluates the clinical utility of candidate genomic applications in clinical practice. For example, this type of research would include whether a genomic application performs better than the standard of care in improving health outcomes or developing evidence from the clinical setting to informed evidence-based guidelines. T3 research includes studies that assess implementation and integration of genomics into routine clinical practice. T3 research would include, for example, the evaluation of implementing genomic applications in community-based centers. T4 research evaluates population health impact of genomic medicine. An example of T4 research would be performing nationwide surveillance to evaluate how the implementation of a particular genomic test has affected population health.

Currently, there is very little genomics research conducted and published in T2-T4 research. For example, the NCI's Cancer Genomics and Epidemiology Navigator (CGEN <http://epi.grants.cancer.gov/cgen>), an online freely accessible tool about resources and publications for cancer genomics and epidemiology research, indicates that there are over 22,500 cancer-related genomic epidemiology (Human Genomic Epidemiology (HuGE)) publications. From the same database we see that there are currently 344 genomic applications that have been proposed for cancer care and prevention since 2009. In addition, there are only 70 evidence-based recommendations that address cancer-based genomic test. Only 26 are recommended for use of the application in a health care setting by professional

groups or guideline developers (tier 1 applications). The vast majority have insufficient evidence base or negative recommendation for use. Additionally, groups such as the Office of Public Health Genomics at the Centers for Disease Control and Prevention have made an attempt to categorize genomic applications in terms of the level of synthesized evidence for their use in a clinical setting [8] to help guide researchers, policy makers and practitioners. This is the same trend that we see over and over again in the field of genomics. There are thousands of studies that show promising genomic discoveries that lead to promising interventions. However, only a few of these interventions “stick” and make an impact on healthcare. Schully et al. [7,9] as well as Clyne [10] found that less than 2% of cancer genomics research funded by the National Cancer Institute and less than 0.5% of published cancer genomics research is T2 and beyond. Additionally, a recent analysis of the National Heart Lung and Blood Institute's genomics portfolio shows a similar trend [10]. Implementation of genomic applications that lack an evidence base can have high costs in terms of adverse health outcomes and increased health care costs.

Since it is unlikely that randomized clinical trials (RCTs) will be performed on every promising genomic application, researchers must strive to gain an evidence base for these applications by conducting appropriate observational studies [11] and comparative effectiveness research [12].

Once a promising intervention is identified in genomics, critical research is needed in order to determine if the application should be recommended for routine use in a health care setting. Behavioral and communication research also are needed to determine patterns of utilization and patient communication. Comparative effectiveness research (CER) also is needed to determine the clinical validity and utility of the applications, in comparison with existing practice. Additionally, health services and implementation research can track integration of tests in practice and measure disparities in access [13]. Additionally, multi-level research should also be performed to evaluate how an individual's external environment (family dynamics, neighborhood factors, state and federal policies, etc.) affects the overall outcomes of the genomic application [14].

If we continue to perform T0-T1 research without also addressing behavioral, CER, implementation, utilization, surveillance, and multi-level research, the promise of genomic medicine for improving health and preventing disease will not be fulfilled. All phases of translation research, especially T2+ research are integral to making a population health impact.

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