Reflections on the Founding of the International Cancer Genome Consortium

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Five years have passed since the strategy meeting that launched the International Cancer Genome Consortium (ICGC)4 in October 2007. The intervening 5 years have been a time of remarkable progress in cancer genome research, with great strides having been made toward understanding the mutational landscape of cancer and the early adoption of genome analyses in the clinical management of patients. Although progress in the field of cancer genomics has received wide coverage in the scientific literature and lay media, not much has been written about the events that led to the founding of the international consortium. Given our involvement in these events, we were asked to look back at the circumstances that attracted many of the world’s leading cancer agencies, genome and cancer scientists, ethicists, computer scientists, and other experts to work together. The common purposes were to accelerate the discovery of many new cancer biomarkers and potential cancer targets and to spur the development of new clinical tests and therapeutic interventions that would benefit cancer patients worldwide.

Fig. 1 is a slide from the opening talk at the International Cancer Genomics Strategy Meeting held in Toronto, Canada, on October 1 and 2, 2007. This meeting was convened by 6 organizations—the European Commission, Genome Canada, the National Cancer Institute, the National Human Genome Research Institute, the Ontario Institute for Cancer Research, and the Wellcome Trust. The meeting drew 122 participants from 22 countries, including world leaders in cancer genomics research, ethics, statistics, informatics, and pathology, as well as directors of funding agencies. International researchers and funding agencies used the forum to exchange knowledge and discuss the range of opportunities for a consortium initiative that would generate an atlas of genomic abnormalities in cancer.

Several motives lay behind the creation of an international consortium. First, building a comprehensive cancer genomics atlas that would cover all major tumor types and subtypes is a daunting project, one that would benefit from collaboration among countries. An international consortium could also streamline global efforts, improve standardization, facilitate comparable studies of different types of cancer, and address the spectrum of cancers worldwide. The social value of such a project was obvious, given the staggering toll of cancer on human life and the serious strain on healthcare resources due to growing cancer rates.

Meeting participants recognized, however, that several impediments and even possible adverse results could arise from creating a consortium. The high cost of the project could take resources away from other useful initiatives in cancer prevention, early detection, and treatment. The consortium could inadvertently lead to a small number of groups holding onto information for commercial purposes. If cancer genome analyses were used to develop costly new tests and therapies, future medical care might become unaffordable. The effort to standardize and share patient clinical and genomic data among countries would be confounded by differing legal frameworks among nations.

Before debating the issues involved in creating an international collaboration, pioneers in large-scale cancer genome studies shared their results and the lessons learned (1–4). One thought predominated after this session: This will be hard! We realized that existing biospecimen collections would likely not meet technological and ethics requirements, so prospective recruitment of cancer patients would be needed. It was clear that next-generation sequencing would be the key to large-scale mutational screens of many types of tumors but that this technology would evolve rapidly. Nevertheless, the opportunity to obtain truly exciting insights from a comprehensive analysis of cancer was evident and compelling. The meeting was divided into plenary and small-group sessions where a range of issues pertinent to clinical issues, tissue samples, technology, informatics, and ethics were discussed.

Meeting participants were asked to consider the issues and challenges in the context of possible consortium models. These models ranged from an “open” model in which different groups would define the different types of projects they would undertake while en-
The first strategy meeting ended with a common conviction that major advances in cancer genome research have the potential to benefit cancer patients. We tentatively agreed that the consortium would attempt to obtain a comprehensive description of all relevant genomic and epigenomic changes for 50 different tumor types. In recognition of the numerous challenges specific to each tumor type (and subtype), we agreed that the unit of organization within the ICGC would be at the level of specific cancer type or subtype. There were unanimous decisions that the consortium should adopt principles of the Human Genome Project (5, 6) regarding early release of data sets to the scientific community and that members would not make claims to possible intellectual property derived from primary data. The meeting’s immediate items were to create a secretariat in Toronto to help administer the consortium and to launch working groups that would define governance, structure, policies, and guidelines with sufficient detail so that funding organizations and scientists would know the expectations before joining the ICGC.

In April 2008, a document entitled “International Cancer Genome Consortium (ICGC) Goals, Structure, Policies and Guidelines” and coauthored by 87 participants in 9 committees and working groups was released to the scientific community (http://www.icgc.org/files/ICGC_April_29_2008.pdf). The document defined the ICGC as a confederation of members who share common goals and principles and agree to work in a coordinated and collaborative manner within a defined structure. Members include financial backers and scientific teams that take responsibility to undertake at least 1 cancer genome project, which in most circumstances involves the characterization of a minimum of 500 unique cases of a cancer type or subtype. With the potential cost of undertaking 1 cancer genome project being US$20 million, we recognized that it would take time for members to commit. We anticipated that some projects would be ready to start within 1 year, whereas others would require more time. The expecta-
tion was (and still is) that the consortium would take 1 decade to reach its goals.

Where are we today? As of October 2012, the ICGC has received commitments from researchers and funding organizations in Asia, Australia, Europe, and North America for 47 project teams in 15 jurisdictions to study more than 20,000 tumor genomes. For many of the countries that joined the project, their support to the participating scientists was the largest grant ever awarded, a testament to both the importance of the initiative for cancer patients and the belief that an international collaboration will enhance the adoption of new sequencing technologies and increase the bioinformatics capabilities of their scientific communities. More than 23,000 tumors that meet ICGC requirements for consent have been obtained, and >20,000 samples have been approved by research pathologists as meeting ICGC standards. The raw data sets now existing for >10,000 tumors include >1700 whole-genome sequences, >5130 exomes, >9700 copy number–alteration data sets, >4900 transcriptomes (RNASeq), and >6600 methylomes. Processed data are available via the Data Coordination Centre (http://dcc.icgc.org), which is based at the Ontario Institute for Cancer Research and is updated bimonthly. The latest data release (version 10) in October 2012 includes data sets from 33 ICGC members and 5 additional groups. In total, ICGC data release 10 comprises data from 7022 cancer genomes. The number of users of ICGC data sets is increasing rapidly.

More than 230 authors engaged in ICGC projects published a marker report in April 2010 (7). The report outlined the ICGC’s ethical framework, study design, use of common standards of data collection and analysis, and how the projects would proceed. The report was accompanied by the first ICGC data release, which included data sets for breast, liver, and pancreatic cancer. Since then, ICGC members have published more than 2 dozen reports on cancer genome data sets and follow-up validation studies of cancer mutations (often with associated clinical correlates for prognosis), as well as concept, methods, and policy reports [see (8–20) for examples of these publications]. The ICGC has also attracted substantial international media attention.

ICGC members are actively engaged in international working groups that discuss and refine guidelines on a number of topics, including technologies, data quality, bioinformatics, and data coordination. Although most interactions occur through teleconferences and the Internet, ICGC members meet at international workshops every 9 months.

Ethical issues, including oversight of data-access mechanisms, are coordinated by the Ethics and Policy Committee, which comprises international experts on the ethical, legal, and social issues of genomics research. The International Data Access Committee (IDAC) was formed to have oversight responsibility for the Data Access Compliance Office (DACO) and to report on data use and access issues. The DACO, housed at McGill University, handles requests for access to controlled data, which are defined as data sets containing germline genomic data and detailed clinical information from specific individuals whose personal identifiers have been removed.

The consortium’s task is far from done. Although many members are engaged in exciting translational projects (21–23), the consortium needs to focus on achieving its primary goal of generating comprehensive descriptions of genomic, transcriptomic, and epigenomic changes in 50 different tumor types to provide the comprehensive perspective that motivated the consortium from the outset. Most projects under way have generated data for only a subset of planned samples and usually only 1 or 2 of the data types that are required. In the next 5 years, the ICGC will deliver on its initial objectives and new ones, including: (a) sequencing a cumulative number of >25,000 tumor genomes from 50 or more tumor types; (b) improving the data quality of ICGC data sets; (c) developing a scalable software infrastructure to support data management and cancer genome research; (d) streamlining data-access mechanisms to accelerate usage and downstream discoveries without compromising the need to protect patient confidentiality; (e) coordinating cross-tumor analyses; and (f) training basic and clinician scientists to use ICGC data sets and tools. This final point is not to be underestimated, given that ICGC catalogues of mutations will only drive the development of new cancer biomarkers and targeted therapies and transform clinical practice, if there is strong degree of adoption by the cancer research community.

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