Advancing Clinico-Genomic Clinical Trials on cancer Workshop

E8. ACGT: A platform to facilitate future clinico-genomic research on breast cancer

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With the advent of array-based technology and the sequencing of the human genome, comprehensive analysis of the transcriptional variation at the genomic level has become possible and the knowledge derived from gene expression profiling studies is already impressive in terms of improving our understanding of the basic biology of breast cancer.

These discoveries have also challenged the current classification of breast cancer and have provided new tools to predict disease recurrence and response to different treatments, as well as new insights into various oncogenic pathways and the process of metastatic progression (reviewed in [1]).

Currently, there are even two clinical trials running which aim to achieve level I evidence for two expression-profiling signatures – the Oncotype DX recurrence score [2] and the 70-gene Amsterdam signature (Mammaprint- [3]).

In order to further refine our understanding of prognosis and prediction of response to commonly administered treatments to breast cancer patients, an increasing number of trials are characterising the tumours further using gene expression profiling or other high-throughput technology, which we will refer to as 'clinico-genomic trials' hereafter. While the goal is clear, the path to such discoveries has been fraught with roadblocks in terms of technical, scientific, ethical and legal challenges.

The underlying motivation of the EU-funded Advancing Clinico-Genomic Clinical Trials on Cancer (ACGT) project is to provide researchers and clinicians with optimal computational and IT means and resources to fight cancer, with a particular focus on breast cancer treatment. The ACGT project is responding to this vision by: 1) defining common standards of data storage at each level of investigation; 2) developing the ACGT Master ontology for cross-referencing terms and their biological contexts; 3) defining and implementing a secure architecture allowing the seamless integration of data at all levels; and 4) implementing a bio-medical GRID infrastructure offering seamless mediation services for sharing data and data-processing tools. ACGT will therefore deliver a unifying infrastructure allowing cancer researchers to share their data and to benefit from the innovative informatics tools that have been developed by other researchers.

ACGT aims to facilitate both retrospective and prospective clinical cancer research. For example, it will allow users to retrieve sets of data from public databases and query the combined data to retrieve information. To this end, ACGT will make new open source tools available for multi-level, biomedical data analysis and knowledge discovery as well as adaptation/modification of existing ones, utilise the advantages of Grid computing, and enable high-performing data-mining and biomedical knowledge extraction operations. [4]

In this way, ACGT will also help clinicians to set up new clinical trials that interconnect with the ACGT infrastructure, making future sharing and integration of the data and results easier. Specifically, ACGT is developing the 'ACGT Trial Management System' (ObTIMA), [5] which consists of: 1) the ACGT Trial Builder, which is based on the Master Ontology, developed within the project and includes the Trial Outline Builder and the Case Report Form (CRF)-Creator; 2) the Patient Data Management System, and 3) the Repository, which stores already developed CRFs and complete trials. Importantly, all security, legal and ethical conditions are and will be considered, including pseudonymisation or anonymisation of personal data, a roles and rights system and the encryption of data if necessary.

The goal of clinical cancer research will be to integrate several potential clinically relevant parameters into a comprehensive clinical decision-making algorithm that will lead us towards individualised medicine. This procedure should include traditional clinico-pathological parameters as well as imaging data, and incorporate data generated by using the new molecular tools. However, this highly complex and multi-level information will impose specific data integration requirements. So far, these different types of data are not only maintained in a variety of different data sources but are also managed by different complex data management and analytical systems. Additionally, they involve many institutions and

[1] ACGT – Advancing Clinico-Genomic Clinical Trials on Cancer. Website: http://www.eu-acgt.org; Project Identifier: FP6-2005-IST-026996; Project Coordinator*:* ERCIM (European Research Consortium for Informatics and Mathematics) – France (*Contact person:* Rémi Ronchaud); Scientific Coordinator: FORTH (Foundation for Research and Technology Hellas) – Greece *(Contact person:* Manolis Tsiknakis).

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numerous complex workflows. Projects such as ACGT are important steps towards the integration of those environments into a single comprehensive biomedical platform, herewith contributing significantly to the ultimate goal of individualised medicine.

Conflict of interest statement

None declared.

References

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