Coordinated Research Infrastructures Building Enduring Life-science services
- CORBEL -

Deliverable D3.11
Report describing informational lacunes and data enrichment strategy: Expanding the consortium and selecting samples for CORBEL Use case

WP3 – Community Driven Cross-Infrastructure joint research – Medical

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Lead partner for Task 3.5: BBMRI-ERIC (LUMC)
Contributing partner(s): ErasmusMC and BBMRI-ERIC linked 3rd parties: LUMC, THL, UTARTU, NTNU

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Content

Executive Summary

This report presents an overview of the samples of participants in four major large population cohorts, in Finland, Estonia, Norway and the Netherlands, who have developed pancreas cancer in the years after their enrolment ('cases') as well as a twice as high nr of samples of participants of the same biobanks, matched for age and gender, who have not developed this disease ('controls'). Subsequently, in close consultation with the biobanks themselves, the status of the samples has been reviewed (actual availability, presence of informed consent, availability of phenotypic data, required local and national approvals procedures and completion thereof), followed by their shipment to the centralized address of THL (Helsinki, FI). In the next phase of the research, the samples will be subjected to metabolomics data generation at Brainshake Ltd (Helsinki, FI), after which all the data will be jointly analysed by the academic groups involved, with the aim of defining early metabolomic biomarkers for presymptomatic pancreas cancer.

Project objectives

With this deliverable, the project has reached/this deliverable has contributed to the following objectives. This report covers the objectives of the first two WP3 task 3.5 sub-items:

a) Subtask 3.5.1 Collating and expanding the consortium.
b) Subtask 3.5.2 Sample selection and verification.

Detailed report on the deliverable

Background

D3.11 is part of Task 3.5: Gaining and harmonizing access to prospective patient cohorts for the development of prognostic biomarker data.
Use case: Developing robust prognostic NMR-metabolomics biomarker data for pancreas cancer: lethal, untreatable, fifth commonest cancer, unmet medical need for early detection, improved treatment and prevention). Models similar approaches.
Subtask 3.5.1 Collating and expanding the consortium.
Subtask 3.5.2 Sample selection and verification.
Subtask 3.5.3 Data generation and analysis.
Subtask 3.5.4 Dissemination.

The core of the joint activity of WP3.5 is the identification of cases and controls across several large prospective cohorts in Europe. Four of these, participating in BBMRI-ERIC, THL (FI), UTARTU (EE), NTNU (HUNT, NO), and ErasmusMC (NL), were willing to connect as a primary sample- and data-

provider user consortium. This ensured a rapid start with the definition, and where necessary, harmonization of molecular and clinical parameters, treatment outcomes and other data types.

The initially participating population cohorts and provided summary statistics suggested the availability of ~300 incident cases, consistent with the estimated pancreas cancer incidence of 5-7/100.000 or even suggesting that this may have been underestimated due to incomplete ascertainment in disease registries. Considering the size of the national population cohorts, we expect that this figure can be easily doubled in a later rollout through Europe.

Description of Work

A table of required phenotypes was agreed upon as per below:

Table 1: Required sample data (admin and phenotypes)

Sample ID
Sample date (dd-mm-yyyy)
Material available (Plasma)
Fasted/nonfasted (F/N/F+N)
Age (yr)
Gender (M/F)
Date diagnosis (dd-mm-yyyy)
Deceased (y/n)
Date of death (dd-mm-yyyy)
Brainshake metabolomics done (y/n)
Smoker (cig/d)
Past smoker (cig/d)
Smoked till (dd-mm-yyyy)
BMI
Alcohol consumption (qty/t)
Past alcohol consumption (qty/t)
Alcohol till (dd-mm-yyyy)
Type2Diabetes (Y/N)
Blood pressure (sys/dia)
Any other morbidities recorded

Subsequently an inventory was made of the number and status of the samples in each biobank, which fulfilled the criteria of cases or controls. The existing phenotypic data (Table 1) are to be complimented by metabolomic analysis from the inventoried samples. The analysis will be conducted by Brainshake Ltd applying quantitative nuclear magnetic resonance (NMR) metabolomics platform, which offers a wide range of metabolites to identify biomarkers for pancreatic cancer.

Table 2: Summary of cases and controls per participating data/sample provider

Source	Cases (n)	Controls (n)	Required Metabolomics (n)
THL	60	120	60*
UTARTU	81	162	243
NTHU/HUNT	235	470	705
ErasmusMC	115	230	345
Total	491	982	1343

* Of the 120 THL controls Brainshake metabolomics data are already available

The final sample count (Table 2) was in fact higher than initially anticipated (around 350 cases and 700 controls). This is mostly due to initial counts being somewhat outdated while once the actual project started, most biobanks had more recent data available from the cancer registries. This is only beneficial from statistical point of view, while the additional cost has in fact been offset by volume cost reductions.

In all the respective countries the material transfer procedures have been initiated as early as possible (even before all the actual data and precise sample counts were obtained). This entailed ethical and legal permission to share and analyse samples transnationally, which in the different countries turned out to be subject to very different procedures and requirements, and this was a very lengthy procedure. It started in the spring of 2015 and was only recently completed. This is a point worth emphasising as many current projects require transnational sample- and data sharing. In all cases this required the generation of *de novo* MTAs in which the specifics of this project needed to be duly taken into account. Presently all the MTAs are signed, the Estonian, Finnish and Norwegian samples have arrived at THL while the Dutch samples are ready for shipment and are expected at the end of August – they were held over the holidays to reduce sample shipment risks during the summer vacation period.

Next steps

The next step, to be accomplished in the fall of 2016, is the actual metabolomics data generation. There is little delay foreseen in this phase as the cost estimates have been received – and fit the budgeted funds – and Brainshake Ltd deals with both larger and smaller sample batches on a regular basis.

Publications

No publications have as yet been generated, but one of the publications will deal specifically with the practicalities of hands-on transnational sample- and data sharing.

Delivery and schedule

The delivery is completed herewith.

Adjustments made

We note that we may need to postpone one of the next milestones, enrolling additional biobanks. Due to the delays sustained in the material transfers, the actual data analysis in the discovery phase may need more time than anticipated, and it is not useful to approach biobanks for validation before we actually have results that require validation. Adjustments are therefore expected.

Appendices

N/A