COBRED
Colon and Breast cancer Diagnostics

Summary

COBRED aims at the discovery of colon and breast cancer biomarkers for patient follow-up (monitoring markers). COBRED will exploit the high-throughput analysis capacity of transcriptomics, proteomics and metabolomics technologies in an integrated systems biology approach and the expertise of biotech SMEs and academic partners to discover biomarker candidates. Two clinical institutes renowned for their expertise in colon and breast cancer will participate in the study with the design and execution of a prospective clinical collection and will carry out the biological and clinical validation of the efficiency of the identified biomarkers. After 3 years COBRED will deliver a set of biomarker candidates verified in preclinical studies, ready for large scale clinical validation and further development for commercialization by the respective SME partners. Furthermore COBRED will have demonstrated the potential to explore consolidated data resulting from different high-throughput technologies and clinical profiles with advanced data mining technologies for enhanced biomarker discovery.

Although within the project scope COBRED focuses on biomarkers for follow-up diagnostics, it has the potential to evolve to an early cancer detection & screening tool.

Problem

An apparent paradox of current cancer epidemiology is that while new therapies and diagnostics improve survival rates in common cancers, e.g. colon and breast cancer, the incidence rates are also increasing, thus the net effect is negative.

Colorectal cancer (CRC) is the third commonest cancer type worldwide: in the year 2000 the global incidence was about 1 million, close to 10% of all cancers, and it resulted in about 0.5 million deaths, equalling of about 8% of all cancer mortality. Breast cancer (BC) is the most common cancer in Western women. In these patients, it is not the primary tumour, but its distant metastases that are the main cause of mortality. The yearly incidence rate is over 0.5 million (630 000 new breast cancer cases) that results in about 0.2 million deaths. Recently, the rates of metastasis and mortality in BC patients have decreased as a result of early diagnosis by mammographic screening and the implementation of systemic adjuvant therapy similarly to CRC. There is ample, but ‘only’ circumstantial evidence that derives from survival data of patients with early stages of cancer, suggesting that earlier diagnosis would allow 10-20% survival rates improvement. In fact, the potential benefits of early CRC and BC diagnosis are so high that a wide range of community and governmental efforts have been implemented for population wide screening.

Biomarkers are substances found in the blood, other body fluids (e.g., urine) or tissues that alone or in combination may signal the presence of cancer or the risk for cancer. Diagnostics based on biomarkers have the potential to significantly improve current cancer diagnostic means, providing a higher sensitivity (i.e. much smaller tumours can be detected), easier and faster and at a much lower cost. Biomarker discovery and validation, similarly to drug discovery and validation, is a long process with high rate (60-80%) of attrition of candidate biomarkers along the major steps of qualification that ultimately ends in the approval by the Food and Drug Administration (FDA) in the US and the European Agency for the Evaluation of Medicinal Products (EMEA) in the EU. Often, seemingly good candidates that have been identified and found valuable in one study do not show the expected predictive values in the second study. In fact, the number of new diagnostics approved per year is decreasing in sharp contrast to the intensifying biomarker discovery efforts. Thus, despite having the highest potential value in numbers, COBRED choose not to pursue the discovery of screening markers because of economic and logistic impracticalities of a large scale screening-maker validation in BC and CRC. Instead, we focus on the second largest clinical need, the improvement of patient follow up, by the discovery of monitoring markers, which are expected to report relapse, metastasis and minimal residual disease at earlier stages, which are more amenable to surgical and chemotherapy treatment, and more likely to improve cancer patient survival.

Aim

The specific RTD objectives are to:

- design a clinical protocol for prospective clinical BC and CRC collections that fit the needs of the 3 high-throughput screening technologies used: transcriptomics, proteomics and metabolomics;
- identify biomarker candidates (metabolites, proteins, PBL derived mRNAs) capable to detect and assess the status of minimal residual disease, metastases and recurrence after surgery and chemotherapy;
- develop a centralized database to integrate the data generated by the 3 technology platforms with the anatomo-clinical information of the clinical collections;
- discover biomarkers with better specificity and sensitivity using across-platform advanced data-mining techniques on the combined data from the consolidated database;
- validate the biological relevance and diagnostic potential of the identified biomarkers by testing their specificity on tissue arrays and in relevant preclinical models.
Expected results

Specific project results will include:
- sets of biomarkers (gene signatures, proteins, metabolites or a combination of these) that will be considered clinically relevant for early diagnosis of primary BC and CRC and relapses;
- central repository system hosting the results from the technological platforms and the relevant clinical data;
- prospective clinical collection of BC and CRC;
- clinical validation for the diagnostic potential of subsets of the identified biomarkers in comparison to existing biomarkers and to currently available imaging techniques;
- preclinical models for the biomarker evaluation and biological studies.

Potential applications

Diagnostic kit for the detection of cancer recurrence and metastasis, with the longer term goal to develop early cancer detection tests amenable for population screening.