Success Story 2018
COMET

CBmed GmbH
Center for Biomarker Research in Medicine
Programme: COMET – Competence Centers for Excellent Technologies
Programme line: K1-Centers
COMET sub-project 2.51, duration and type of project:
FUSION Technology – Showcase Study Colon Cancer Stage II
07/2016 – 12/2018, strategic

FUSION Technology – A Systems Biology Approach Towards Predictive Biomarkers for Relapse Risk in Stage II Colon Cancer

Colon cancer (CC) belongs to the most commonly diagnosed malignancies among men and women in the developed world, with an estimated 140,250 new cases being diagnosed in 2018 in the US alone, including 50,630 estimated deaths in 2018. Identification of high-risk patients with stage II CC is difficult and currently defined by several clinicopathological risk factors. Although the current risk definition for stage II CC-patients is still recommended, new prognostic and predictive markers for patients potentially profiting from adjuvant chemotherapy (CTX) represent a clinical need. CBmed therefore took a FUSION Technology – assisted multi-platform approach towards biomarker discovery for stage II colon cancer risk prediction.

FUSION Technology Showcase Study: Stage II Colon Cancer

To tackle this problem, we aim to identify novel biomarkers predictive of stage II CC relapse risk, utilizing an integrated, data-driven multi-scale approach for combined analyses of biological data layers obtained through six different CBmed technology platforms: NGS, LC-MS/MS Proteomics, MALDI-MS, Metabolomics, Immune Profiling, and Digital Pathology plus Clinical Data.

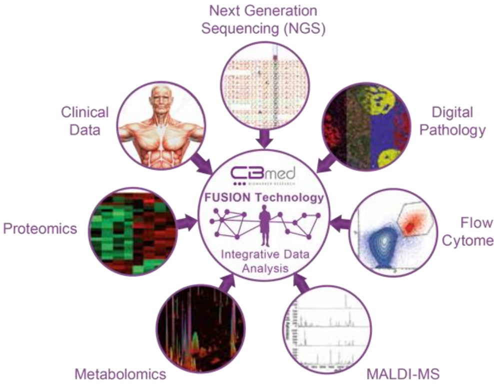

Fig 1: FUSION Technology Multi-Platform Approach

FUSION Technology IT Infrastructure

Data processing and computational data analysis capabilities are required to handle the resulting heterogeneous complex data sets. To this end we set up an in-house IT infrastructure providing capability for efficient data processing and bioinformatics downstream analyses.

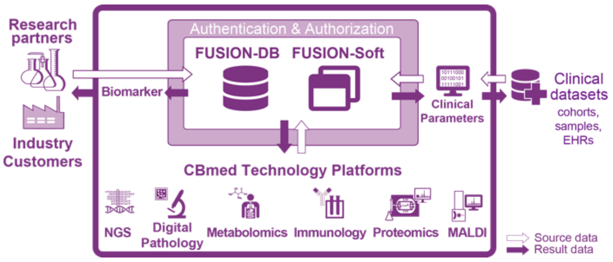

Fig 2: FUSION Technology IT Infrastructure

A versatile FUSION-DB database infrastructure organizes both structured (SQL) and unstructured (NoSQL) data to facilitate fast and flexible data access for statistical analyses. Data access and analysis are supported by FUSION-SOFT.

bmwfw Bundesministerium für Wissenschaft, Forschung und Wirtschaft
bmvit Bundesministerium für Verkehr, Innovation und Technologie

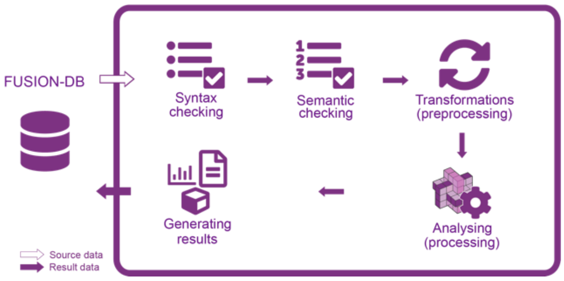

Fig 3: FUSION-SOFT Architecture

FUSION-SOFT is a custom software environment providing a range of relevant opensource and in-house bioinformatics plugins and workflows.

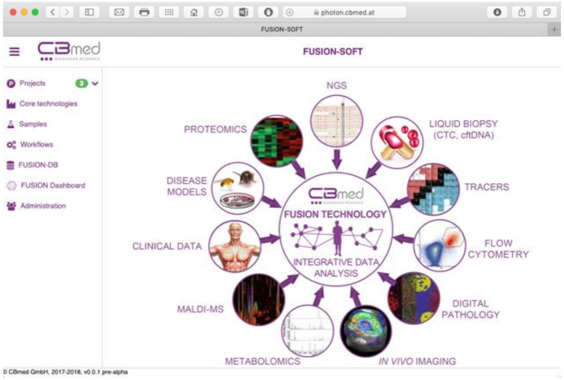

Fig 4: FUSION-SOFT GUI & Dashboard

FUSION-SOFT includes dashboard capabilities that ease data access and analysis.

Biomarker Candidates for Relapse Risk Prediction in Stage II Colon Cancer

First results obtained from NGS analyses indicated differing mutational patterns in the KIT and KRAS genes comparing relapse vs. relapse-free patients. Systems-level FFPE tissue LC-MS/MS proteomics revealed two clusters, one of which is enriched in relapse. We performed Machine Learning feature selection using Random Forest (RF), and found 4 proteins that were consistently predictive in linear logistic regression models (AUCs > 0.8). Signatures of 3, or 4 increased the predictive performance to AUCs ≥ 0.9.

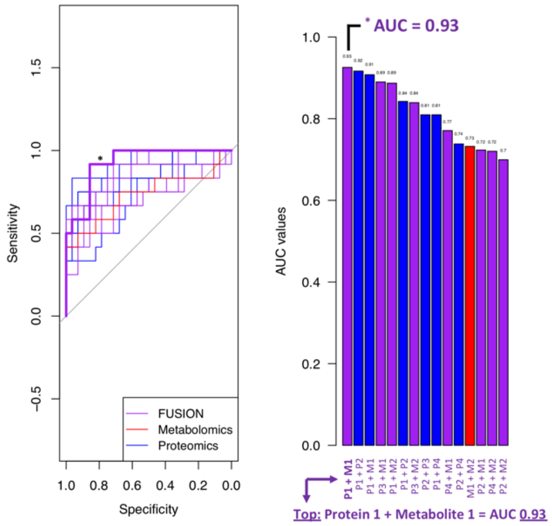

Fig 5: FUSION Technology Multi-Omics Biomarker Candidates of Stage II Colon Cancer Relapse

RF analysis identified 2 high-confidence predictive metabolites (AUCs > 0.7). Strikingly, combination of protein and metabolite features (Fig. 5, purple) can increase predictive performance. and the best predictor is comprised of a tissue-derived protein and a liquid biopsy-derived metabolite. This underlines the power of a multi-scale, systems-level FUSION Technology approach to biomarker discovery. Further analyses will assess additional integrated analyses, machine learning, and integrated network modeling, towards validation of these candidates.

Benefits & Impact of FUSION Technology

FUSION Technology computational data science capabilities and infrastructure enable CBmed biomarker research through support in data management and processing of complex multi-platform, data-driven projects. Already, FUSION-DB, bioinformatics expertise, and first algorithmic workflows in FUSION-SOFT support CBmed core technology platforms, such as next-generation sequencing (NGS) and digital pathology data analyses. In the future, these assets will support CBsolutions (non-K) projects.

Contact Details and Information

K1-Centre CBmed

CBmed GmbH
Stiftingtalstrasse 5, 8010, Graz
+43 316 385 28801
office@cbmed.at
www.cbmed.org

Project coordinator
Dr. Marc Brehme, M.Sc., Ph.D.

Project Partner

Organisation	Country
Joanneum Research GmbH (JR)	Austria
Medical University of Graz (MUG)	Austria
Medical University of Vienna (MUW)	Austria