Molecular Oncology

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EACR 2023 Congress Abstracts

Contents

Proffered Papers

10-minute talks awarded for the highest scored abstracts, embedded in the scientific symposia sessions. These presentations are not accompanied by a poster.

Posters in the Spotlight

Tuesday 13 June, 17:30 - 18:30, Poster and Exhibition Hall
Wednesday 14 June, 17:15 - 18:15, Poster and Exhibition Hall

Dedicated sessions taking place in the spotlight area within the Poster and Exhibition Hall. Poster presenters with high scoring abstracts will give short presentations of up to 10 minutes. Their posters will also be available to view during the Poster Discussion Sessions.

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Introduction

Intra-tumoral heterogeneity represents a major challenge for the effective implementation of precision oncology and underlies the modest predictive value of biomarker discovery based on cancer cell lines. Previous work by our group has shown that breast cancer patient-derived xenografts (PDTXs) and PDTX-derived tumour cells (PDTCs) robustly recapitulate intra-tumoral heterogeneity. It also developed a platform for high-throughput drug screening in PDTCs. This study aims to integrate the baseline molecular landscape of tumours with response data from breast cancer PDTC high-throughput drug screening using machine learning to characterize pharmaco-omic associations.

Material and Methods

PDTCs from 34 different models were treated ex vivo with 67 different compounds at 7 different concentrations. The compounds were either approved cancer treatments or drugs targeting key cancer pathways. Viability was measured by Cell-Titer-Glo (CTG) after 7 days and area under the dose-response curve (AUC) was calculated to determine therapy effectiveness. Shallow whole genome sequencing, whole exome sequencing, RNA sequencing, methylation-sequencing, protein mass cytometry and reverse phase protein array profiles were obtained from the same models. A defined set of metrics were computed and integrated to build a predictive model of drug-response using machine learning characterizing the landscape of pharmaco-omic associations.

Results and Discussions

Compounds were filtered based on the response pattern across the models. 67/67 drugs tested had at least 2 models showing response (AUC>0.2) and at least 2 models showing resistance (AUC<0.2). A wide range of low- and high-level features were computed. We show that several molecular features such as tumour mutational burden and chromosomal instability are associated with in vitro drug response in high-throughput drug screening, and that results recapitulated known mechanisms of sensitivity and resistance while identifying multiple new candidate biomarkers. In addition, we show that the integration of multi-omic features using machine learning achieves superior predictive performance after cross-validation and suggests novel biomarkers.

Conclusion

PDTXs and PDTCs are a powerful platform in pre-clinical cancer research. Here, we have demonstrated the potential of coupling high-throughput drug screening with multi-omic profiling for novel biomarker discovery and drug development.

EACR23-0485

Biomarker potential of the transcript PHF19-207 in colon cancer

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Introduction

Recent data from a comprehensive pan-cancer transcriptome analysis demonstrated differential activity of two alternative *PHF19* gene promoters in malignant vs. non-malignant gut mucosa. The promoter found to be up-regulated in colon and rectal cancer gives rise to the transcript PHF19-207. This finding has pointed to the biomarker potential and possible tumor-promoting role of this transcript. Our study aimed to evaluate the expression of PHF19-207 in colon cancer, as well as to investigate its potential function using *in silico* tools.

Material and Methods

Immortalized colonic epithelial cell line isolated from healthy tissue (HCEC-1CT) and a set of colon cancer cell lines (Caco-2, HCT116, HT29, DLD-1, SW480 and SW620) were used. The expression analysis of PHF19-207 transcript was performed using qPCR. For *in silico* analysis, Coding Potential Calculator tool and AnnoLnc tool were used.

Results and Discussions

The expression analysis demonstrated that the expression of PHF19-207 was increased in all malignant cell lines in comparison to the non-malignant cell line HCEC-1CT (2 to 5-fold). Also, the more prominent increase was observed in the cell lines originating from later stages of colon tumors. Based on Coding Potential Calculator tool, PHF19-207 was classified as non-coding, with coding probability of 0.2. The AnnoLnc tool indicates its downregulation of PHF19-207 in normal colon tissue and its upregulation in cancer tissue samples. The same tool indicates nuclear localization of the PHF19-207 transcripts.

Conclusion

The results of expression analysis confirm potential of PHF19-207 as diagnostic biomarker, while the results of *in silico* analysis suggest that this transcript may be a lncRNA with role in gene expression regulation. Further research on this RNA molecule should aim for functional studies to investigate its role in colon carcinogenesis.

EACR23-0495

An activity-based biomarker for identifying homologous recombination deficiencies across cancer types in real-time

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Introduction

Homologous recombination (HR)-mediated DNA repair is a prerequisite for maintaining genome stability. Cancer cells displaying HR deficiency (HRD) are selectively