

BITS :: Call for Abstracts 2024 - Oral communication

<i>Type</i>	Oral communication
<i>Session</i>	Multi-Omics
<i>Title</i>	Unveiling Drug sensitivity and GPCR Expression Patterns: A Gateway to Targeted Cancer Therapy
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<i>Motivation</i>	<p>In the intricate ecosystem of cancer biology, G protein-coupled receptor (GPCRs) play a key role exerting substantial influence on cell signaling networks and the complexity of the tumor microenvironment. These versatile receptors, which include a wide range of ligands and downstream effectors, act as channels for extracellular cues, finely regulating cellular behaviors such as proliferation, migration and survival. Given their role as gatekeepers of cellular responses to endogenous and exogenous stimuli, GPCRs represent promising targets for pharmacological intervention in cancer therapy.</p> <p>Numerous studies are emerging on the effectiveness of both agonists and antagonists in modulating GPCR signaling pathways and their impact on tumor progression. Intriguingly, the dichotomy between agonist and antagonist actions of GPCR-targeting drugs can exert divergent influences on cellular signaling pathways and tumor progression. Our main motivation was to meticulously organize the wealth of data regarding the expression of G-protein-coupled receptors (GPCRs) in cancer cell lines and the consequent effects of GPCR-targeted drugs. By synthesizing and structuring this knowledge, our goal is to provide a resource that not only elucidates the complex interplay between GPCRs and cancer, but also enables the scientific community to develop more effective therapeutic strategies.</p>
<i>Methods</i>	<p>We based our analysis by integrating the DepMap transcriptomic database to extract basal gene expression data from various cancer cell lines and on the L1000 database for its differential gene expression profiles after treatment with various compounds. To evaluate the response to these GPCR-targeted drugs, we cross-referenced the data obtained with the Prism response database.</p> <p>Intersecting these data sets, we delineated the impact of GPCR-targeted drugs on gene expression of cancer cell lines. In addition, Gene set enrichment analysis (GSEA) was conducted to identify significant alterations in gene expression patterns after drug treatment. We implemented such an integrated resource through a Shiny webapp called DISCOVER: Drug impact, sensitivity modification and viability response on GPCRs expression patterns in cancer cell lines. DISCOVER collects and analyzes transcriptomic data in correlation to drug response based on the specific tumor subtype of the cell lines, providing multiple descriptive and analytical graphs. The R packages ComplexHeatmap, clusterProfiler, pathview and enrichplot were applied to these analyses.</p>
<i>Results</i>	<p>Our application makes use of several comprehensive databases of cell line transcriptomes to analyze the GPCR landscape and assess how specific GPCR-targeting drugs influence cancer cell viability and the expression profiles.</p> <p>By integrating high-throughput transcriptomic data from diverse cancer cell lines our resource enables researchers and clinicians to explore the dynamic interplay between GPCRs, G-protein and cancer phenotypes. Through analytical tools and interactive visualizations, users could discern patterns of GPCR expression, identify candidate receptors driving oncogenic signaling pathways. Moreover, our platform facilitates the evaluation of GPCR-targeting drugs, enabling users to assess their efficacy, specificity on the different cancer type. For instance we found a wide number of cases where a GPCR drug elicit potent sensitivity responses only on specific cell lines (e.g. CHRM3 antagonist Xanomeline in hepatocellular carcinoma lines). Intriguingly, we also found that agonists and antagonists for the same receptor family (e.g. adrenergic receptors) display potent growth inhibition capabilities in a cell line dependent manner, underlining the importance of specific transcriptional programs in dictating the response to the drug. The app provides a user-friendly interface for querying, analyzing, and interpreting transcriptomic data, empowering researchers and clinicians to identify potential therapeutic targets and optimize treatment strategies for various cancer types.</p>
<i>Info</i>	-
<i>filename</i>	-
<i>Figure</i>	-
<i>Availability</i>	-
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Summary

GPCRs have been shown to have considerable influence on cancer biology. Our research dives deep into their role, revealing how targeted drugs can reshape cancer's landscape. With our platform, researchers can pinpoint new treatment avenues, pushing forward knowledge of possible therapies for cancer.

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