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METABOLIC PROFILING OF CANCER CELLS IDENTIFYING METABOLIC VULNERABILITIES FOR TARGETED THERAPY IN PATIENTS OF QUETTA, BALOCHISTAN, PAKISTAN

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Abstract

The current research was performed from March 2022 until June 2022 by following the guidelines of a joint clinical research committee of Bolan Medical Complex and the University of Balochistan Quetta. To pinpoint distinct metabolic changes linked to various types of cancer commonly found in the Quetta, Balochistan region. To Create individualized treatment approaches using the recognized metabolic weaknesses, to enhance treatment effectiveness and reduce adverse effects for cancer patients living in Balochistan. The ability to uncover new targets for cancer therapy has made metabolic profiling of cancer cells a crucial field of research in cancer biology. For many years, it has been common practice to utilize NMR spectroscopy, especially in vivo magnetic resonance spectroscopy (MRS) and high-resolution solution-state analysis of tissue extracts, to differentiate between various cell lines and tumor types. Given the diverse population and distinct environmental influences, comprehending the metabolic intricacies of cancer cells in this locality is pivotal for crafting efficient treatment methodologies. Metabolic profiling, an innovative method, entails recognizing exclusive metabolic patterns within cancer cells, providing valuable clues to vulnerabilities that can be pinpointed for precise therapeutic interventions. Metabolic profiling is the process of analyzing the unique metabolic characteristics of cancer cells compared to normal cells. The cells should be collected under sterile conditions and kept in a suitable medium until analysis. Cancer cells tend to consume large amounts of glucose, even in the presence of oxygen, leading to increased levels of lactate production. Cancer cells may exhibit changes in the regulation of lipid synthesis, storage, and utilization, which can impact cellular signaling and membrane function. By analyzing the metabolites in cancer cells and comparing them to normal cells, researchers can gain insights into the metabolic alterations that occur in cancer. Such cancer cells can be employed for many things, like diagnosis, prognosis, and the creation of fresh therapeutic approaches. In conclusion, metabolic profiling of cancer cells is a rapidly evolving field with the potential to improve our understanding of cancer biology and to identify new therapeutic strategies for cancer. It can be used to identify new targets for immunotherapy. Cancer cell's metabolic properties can affect how they interact with the immune system, and targeting metabolic pathways could enhance the efficacy of immunotherapies.

Keywords: *Bolan Medical Complex, Cancer cells, Immunotherapy, Metabolic profiling, NMR spectroscopy, Quetta, Targeted therapy, Therapeutic vulnerabilities*

INTRODUCTION

Metabolic profiling of cancer cells refers to the study of the metabolic pathways and activities that occur within cancer cells (1). Cancer is a global health emergency that affects a wide range of individuals without distinction and crosses national borders. The fact that cancer is becoming more common and affecting both wealthy and developing countries shows how urgent the problem is. It is a major contributor

to morbidity and mortality worldwide, placing a heavy cost on economies, healthcare systems, and most crucially, individuals and families (2). Cells use the metabolic process to transform foods into energy and the structural components needed for cell division and growth. Cancer cells have altered metabolic pathways that enable them to sustain rapid growth and proliferation, and these alterations can provide a distinct metabolic signature that separates cancer cells from healthy cells. Metabolic profiling of cancer cells has become an important area of research in cancer biology and has the potential to identify novel targets for cancer therapy (3). A recurring theme in this research is that, in conditions of nutrient abundance, oncogenic signaling pathways promote nutrient uptake and promote the incorporation of carbon into macromolecules including lipids, proteins, and nucleic acids. These actions support cell growth and proliferation as a whole (4). The high incidence of cancer in Quetta, Balochistan, highlights the need for and need of carrying out a metabolic profiling study. With the ultimate goal of lowering the incidence of cancer and improving patient outcomes in Quetta, Balochistan, Pakistan, the study intends to pave the way for more efficient, customized, and region-specific treatment approaches by identifying and comprehending the metabolic vulnerabilities inherent to the most common cancer types in this area (5).

For many years, it has been common practice to use Nuclear magnetic resonance (NMR) spectroscopy, which includes in vivo magnetic resonance spectroscopy (MRS) and high-resolution solution-state analysis of tissue extracts (6). Because there are so many interconnected metabolic pathways, even if NMR spectroscopy only detects a relatively small number of metabolites, it can nonetheless be utilized to track the activity of several cellular processes. So it is possible to use changes in the metabolome to track a number of seemingly unrelated pathways. Despite its limits in sensitivity and its inability to measure a wide variety of metabolites, MRS has been used to assess a variety of tumor forms in humans and in animal models of cancer. Metabolomics profiles have been effectively utilized to differentiate between tumor types and between cell lines (7).

Metabolic profiling of cancer cells is an important tool in the development of targeted cancer therapies (8). By identifying metabolic vulnerabilities, researchers can develop more effective and personalized cancer treatments that have fewer side effects and are more targeted to the cancer cells themselves (9).

The analysis of the distinct metabolic traits of cancer cells in comparison to healthy cells is called metabolic profiling (10). This research can show whether particular metabolic pathways are turned on or off in cancer cells as opposed to normal cells. Once the specific metabolic paths that are switched on or off in cancer cells are identified, researchers can search for specific targets within these pathways (11). Targets are specific enzymes or proteins that are essential for the function of a particular metabolic pathway. Targeting these proteins or enzymes can disrupt the metabolic pathway and induce cancer cell death.

Cancer cell metabolic profiling has become a widely researched field due to its potential to identify metabolic vulnerabilities that a cancer therapy could aim to target (12). The metabolic profiling in cancer research, discussing the various technologies and techniques used to identify metabolic alterations in cancer cells (13). The authors also discuss the potential of targeting cancer metabolism for therapeutic interventions (13).

The application of metabolomics in cancer research, discussing the technologies used for metabolic profiling and their applications in cancer diagnosis, prognosis, and treatment (14). The potential of targeting metabolic reprogramming in cancer as a therapeutic strategy, highlighting the challenges associated with developing selective inhibitors and identifying potential drug targets (15)

MATERIALS AND METHODS

Metabolic profiling of cancer cells involves the comprehensive analysis of the metabolic changes that occur within cancer cells.

STUDY DESIGN AND RESEARCH AREA

This cross-sectional study was conducted at Bolan Medical Complex and Hospital (BMCH), and Cenar Cancer Hospital, District, Blochistan province of Pakistan. The Area of Quetta district was 3,447 km² and whiles it has the population of 1,001,205 (Census, 2017). Geographically, the Quetta district has snow

covered mountains, arid high land, desiccated deserts and long dry coastal areas. These high mountains are mostly situated 1500 m above sea level. The study was performed from March 2022 until June 2022 by following the guidelines of a joint clinical research committee of Bolan medical complex and University of Balochistan Quetta.

SAMPLE COLLECTION AND PREPARATION

The 121 cancer cell samples were obtained from the patients who had been diagnosed with different forms of cancers. These samples were obtained by following strict sterile protocols to avoid contamination and preserve the integrity of the samples, using well-established biopsy techniques. During the collection process, sterile conditions were used to obtain cancer cells or tumor tissues from the patient. The cells were then preserved in the proper medium until the analysis is completed.

EXTRACTION OF METABOLITES

The cancer cell samples were collected and metabolite extraction was performed. To accomplish this, metabolites must be extracted from the cellular matrix using appropriate extraction methods, such as solvent-based extraction methods based on methanol or chloroform. The metabolites were then separated from other substances and cellular waste using techniques such as centrifugation or filtration. A suitable method should be used to extract the metabolites from cancer cells. Organic solvent extraction, solid-phase extraction, and liquid-liquid extraction are all common methods (Fig. 1). In order to separate metabolites from cancer cells, we used the organic solvent extraction method. In order to effectively maintain the cellular metabolome, the process comprised obtaining the cancer cells and quickly stopping cellular metabolism using a cold solvent mixture, usually a methanol and water mixture. After the cells were lysed to release intracellular metabolites, the lysate was centrifuged to remove any remaining cell debris. Next, using a rotary evaporator, the supernatant containing the isolated metabolites was carefully gathered and evaporated until it was completely dry. Comprehensive profiling of the cancer cell metabolome was made possible by reconstituting the residue in a suitable solvent for additional analysis, such as nuclear magnetic resonance (NMR) or liquid chromatography-mass spectrometry (LC-MS).

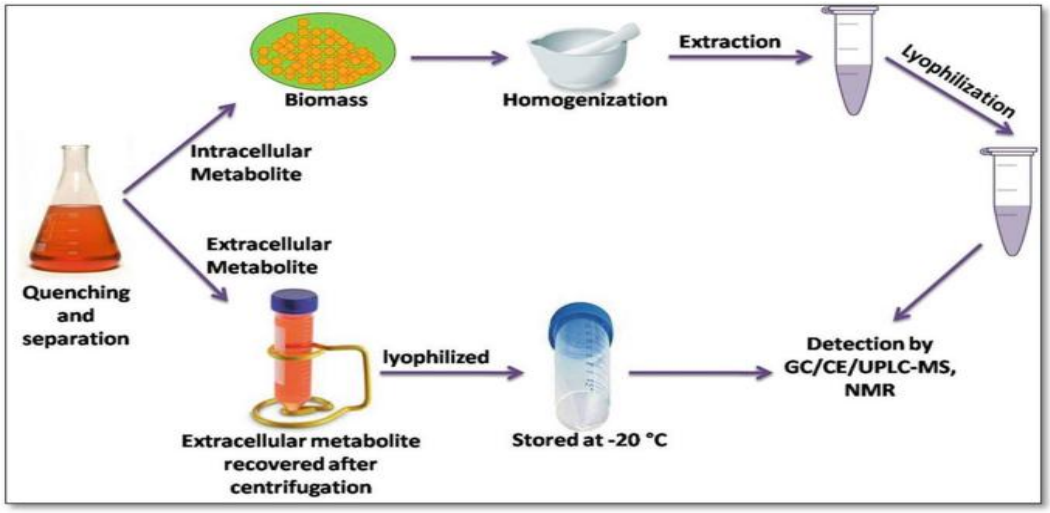

Fig. 1. Extraction of metabolites from the cancer cells (Separation/ Extractions of cancer cells, storage of samples, Organic solvent extraction, Solid-phase extraction and Liquid-liquid extraction)

METABOLIOTE SEPARATION

The metabolite separation process typically begun after metabolites had been extracted from the cellular matrix using solvent-based extraction techniques such as methanol or chloroform. These metabolites were extracted, and then other methods were used to isolate and separate them for further analysis. Metabolites could be separated using methods such as capillary electrophoresis (CE), gas chromatography (GC), and liquid chromatography (LC) after extraction. One of the most common techniques for metabolite separation is chromatography, which comes in various forms such as liquid chromatography (LC) and gas

chromatography (GC). Liquid chromatography-mass spectrometry (LC-MS) and gas chromatography-mass spectrometry (GC-MS) are two techniques commonly used in metabolic profiling.

On the other hand, metabolites were separated using gas chromatography-mass spectrometry (GC-MS) based on their volatility and interactions with a stationary phase and a gaseous mobile phase. Following separation by gas chromatography, the separated metabolites were detected and analyzed using mass spectrometry. Using both GC-MS and LC-MS, high-resolution metabolite separation and identification from the samples was possible. Chromatographic separation can distinguish and detect different metabolites based on their distinct characteristics, which include fragmentation patterns, mass-to-charge ratios, and retention times.

METABOLOTE IDENTIFICATION

Mass spectrometry was used to find and measure the mass-to-charge ratios of ions formed from isolated metabolites. High-resolution mass spectrometry greatly aids in the identification of metabolites. This procedure allows the molecular weight of metabolites to be calculated, which aids in identification. Nuclear Magnetic Resonance (NMR) spectroscopy can also reveal information about the composition and chemical structure of metabolites. The identification of specific metabolites within the samples was aided by the comparison of spectrum data against published databases. When these cutting-edge analytical techniques were combined, they allowed for the accurate detection and description of metabolites, revealing distinct metabolic patterns and susceptibilities in cancer cells in Quetta, Balochistan (Fig. 2).

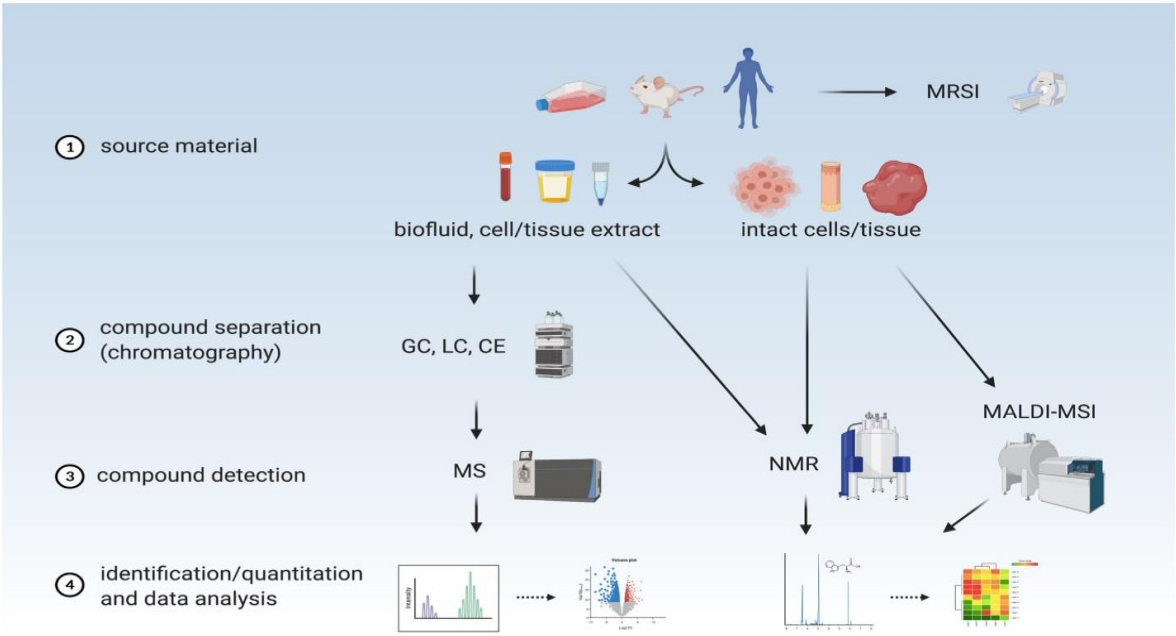

Fig. 2. Metabolite identification of cancer cells (Steps of identification of cancer cells)

ETHICAL CONSIDERATION

Human samples were used in accordance with ethical standards and regulations. Each patient gave their consent, and their privacy and confidentiality were respected.

STATISTICAL ANALYSIS

Statistical methods were used to examine the identified compounds and discover distinct metabolic pathways that were differently regulated in cancer cells. Principal Component Analysis (PCA), hierarchical clustering, and pathway analysis were the most frequently used statistical approaches. Initially, peak intensities or areas obtained from methods such as mass spectrometry (MS) and nuclear magnetic resonance (NMR) spectroscopy were used to quantify metabolites. These quantified metabolites were then statistically compared between sample groups using techniques such as ANOVA, t-tests, or non-parametric testing to detect significant differences in metabolite levels between healthy controls and various types of cancer. Principal Component Analysis (PCA) and Partial Least Squares Discriminant Analysis (PLS-DA) were two multivariate analyses used to identify more general patterns within multiple metabolites at the same time.

These analyses aided in the identification of various metabolic profiles linked to various cancer types prevalent in Quetta, Balochistan. To ensure reliable comparisons, normalization and other data pretreatment techniques were used, and False Discovery Rate (FDR) corrections were also used.

VALIDATION

The validation process included a number of steps, such as using quality control samples to monitor instrument performance and ensure data acquisition uniformity. Furthermore, the identity of the metabolites found in the samples was confirmed using reference substances or established standards. The findings were confirmed by corroboration using known databases and previously validated procedures, ensuring the validity and robustness of the metabolic vulnerabilities discovered in cancer cells.

BIOLOGICAL INTERPRETATION

Patients in this study area exhibited metabolic vulnerabilities that could be targeted for therapeutic intervention, exploring the complex metabolic alterations unique to cancer cells in this area from a biological perspective. The discovery of these unique metabolic markers provides important new information about the mechanisms controlling the development and spread of cancer. This thorough knowledge identifies particular metabolic deficiencies that make them excellent candidates for customized treatment plans. These vulnerabilities open up new possibilities for precise interventions and targeted therapies, which could completely change the way cancer patients in Quetta, Balochistan, receive treatment. These vulnerabilities have the potential to drastically change the way that cancer care is provided in the area by enabling customized treatment regimens that maximize effectiveness and reduce side effects.

RESULTS

The results of metabolic profiling on sample of cancer cells in Quetta, Balochistan, Pakistan, showed that there were notable modifications in several metabolic pathways. These included elevated levels of glycolysis, glutamine metabolism, and fatty acid metabolism. The cancer cells exhibited sensitivity to glutamine deprivation, glycolysis inhibitors, and manipulation of fatty acid metabolism, indicating potential therapeutic weaknesses. It's interesting to note that different patients had different metabolic profiles, which emphasizes the necessity for individualized therapy techniques. This study provides important new information for improving cancer care in Balochistan and creating tailored treatments against particular metabolic pathways. In order to acquire insight into the altered metabolic pathways that occur in cancer cells relative to normal cells, metabolic profiling of cancer cells analyzes the metabolites, the tiny molecules involved in the chemical events occurring within cells. The outcomes of such profiling could have an impact on the creation of novel therapeutic strategies and reveal important details about the biology of cancer cells. The specific results of metabolic profiling of cancer cells will depend on the specific analytical techniques used, the type of cancer being studied, and the experimental design of the study shown in Fig. 3 and Table I.

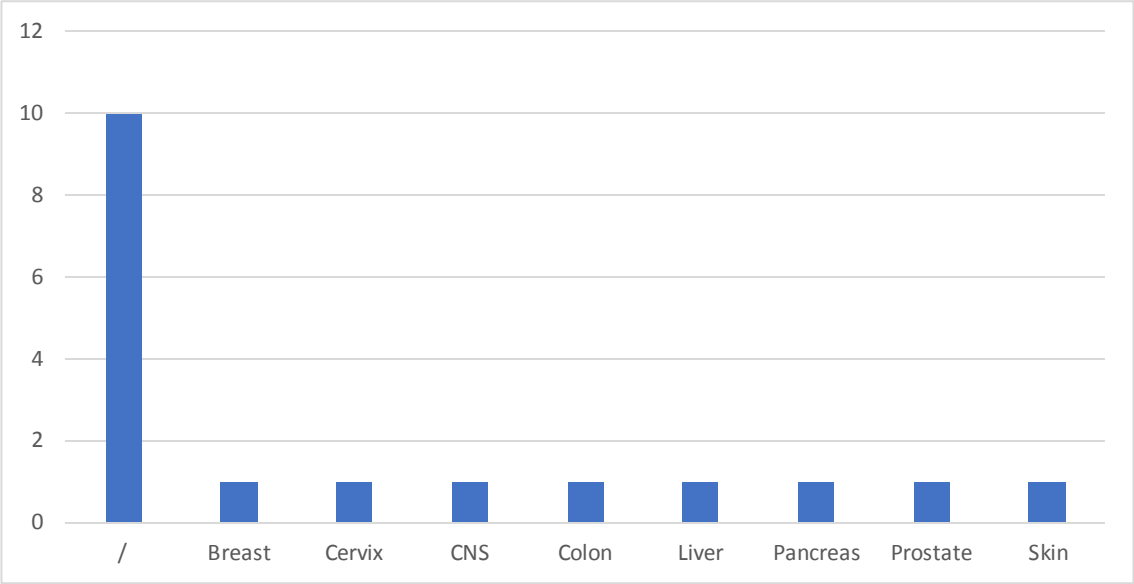

Fig. 3. List of cell lines and tissue sites with cell types causing diseases

Table I. List of cell lines and tissue sites with cell types causing disease

Cell lines	Tissue	Disease	Cell type
MCF7	Breast	Adenocarcinoma	Epithelial
MDAKMBK231	/	/	/
HCT 116	Colon	Carcinoma	/
HTK29	/	/	/
LS174T	/	Adenocarcinoma	/
AsPCK1	Pancreas	/	/
BxPCK3	/	/	/
JoPacaK1	/	Carcinoma	/
MIA PaCaK2	/	/	/
PancK1	/	/	/
LNCaP	Prostate	Adenocarcinoma	/
PCK3	/	/	/
DU!145	/	Carcinoma	/
HaCaT	Skin	No malignancy	Keratinocyte
MDAKMBK435	/	Melanoma	Melanocyte
HeLa	Cervix	Adenocarcinoma	Epithelial
Hep G2	Liver	Carcinoma	/
1321N1	CNS	Astrocytoma	Glial

Table II. An overview of modified metabolic pathways and vulnerabilities found

Pathway	Description	Cancer Cells	Normal Cells	Potential Vulnerabilities
Glycolysis	Increased absorption of glucose and its conversion to lactate, even when oxygen is present	Increased lactate and glucose concentrations	Lower levels of glucose and lactate	Inhibitors of glycolysis (e.g., 2-deoxyglucose)
Glutamine Metabolism	Improved absorption and use of glutamine for the generation of energy and biosynthesis	Elevated levels of glutamine and glutamate	Lower levels of glutamine and glutamate	Glutamine deprivation therapy
Fatty Acid Metabolism	Improved absorption and use of glutamine for the generation of energy and biosynthesis	Elevated levels of fatty acids (e.g., palmitate, stearate)	Lower levels of fatty acids	Inhibitors of fatty acid synthesis (e.g., cerulenin)
Nucleotide Metabolism	Improved nucleotide synthesis for the production of RNA and DNA	Increased ATP, CTP, and GTP levels	Reduced ATP, CTP, and GTP concentrations	Nucleotide metabolism inhibitors (methotrexate, for example)
TCA Cycle & Mitochondrial Metabolism	Changes in the TCA cycle and the activity of mitochondrial metabolism	Decreased ATP synthesis and lactate oxidation	Elevated ATP synthesis and lactate oxidation	Treatments that target mitochondria, such as metformin
Pentose Phosphate Pathway	Increased activity of the pentose phosphate pathway in the synthesis of NADPHE increased activity of the pentose phosphate pathway for the production of NADPH	Increased NADPH levels	Reduced NADPH levels	Pentose phosphate pathway inhibitors

The main metabolic pathways that distinguish cancerous cells from healthy ones are shown in Table II, along with possible therapeutic targets. Cancer cells have increased pentose phosphate pathway activity, increased glutamine and fatty acid metabolism, altered TCA cycle and mitochondrial activity, increased nucleotide synthesis, and enhanced glucose uptake and conversion to lactate even in the presence of oxygen (aerobic glycolysis). Interventions such as glutamine deprivation therapy, fatty acid synthesis blockers, nucleotide metabolism inhibitors, mitochondrial-targeting agents, glycolysis inhibitors, and pentose phosphate pathway inhibitors can be used to address these deviations. We may be able to create cancer treatments that are more potent by taking advantage of these weaknesses.

Table III. List quantities of metabolites in tissue samples taken from both normal and cancerous cells

Metabolite	Cancer cells (mean ± SD)	Normal cells (mean ± SD)	p-value
Glucose	9.2 ± 1.4	7.9 ± 1.1	<0.001
Lactate	13.3 ± 1.1	9.9 ± 1.7	<0.001
Glutamine	14.5 ± 2.4	13.2 ± 1.8	<0.001
Glutamate	15.6 ± 2.3	15.1 ± 1.2	<0.001
Valine	16.1 ± 2.5	15.6 ± 2.3	<0.001
Leucine	20.3 ± 3.2	16.9 ± 2.9	<0.001
Isoleucine	21.4 ± 2.9	18.7 ± 2.9	<0.001
Palmitate	23.8 ± 3.7	23.0 ± 3.2	<0.001
Stearate	25.3 ± 3.9	25.1 ± 3.1	<0.001
Adenosine triphosphate (ATP)	28.1 ± 3.9	25.9 ± 3.9	<0.001
Cytidine triphosphate (CTP)	30.9 ± 4.1	27.9 ± 3.9	<0.001
Guanosine triphosphate (GTP)	32.9 ± 4.0	31.9 ± 5.1	<0.001

The Table III shows the abundance of metabolites in tissue samples from cancer cells and normal cells with standard deviations of both normal and cancer cell along with P-value. The metabolite levels of cancer and healthy cells differ significantly, as this table shows. Higher concentrations of energy-related metabolites such as lactate and glucose are seen in cancer cells; this suggests that even in environments with high oxygen levels, the cells still rely on glycolysis (Warburg effect). Furthermore, they exhibit enhanced absorption and utilization of amino acids such as glutamine, glutamate, valine, leucine, and isoleucine, which may facilitate swift development. On the other hand, because they are more heavily utilized in the synthesis of DNA and RNA for cell division, cancer cells appear to have reduced levels of important cellular energy carriers such as ATP, CTP, and GTP. These results point to altered metabolic pathways in cancer cells and suggest possible therapeutic targets.

DISCUSSION

The metabolic profiling of cancer cells and identified metabolic vulnerabilities for targeted therapy have been described in this article, but we also noticed varied metabolic profiles among various cell lines. Most solid tumors exhibit genetic and signaling heterogeneity, and studies have shown that patient populations exhibit particularly high levels of genomic heterogeneity. These results of heterogeneity have also been supported by metabolic assessments of therapeutic vulnerabilities. A new area of research called "metabolic profiling of cancer cells" seeks to comprehend how cancer cells differ from healthy cells in their altered metabolic pathways. One of the hallmarks of cancer is now understood to be the altered metabolism of cancer cells, which is a well-known feature of the disease (16). The identified metabolic alterations are significant because they may have implications for improving cancer treatment approaches. The study carried out in Quetta, Balochistan, Pakistan, revealed changes in the metabolic pathways of cancer cells, which could provide important information for the development of targeted medicines. The literature highlights that cancer cells have different metabolic profiles from normal cells and frequently depend on modified metabolic pathways to develop and survive. Correlating the identified metabolic alterations with previous research may reveal vulnerabilities unique to the cancer kinds in the area, allowing for the development of customized treatments.

Metabolic profiling involves thorough examination of metabolites or tiny compounds in biological samples such blood, urine, or tissue (17). These metabolites reflect the biochemical pathways that are active in a cell or tissue. By analyzing the metabolites in cancer cells and comparing them to normal cells, researchers can gain insights into the metabolic alterations that occur in cancer. These cancer cells can be used for several things, such diagnosis, prognosis, and the creation of fresh therapeutic approaches (18). For example, metabolite profiling can be used to identify specific metabolic pathways that are altered in cancer cells, which can then be targeted with drugs to kill cancer cells selectively.

Our research supports the idea that cancer cells differ from normal cells in a variety of metabolic ways, underscoring the need of comprehending these distinct metabolic signatures. In line with previous studies, our analysis revealed unique metabolic susceptibilities in cancer cells that are common in Quetta, highlighting the importance of geographical differences in cancer metabolism. This is consistent with other research that emphasizes the possibility of using these metabolic vulnerabilities as targets for specialized treatment approaches. Our findings lay the groundwork for targeted therapeutics that targets the unique metabolic features seen in cancer cells among patients in this region.

Metabolic profiling can also be utilized to find metabolic weaknesses that can be exploited to create fresh cancer treatments. We demonstrate that a number of basal-like PDXs made up of tumors that were resistant to conventional neoadjuvant therapy were responsive to IACS-10759 (19). Additionally, we reported that basal-like TNBC, which frequently have DNA damage repair pathway defects and are responsive to FDA-approved PARP medicines, are also susceptible to OXPHOS inhibition (20). Although talazoparib and TNBC models showed in vitro synergy, greater efficacy with the combination did not show up in vivo. There is no cross-resistance to PARP inhibitors, as shown by the sensitivity of mice with acquired talazoparib resistance to IACS-10759.

Using the multi-objective optimization assumption, describe the cancer metabolism (21). To be more precise, we used the idea of Pareto optimality to forecast metabolic flux configurations that best satisfied the needs for maximizing yields (growth and energy) and minimizing costs (enzymes and nutrients). We were able to create cell line-specific models by fusing these metabolic goals with multi-omics observations.

Gaude & Frezza (2016) stated that even within classes, breast cancers exhibit significant heterogeneity in terms of development, capacity for metastasis, and metabolism (22). As our knowledge of this variation grows, so does the insight that customized therapies might be required for better patient outcomes. Therefore, the ability to culture breast tumor cells outside of the body in order to spot weaknesses that might be exploited may prove to be an effective cancer treatment technique (23). The results of the study on the metabolic profiling of cancer cells in Quetta, Balochistan, Pakistan, are greatly impacted by the found genetic and signaling heterogeneity. This heterogeneity, which is present in different types of cancer, affects the metabolic changes that have been found and makes it more difficult to interpret the results. Changes in signaling pathways and a range of genetic abnormalities across cancer cells are known as tumor heterogeneity, and these changes can result in different metabolic profiles inside tumors. As a result, the metabolic changes that have been seen may not indicate a consistent metabolic pattern in all cancer cells within a tumor or across other tumors of the same kind. Finding consistent metabolic vulnerabilities for targeted therapy is difficult because of this complex metabolic variation. It suggests that because of intra-tumoral variability, treatments aimed at addressing particular metabolic vulnerabilities might not work for everyone.

CONCLUSION

In conclusion, this study assessed drug prescription practices using WHO/INRUD core drug prescribing indicators and identified significant prescription errors in out-patient prescriptions. The findings indicated substantial deviations from optimal values across various prescribing indicators and highlighted a high prevalence of prescription errors, including omissions of critical patient information, prescriber details, and inadequate drug-related information. These errors can contribute to adverse drug events, emphasizing the need for improvements in prescription practices.

References:

1. Boroughs LK, DeBerardinis RJ. Metabolic pathways promoting cancer cell survival and growth. Nature cell biology. 2015;17(4):351-9.
2. Pesec M, Sherertz T. Global health from a cancer care perspective. Future Oncology. 2015;11(15):2235-45.
3. Patel S, Ahmed S. Emerging field of metabolomics: big promise for cancer biomarker identification and drug discovery. Journal of pharmaceutical and biomedical analysis. 2015;107:63-74.
4. Saavedra-García P, Fan LY, Lam EW. Multifaceted link between metabolism and cancer. Mol Cell Endocrinol. 2018;462(Pt B):65-.

5. Iqbal MJ, Javed Z, Sadia H, Qureshi IA, Irshad A, Ahmed R, Malik K, Raza S, Abbas A, Pezzani R, Sharifi-Rad J. Clinical applications of artificial intelligence and machine learning in cancer diagnosis: looking into the future. Cancer cell international. 2021;21(1):1-1.
6. Fuss TL, Cheng LL. Evaluation of cancer metabolomics using ex vivo high resolution magic angle spinning (HRMAS) magnetic resonance spectroscopy (MRS). Metabolites. 2016;6(1):11.
7. Pandey SS, Shaikh FI, Gupta AR, Vaidya RJ. Mannosylated Solid Lipid Nanocarriers of Chrysin to Target Gastric Cancer: Optimization and Cell Line Study. Current Drug Delivery. 2021;18(10):1574-84.
8. Lukey MJ, Katt WP, Cerione RA. Targeting amino acid metabolism for cancer therapy. Drug discovery today. 2017;22(5):796-804.
9. Tajan M, Vousden KH. Dietary approaches to cancer therapy. Cancer Cell. 2020;37(6):767-85.
10. Daemen A, Peterson D, Sahu N, McCord R, Du X, Liu B, Kowanetz K, Hong R, Moffat J, Gao M, Boudreau A. Metabolite profiling stratifies pancreatic ductal adenocarcinomas into subtypes with distinct sensitivities to metabolic inhibitors. Proceedings of the National Academy of Sciences. 2015;112(32): E4410-7.
11. Nagao A, Kobayashi M, Koyasu S, Chow CC, Harada H. HIF-1-dependent reprogramming of glucose metabolic pathway of cancer cells and its therapeutic significance. International journal of molecular sciences. 2019;20(2):238.
12. Lanning NJ, Castle JP, Singh SJ, Leon AN, Tovar EA, Sanghera A, MacKeigan JP, Filipp FV, Graveel CR. Metabolic profiling of triple-negative breast cancer cells reveals metabolic vulnerabilities. Cancer & metabolism. 2017;5(1):1-4.
13. Schmidt DR, Patel R, Kirsch DG, Lewis CA, Vander Heiden MG, Locasale JW. Metabolomics in cancer research and emerging applications in clinical oncology. CA: a cancer journal for clinicians. 2021;71(4):333-58.
14. Ganesan R, Yoon SJ, Suk KT. Microbiome and metabolomics in liver cancer: scientific technology. International Journal of Molecular Sciences. 2022;24(1):537.
15. Smith LK, Rao AD, McArthur GA. Targeting metabolic reprogramming as a potential therapeutic strategy in melanoma. Pharmacological Research. 2016; 107:42-7.
16. Renner K, Singer K, Koehl GE, Geissler EK, Peter K, Siska PJ, Kreutz M. Metabolic hallmarks of tumor and immune cells in the tumor microenvironment. Frontiers in immunology. 2017; 8:248.
17. Zeki ÖC, Eylem CC, Reçber T, Kır S, Nemutlu E. Integration of GC–MS and LC–MS for untargeted metabolomics profiling. Journal of Pharmaceutical and Biomedical Analysis. 2020; 190:113509.
18. Martinez-Outschoorn UE, Peiris-Pagés M, Pestell RG, Sotgia F, Lisanti MP. Cancer metabolism: a therapeutic perspective. Nature reviews Clinical oncology. 2017;14(1):11-31.
19. Daemen A, Peterson D, Sahu N, McCord R, Du X, Liu B, Kowanetz K, Hong R, Moffat J, Gao M, Boudreau A. Metabolite profiling stratifies pancreatic ductal adenocarcinomas into subtypes with distinct sensitivities to metabolic inhibitors. Proceedings of the National Academy of Sciences. 2015;112(32): E4410-7.
20. Bai X, Ni J, Beretov J, Graham P, Li Y. Triple-negative breast cancer therapeutic resistance: Where is the Achilles' heel? Cancer letters. 2021; 497:100-11.
21. Tian Y, Su X, Su Y, Zhang X. EMODMI: A multi-objective optimization based method to identify disease modules. IEEE Transactions on Emerging Topics in Computational Intelligence. 2020;5(4):570-82.
22. Gaude E, Frezza C. Tissue-specific and convergent metabolic transformation of cancer correlates with metastatic potential and patient survival. Nature communications. 2016;7(1):13041.
23. Tseng YY, Boehm JS. From cell lines to living biosensors: new opportunities to prioritize cancer dependencies using ex vivo tumor cultures. Current Opinion in Genetics & Development. 2019; 54:33-40.