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REVIEW

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Isothermal calorimetry calscreener in the metabolism gauge of human malignant neoplastic cells: a burgeoning nexus in cancer biochemical metrology and diagnostics

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Abstract

Background At present, the function of isothermal microcalorimetry (IMC) calscreener in detecting alterations in the metabolic pathways of cancer cells remains unexplored. We disclosed the shortcomings of current screening methods and the need for precise and dependable instruments in the detection and informed treatment of cancer via the IMC in relation to the experimental procedures required to obtain accurate results.

Main body of abstract We examined the intricate technical aspects of isothermal calorimetry. The application of the IMC calscreener in cancer research is then discussed in depth, including how it can be used to evaluate the efficacy of treatments, identify metabolic inhibitors, and assess metabolic rates. We also investigated the diagnostic potential of isothermal calorimetry, particularly for early cancer detection and tracing therapy efficacy.

Conclusions General findings shed light on the present issues and potential approaches for isothermal calorimetry application in cancer research and diagnosis. We underline the potential for isothermal calorimetry to fundamentally alter how to understand and treat cancer, as well as the need for additional studies to maximize its application in clinical settings. This in turn offers a thorough and fascinating account of the emerging relationship between isothermal calorimetry and cancer biochemistry, as well as its potential to revolutionize cancer detection and therapy.

Keywords Cancer cells, Cancer diagnosis, Cancer metabolism, Cancer treatment, IMC calscreener

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Background

Isothermal microcalorimetry calscreener dynamics and intricacies of cancer biology

Cancer, a complex and multifaceted disease, continues to be a global health challenge. Its prevalence and impact on human lives demand continuous advancements in the field of cancer biology research (Ibisanmi et al. 2023). Understanding the intricate biochemical processes within cancer cells is paramount to developing effective diagnostic tools and therapeutic strategies (Yang et al. 2022). Over the years, various techniques have been employed to investigate cancer cell metabolism, unraveling critical insights into its aberrant behavior (Cho et al. 2023). Isothermal calorimetry (IMC) has emerged as one of the most effective methods for investigating metabolic changes in cancer cells (Kang et al. 2018).

Isothermal calorimetry is a powerful analytical procedure that allows the measurement of heat flow associated with physical and chemical processes occurring in a sample (Bastos et al. 2023). It provides valuable insights into various thermodynamic and kinetic properties of substances, such as heat capacity, reaction enthalpy, reaction rates, and heat release (Cavalcanti et al. 2023). The advancements in calorimetric instrumentation have led to the development of more sophisticated and efficient devices, such as the calscreener, which has revolutionized the field of isothermal calorimetry (Vasala et al. 2020). The fundamental principle of isothermal calorimetry is measuring heat flux in a controlled environment. The method entails measuring heat transfer as a function of time, which is typically expressed in watts (W) (Zogg et al. 2004). A highly sensitive sensor, such as a thermopile or thermistor, detects the heat flow by turning the heat into an electrical signal. The signal is then recorded and analyzed to determine the thermodynamic and kinetic properties of the sample under investigation. Given below is the fundamental equation governing isothermal calorimetry:

$$Q = Cp \times \Delta T \tag{1}$$

where Q represents the heat flow, Cp is the heat capacity of the sample, and ΔT is the change in temperature (Eq. 1). By measuring the heat flow and knowing the heat capacity, one can calculate the enthalpy change associated with a process occurring in the sample.

IMC is a well-established method used to measure heat changes associated with biochemical reactions. It offers a unique advantage by providing a direct and real-time measurement of heat production or consumption during cellular processes (Vogel et al. 2021). By quantifying heat exchange, IMC can elucidate the metabolic pathways and energy fluxes within cells, shedding light on the metabolic alterations that occur in cancer. In recent years, the application of IMC in cancer research has gained significant momentum, especially in the context of studying human malignant neoplastic cells (Faubert et al. 2020). Malignant neoplastic cells, commonly known as cancer cells, exhibit distinctive metabolic characteristics compared to normal cells. These metabolic changes are essential for cancer cell survival, proliferation, and immune evasion. Understanding the metabolic nuances of cancer cells is vital for the development of targeted therapies and accurate diagnostic tools (Faubert et al. 2020).

The advancement of the IMC calscreener has further accelerated the exploration of cancer cell metabolism. The calscreener is specifically designed to analyze the metabolic activity of malignant neoplastic cells, enabling researchers to probe the intricacies of cancer cell metabolism with unprecedented precision and sensitivity (Faubert et al. 2020). Using the IMC calscreener, scientists can track the heat fluxes and thermodynamic properties of metabolic processes in cancer cells. This gives them important information about the biochemical changes that cause cancer to spread (Faubert et al. 2020). By utilizing the IMC calscreener, researchers can not only deepen their understanding of cancer cell metabolism but also develop novel biomarkers and diagnostic approaches in cancer biology and metabolism. The ability to accurately measure metabolic changes in real time provides a robust foundation for identifying metabolic signatures specific to different cancer types and stages (Faubert et al. 2020). Such information can revolutionize cancer diagnostics, allowing for earlier detection, personalized treatment plans, and improved patient outcomes.

The importance of isothermal microcalorimetry screening in cancer research

The Isothermal calorimetry calscreener has emerged as a powerful and indispensable tool in cancer research, revolutionizing our understanding of cancer biology and its implications for the advancement of personalized cancer therapies. Its technique to investigate metabolic changes in cancer cells provides valuable insights into tumor growth, drug response, and the identification of novel biomarkers (Faubert et al. 2020). One of the hallmarks of cancer is the altered metabolism of tumor cells, known as the Warburg effect. Cancer cells exhibit a shift in their metabolic pathways, favoring glycolysis even in the presence of oxygen, which is in contrast to the oxidative phosphorylation predominant in normal cells (Chen et al. 2016). This metabolic reprogramming provides cancer cells with a survival advantage by supporting their high energy demands and rapid proliferation. Understanding the intricacies of cancer cell metabolism is crucial for developing effective therapeutic strategies (Allison et al. 2017). Isothermal calorimetry is a procedure that

measures the heat generated or consumed during a biochemical reaction. It offers several advantages over traditional methods, making it an invaluable tool in studying cancer metabolism.

One of the key advantages of the Isothermal calorimetry calscreener is its ability to provide real-time measurements of heat flow (Bayode et al. 2022). This dynamic monitoring allows researchers to observe metabolic activity continuously, capturing subtle changes that occur during different stages of cancer progression or in response to various treatments. By monitoring heat production in real time, researchers gain insights into the metabolic pathways involved in cancer cell growth and survival, as stated by Bayode et al. (2022). The calscreener also enables label-free measurements, eliminating the need for exogenous probes or markers. This is particularly advantageous when studying primary cancer cells or patient-derived samples, as it maintains the physiological conditions and ensures the accuracy of the measurements (Gerdes et al. 2014). Label-free measurements provide a more comprehensive understanding of metabolic changes in cancer cells, allowing for a deeper exploration of the underlying mechanisms driving tumor growth and progression (Gerdes et al. 2014).

Furthermore, the IMC calscreener facilitates the identification of specific metabolic dependencies in cancer cells. By analyzing the heat flow data, researchers can uncover key metabolic pathways that are essential for tumor survival and growth (Zhu et al. 2023). These pathways can serve as potential targets for therapeutic interventions. By disrupting these pathways, it becomes possible to starve cancer cells of the nutrients they require for proliferation, leading to more effective and targeted therapies. The high sensitivity of the IMC calscreener is another crucial feature in cancer research (Zhu et al. 2023). It enables the detection of subtle alterations in heat production, even at low cell concentrations. This sensitivity is particularly important when studying rare or precious cancer samples, where obtaining accurate measurements with small sample sizes is critical (Zhu et al. 2023). A more in-depth description of the metabolic changes in cancer cells can be made possible by the IMC calscreener to detect minute changes in heat flow (Garbett et al. 2010).

The capacity of the IMC calscreener has helped to identify new biomarkers and to better understand cancer cell metabolism. Biomarkers are molecules or characteristics that indicate the presence, progression, or response to the treatment of a disease (Ziemssen et al. 2019). Metabolic biomarkers offer advantages over traditional genetic or protein-based markers as they reflect the functional state of cells and provide real-time information about disease progression. By using the IMC calscreener to look at the metabolic profiles of cancer cells, researchers can find metabolic signatures that are unique to different types of tumors. These metabolic signatures can be used as useful biomarkers for early detection, predicting the likely outcome of treatment, and keeping track of how well treatment is working.

Another crucial application of the IMC calscreener in cancer research is the evaluation of drug efficacy. Traditional methods of assessing drug response often rely on endpoint measurements or surrogate markers (Gindy and Prud'homme 2009). However, these measurements may not accurately represent the overall metabolic changes occurring in cancer cells. The IMC calscreener allows for direct monitoring of the heat flow associated with drug-induced metabolic alterations. This provides a more comprehensive understanding of how different drugs affect cancer cell metabolism and helps optimize drug selection for individual patients (Gindy and Prud'homme 2009). By monitoring the heat flow in real time, researchers can assess the effectiveness of a drug on cancer cells and tailor treatment regimens accordingly.

Moreover, the IMC calscreener has the potential for clinical translation in the field of cancer diagnostics. Analyzing the metabolic profiles of cancer cells can aid in early detection and diagnosis (Gindy and Prud'homme 2009). The ability to measure metabolic changes in real time offers opportunities for developing rapid diagnostic assays, these assays can provide timely information about the presence and progression of cancer, allowing for early interventions and improved patient outcomes. Additionally, the calscreener can be used to monitor treatment response, helping clinicians make informed decisions about adjusting therapeutic regimens based on metabolic changes observed in cancer cells (Bayode et al. 2022).

The isothermal calorimetry calscreener enables the investigation of metabolic changes in cancer cells, providing valuable insights into tumor growth, drug response, and the identification of novel biomarkers. The IMC calscreener real-time monitoring, label-free measurements, sensitivity, and ability to identify specific metabolic dependencies contribute to our understanding of cancer biology and open up avenues for developing personalized cancer treatments (Bokhari et al. 2021). The potential for clinical translation further highlights the significance of the calscreener in improving cancer diagnostics and patient care.

Background information on cancer diagnosis and treatment

In recent years, biomarkers have been introduced and have become increasingly important in pharmaceutical discovery, identifying a drug's mechanism of action, investigating early toxicity and efficacy signals, and

identifying patients who are likely to respond to therapy. Furthermore, multiple potentially powerful tools for deciphering such complexities are emerging in various scientific disciplines, and the use of such knowledge in personalized medicine has increased (De Gramont et al. 2015). Biomarkers are utilized to monitor the progression of disease prior to diagnosis, screening, and risk evaluation. During diagnosis, they can aid in the determination of staging, grading, and primary therapy selection. After diagnosis, they can be employed for monitoring therapy, further therapy selection, and monitoring for recurrent disease (Beasley and Levengood 2012; Godfre et al. 2021). A cancer diagnosis typically involves several steps, including a physical examination, a medical history review, and various tests to determine the presence and extent of cancerous cells in the body. During a physical examination, a healthcare provider may perform a visual inspection of the body to look for lumps or abnormalities, as well as palpate (feel) certain areas of the body to check for enlarged or abnormal lymph nodes, organs, or tissues.

According to Umar and Atabo (2019), imaging tests like X-rays, CT scans, MRIs, and PET scans can take detailed images of the body and find any abnormalities. These images can be used to determine the location and size of cancerous tumors as well as evaluate whether the cancer has spread to other parts of the body. As demonstrated by Siravegna et al. (2017), cancer biopsies are typically conducted to confirm the presence of cancerous cells by removing a small tissue sample from the affected area and examining it under a microscope for abnormal cells.

During the progression of cancer, tumors become highly diverse, forming a population of cells with various molecular characteristics and varying therapeutic responses. This spatial and temporal heterogeneity is the critical factor responsible for the development of resistant phenotypes induced by selective pressure upon administration of the treatment (Dagogo-Jack and Shaw 2018).

Nanomedicine provides a flexible platform of biocompatible and biodegradable systems that can deliver conventional chemotherapeutic drugs in vivo, increasing their bioavailability and concentration around tumor tissues and optimizing their release profile (Martinelli et al. 2019). Nanoparticles can be utilized for a variety of purposes, from diagnosis to therapy (Martinelli et al. 2019).

Due to their anti-proliferative and pro-apoptotic properties, natural antioxidants and numerous phytochemicals have recently been introduced as anti-cancer adjuvant therapies (Chikara et al. 2018; Singh et al. 2016). Targeted therapy is another type of cancer treatment that attempts to target a specific site, such as tumor vasculature or intracellular organelles, without affecting the surrounding area. This significantly improves the treatment's specificity and decreases its drawbacks (Bazak et al. 2015). Gene therapy and the manifestation of apoptosis-initiating genes represent a second promising avenue (Lebedeva et al. 2003) and wild-type tumor suppressors (Shanker et al. 2011).

Nanoparticles can also be used in the treatment of cancer. Due to their small size (1–1000 nm) and high surface-to-volume ratio, nanoparticles possess peculiar physiochemical properties (Tinkle et al. 2014). In cancer medicine, biocompatible nanoparticles are used to surmount some of the shortcomings of conventional therapies, such as the low specificity and bioavailability of drugs or contrast agents (Martinelli et al. 2019). Since nanoparticle encapsulation improves solubility, biocompatibility, stability in body fluids, and retention time in the tumor vasculature, it is a promising approach to treating cancer (Albanese et al. 2012; Maeda 2015). Furthermore, nanoparticles can be designed to be highly selective for a particular target and to release the medication in a controlled manner in response to a predetermined stimulus.

Advantages and limitations of isothermal microcalorimetry calscreener in cancer metabolism measurements

The IMC calscreener is engineered to create a consistent and unchanging temperate environment, ensuring isothermal conditions during an experimental design (Bové, 2022). This design guarantees accurate measurement of the heat effects related to the sample, eliminating any potential impact from temperature fluctuations. The system incorporates advanced temperature control mechanisms to sustain a stable thermal equilibrium, thus ensuring dependable and repeatable outcomes.

One of the key advantages of an isothermal calorimetry calscreener is its versatility. It can be utilized to study various processes, such as enzyme kinetics, protein–ligand interactions, drug binding, polymerization, crystallization, and phase transitions. The technique provides quantitative data on heat effects, allowing researchers to assess reaction energetics, thermodynamic stability, and reaction rates (Vasala et al. 2020).

The isothermal calorimetry calscreener technique provides a non-destructive and label-free method for analyzing samples (Braissant et al. 2015). It necessitates minimal sample preparation and allows for in situ measurements, enabling observations under conditions that closely resemble the natural environment of the sample, as conducted by Logan et al. (2021), who divulged parasitic interactions via isothermal microcalorimetry calscreener. This aspect is particularly beneficial when

studying biological systems and fragile materials that may be susceptible to disturbances from external factors, as illustrated in Table 1.

One crucial area where isothermal calorimetry calscreener excel is in the study of protein–ligand interactions, which are essential for the development of targeted therapies (Mosebi 2022). Measuring the heat exchange during the binding of potential drug candidates to target proteins can provide insights into the strength and specificity of these interactions. This information is crucial for designing and optimizing therapeutic agents that selectively target cancer cells while minimizing off-target effects, improving treatment efficacy, and reducing toxicity (Mosebi 2022).

IMC can provide detailed thermodynamic profiles of enzymatic reactions involved in cancer-related processes. Enzymes play vital roles in cellular metabolism, DNA repair, and signal transduction pathways, all of which are disrupted in cancer, as demonstrated by Qiao et al. (2019). Investigating the thermodynamics of enzyme-catalyzed reactions can reveal the underlying mechanisms of cancer and guide us in developing targeted interventions. These insights can aid in the identification of potential targets for drug development and the design of inhibitors to modulate specific enzyme activities, as similarly observed by Qiao et al. (2019) in their work on the nanotherapeutics response framework for precision drug delivery and cancer therapy.

Isothermal calorimetry calscreener also contributes to the understanding of metabolic alterations in cancer cells. Cancer cells demonstrate unique alterations in their metabolic pathways to sustain their rapid growth and proliferation. This understanding can aid in the identification of metabolic vulnerabilities and the development of therapeutic approaches that selectively target cancer cell metabolism, paving the way for novel metabolic-based treatments, as opined by Intlekofer and Finley (2019).

Nonetheless, the drawbacks of isothermal microcalorimetry especially during the metabolism gauge of neoplastic malignant cells which comprises low cancerous cells' sample throughput, non-specific signals in multichannel-design isothermal microcalorimeters, inherent sluggishness of the metabolism gauge of cancerous cells, the potential solutions to low cancerous cells' sample throughput and the lack of comprehension on the parameters of precise heat flow kinetic for measuring cancer cells' metabolism are painstakingly dissected below respectively:

Potential solutions to low cancerous cells' sample throughput in metabolism gauge of the tumor cells

There are numerous strategies that can be taken into consideration to solve the poor sample throughput issue in malignant cells. Microfluidic devices, which handle several samples simultaneously and enable high-throughput analysis, are one potential remedy as demonstrated by Tavakoli et al. (2019). The sample handling procedure can be streamlined by using automation and robotics, which will save time and boost productivity, innovating sample preparation methods and downsizing analysis systems can also help increase sample throughput as observed by Müller et al. (2020).

Non-specific signals in isothermal microcalorimeters with a multichannel design

Measurements of heat flow in multichannel-design-isothermal microcalorimeters that are not specifically related to the metabolic activity of malignant cells are referred to as non-specific signals (Pini et al. 2021). These signals can come from a variety of instances, including heat fluctuations, unrelated chemical events, and instrument noise. To get accurate findings, non-specific signals must be reduced to a minimum. Advanced signal processing techniques, adequate calibration of the isothermal calorimetry calscreener, and careful experimental design can all help to accomplish this as replicated by Bastos et al (2023).

The inherent sluggishness and hastening the slow mechanism of the metabolism gauge of cancerous cells

The time lag between a metabolic event taking place in malignant cells and the accompanying heat flow signal being observed is referred to as the "inherent sluggishness" in the change of heat flow in the isothermal microcalorimeter system (Vehusheia et al. 2023). The time

Table 1 The merits and Demerits of the Isothermal Microcalorimetry Calscreener (IMC) in Cancer Metabolism Gauge

Advantages of isothermal microcalorimetry	Limitations of isothermal microcalorimetry	References
Label-free analysis	Sample compatibility may require specific conditions or modifications	Bokhari et al. (2021)
Real-time monitoring	Instrument costs can be high, limiting accessibility in certain settings	Butini et al. (2018)
High sensitivity	Data interpretation may require expertise and careful analysis	Bokhari et al. (2021)
In situ measurements	Limited throughput compared to some other techniques	Logan et al. (2021)

needed for heat to travel within the system and thermal diffusion are two elements that can be responsible for this delay. It is possible to look into creative alternatives to speed up this sluggish mechanism. For instance, enhancing the temporal resolution of the measurements can be achieved can boost the thermal conductivity of the sample chamber, or refining the architecture of the calorimeter system during metabolism measurement.

Precise heat flow kinetic parameters for measuring cancer cells' metabolism

Understanding the metabolic meter of malignant cells requires accurate real-time kinetic parameterization of heat flow as revealed by Zhang et al. (2023) who illustrated the prospective advantages of their developed cell temperature tracking system in cancer research and underlines the relevance of real-time kinetic parameterization of thermal flow for examining the metabolic properties of malignant cells. These variables may include the rate of heat generation or consumption, the energy required to initiate metabolic processes, and the system's overall heat capacity. Insights regarding the metabolic activities of cancer cells can be gleaned by researchers by tracking the heat flow over time and evaluating the resulting data. However, reliable kinetic parameter measurement necessitates rigorous experimental planning, data analysis, and validation against pre-existing frameworks or reference samples.

IMC calscreener in cancer biochemical metrology

Esophageal carcinoma is one of the most aggressive forms of cancer, with high rates of metastasis and a poor prognosis. Huo et al. (2021) studied the function of thermogenesis in esophageal cancer cell dissemination. It was hypothesized that increased thermogenesis could promote metastasis by altering the adhesion strength of cancer cells. The authors used a combination of in vitro and in vivo techniques to investigate the adhesion strength and thermogenesis of metastatic esophageal carcinoma cells. The authors used a specialized microfluidic device to measure the adhesion strength of cancer cells under different conditions. They also used a Seahorse analyzer to measure the metabolic activity of cancer cells and the production of heat. The study found that metastatic esophageal carcinoma cells exhibited reduced adhesion strength compared to non-metastatic cells. The authors also observed that the metastatic cells had increased thermogenesis, which was associated with higher rates of metastasis in animal models. Additionally, the authors found that inhibiting thermogenesis reduced the metastatic potential of the cancer cells, as illustrated in the conceptual schematics in Fig. 1.

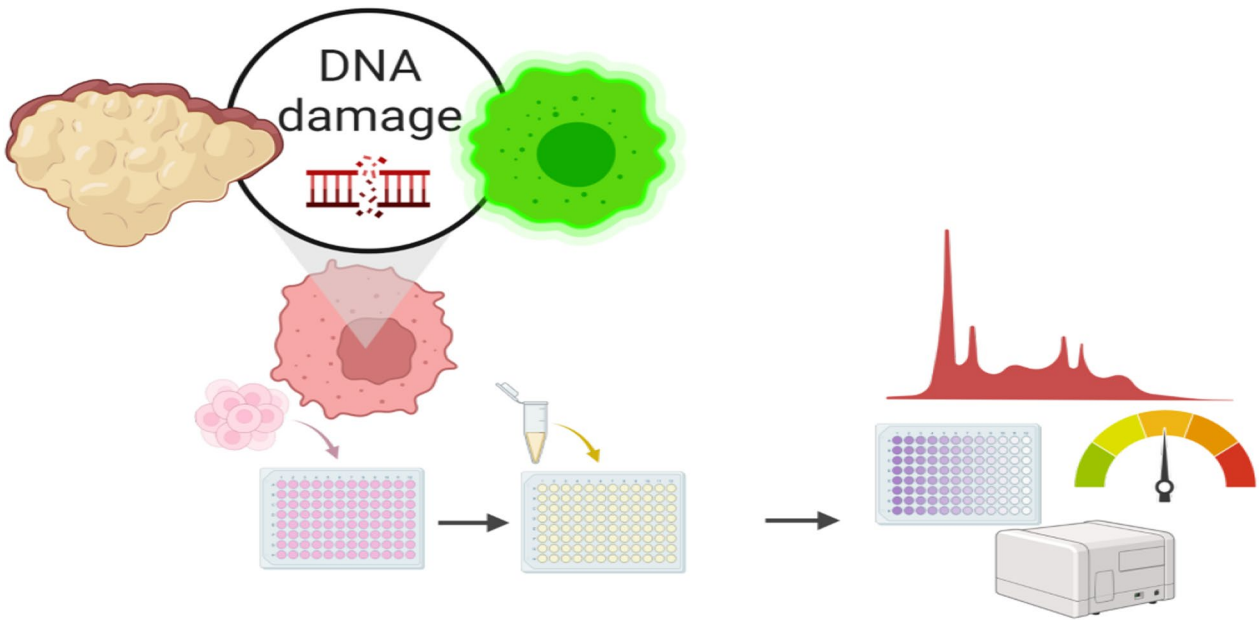

Fig. 1 A schematic breakdown of the metabolism gauge of human malignant neoplastic cells using the IMC calscreener in real time. The isothermal calorimeter is intended for measuring the metabolic activity of human malignant neoplastic cells. It operates by putting malignant cells in micro-well plates and monitoring the heat produced as the cells consume nutrients over time when transferred into the calscreener. The resultant data can be used to find possible targets for cancer therapy and to measure the metabolic rate of the cancerous cells in microwatts (W) in real time

The study by Huo et al. (2021) sheds light on the complex mechanisms underlying metastasis in esophageal carcinoma. The authors suggest that increased thermogenesis could alter the adhesion strength of cancer cells, allowing them to detach from the primary tumor and migrate to other sites in the body. This finding could have important implications for the development of new therapies that target the metabolic pathways involved in thermogenesis. The study by Huo et al. (2021) highlights the potential role of thermogenesis in promoting metastasis in esophageal carcinoma. The authors suggest that inhibiting thermogenesis could be a viable therapeutic strategy for preventing the spread of cancer cells. Further research is needed to fully understand the mechanisms underlying thermogenesis in cancer cells and to develop targeted therapies that can effectively inhibit this process. In a similar vein, Gros et al. (2019) discussed the potential use of carbonic anhydrase IX (CAIX) and aquaporin 1 (AQP1) inhibitors as therapeutic targets for rare childhood tumors and the future implications of their inhibition as a targeted therapy. The challenges of treating rare childhood tumors, which often have limited treatment options and poor prognoses, are far-fetched. This emphasized the need for personalized treatment approaches that take into account the individual characteristics of the tumor in cancer patients. Gros et al. (2019) showed that CAIX and AQP1 are transmembrane proteins that are overexpressed in several types of solid tumors, including renal cell carcinoma, breast cancer, and glioma. Their expression has been linked to tumor growth, angiogenesis, and metastasis. CAIX is a hypoxia-inducible protein that regulates pH homeostasis in the tumor microenvironment, while AQP1 is involved in the regulation of water transport across the cell membrane (Gros et al. 2019). The authors highlight the potential of CAIX and AQP1 inhibitors as targeted therapies for cancer. The inhibition of CAIX could lead to the accumulation of carbon dioxide in the tumor microenvironment, which can trigger apoptosis and decrease tumor growth. AQP1 inhibitors, on the other hand, could prevent tumor angiogenesis and metastasis by blocking the transport of water and other small molecules necessary for tumor growth (Gros et al. 2019).

The authors present data from in vitro and in vivo studies demonstrating the effectiveness of CAIX and AQP1 inhibitors in treating solid tumors. In addition to their potential use in personalized treatment approaches for rare childhood tumors, these inhibitors have also shown promise in the treatment of other types of cancer. Targeted therapies using CAIX and AQP1 inhibitors could provide a more effective and specific approach to cancer treatment, minimizing the side effects of traditional chemotherapy. However, there are several challenges that need to be addressed in the development of CAIX and AQP1 inhibitors as targeted therapies for cancer.

Metabolism gauge of human malignant neoplastic cells

Approximately 10–15% of all cases of paediatric cancer are caused by neuroblastoma, making it the most prevalent extracranial solid tumor in children. Despite advances in treatment, the five-year survival rate for high-risk neuroblastoma remains less than 50% (Pini et al. 2021). Cancer cells have altered metabolic pathways, including enhanced glycolysis and glutaminolysis, which are critical for tumor development and survival. Fructose metabolism has been implicated in various cancers, but its role in neuroblastoma remains poorly understood. In this study, Pini et al. (2021) investigated the effect of fructose metabolism on the proliferation of neuroblastoma cells and its potential as a therapeutic target. The researchers employed isothermal microcalorimetry to assess the metabolic activity of neuroblastoma cells under various glucose and fructose metabolism conditions. The study found that neuroblastoma cells exhibited increased proliferation and metabolic activity under fructose metabolism compared to glucose metabolism. This effect was more pronounced in high-risk neuroblastoma cells. Fructose metabolism also caused changes in neuroblastoma cell cycle progression, with an increase in the S-phase and a decrease in the G1-phase. Furthermore, the study identified key signaling pathways that were activated under fructose metabolism, including the PI3K/AKT/mTOR and MAPK/ERK pathways.

Detection of the metabolism gauge of pathogenic bacterial variants tumorous tissues using isothermal microcalorimetry calscreener (IMC)

Braissant et al. (2015) demonstrated the use of isothermal microcalorimetry for the detection of microorganisms and tumorous microtissues. The researchers measured the heat output of different samples, including bacteria, tumorous microtissues, and parasitic worms, using a high-sensitivity calorimeter. The samples were placed in a 96-well plate, and measurements were taken at regular intervals over a period of up to 72 h. The authors also used microscopy and other conventional methods to verify the presence of the microorganisms and tumorous microtissues.

Using IMC, the researchers were able to detect the metabolic activity of several microbes such as *E. coli*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa*. The authors also demonstrated the ability of IMC to detect the metabolic activity of tumorous microtissues, such as MCF-7 cells, and parasitic worms, such as *Schistosomamansoni*. The authors note that the sensitivity

of the technique was high, with a detection limit of 10^4 cells/ml for bacteria and 10^3 cells/ml for tumorous microtissues.

The use of IMC for the detection of microorganisms and tumorous microtissues has several advantages over conventional methods. Firstly, the label-free nature of the assay eliminates the need for expensive and time-consuming labeling techniques. Secondly, the high sensitivity of the technique allows for the detection of low concentrations of microorganisms and tumorous microtissues. Finally, the real-time monitoring of metabolic activity allows for the determination of the growth rates and drug sensitivity of microorganisms and tumorous microtissues. Braissant et al. has demonstrated the effectiveness of IMC as a label-free, sensitive, and real-time monitoring tool for the detection of microorganisms and tumorous microtissues. The authors noted that further studies are required to validate the technique for clinical applications.

Isothermal microcalorimetry calscreener in cancer diagnostics

Calorimetric assays quantify the amount of heat produced, are label-free, and may be used with materials having a wide range of physical characteristics (Braissant et al. 2015). All living things and many associated biological processes emit heat; hence, bioassays may be carried out using calorimetric methods. Calorimetry, which measures heat generation, has been utilized in bioassays (Gros et al. 2019) and is frequently utilized as a bioactivity monitor in its primary function. Isothermal microcalorimetry is intended for readings in the microwatt range or below (Pini et al. 2021).

Isothermal microcalorimetry can be used to diagnose cancer. The bioenergetic potential of tumor cells was investigated by this biophysical method of tumor cell analysis. Tumor thermogenesis, which is connected to practically all biological activities in the cells' energy turnover, may be measured to assess this, as demonstrated by Huo et al. (2021). Experimental evidence has been shown for a number of cell lines with varying spreading potential, including tongue squamous cell carcinoma, human non-small-cell lung carcinoma, human breast adeno-carcinoma, and murine melanoma, that metastatic cells have increased thermogenesis under these conditions (Lemos et al. 2019).

Braissant et al. (2015) used isothermal microcalorimetry to find the hepatocarcinoma microtissues that produced more heat than the bacteria observed in the same investigation. During the first five hours of the experiment, the maximum thermal power detected was 2.1 W, and it connected directly with the quantity of microtissues placed in the microcalorimetric vial. In a separate experiment, Huo et al. (2021) employed isothermal microcalorimetry to evaluate the differences in heat production between tumor cells originating from the primary tumor and those originating from lymph nodes. According to their results, comparing cell line LN1590 to cell line PT1590, LN1590 produced much more heat over the course of 24 h. In their experiment, Gros et al. (2019) showed that using microcalorimetric measurements of tumor slice cultures alone, it is feasible to identify a response to anti-tumor drugs within 48 h. The fundamental benefit of employing tumor slice culture for assessment is that any tumor piece removed after surgery may be used without first undergoing the time-consuming process of establishing a stable tumor cell culture.

Comparison of isothermal microcalorimetry calscreener with traditional diagnostic methods

Cancer alters a patient's life, eliciting physical, psychological, social, and spiritual anguish (Lewandowska et al. 2021). The sentiments and emotions the illness causes, which disrupt daily life, increase the threat of receiving a cancer diagnosis (Avancini et al. 2020). Three distinct stages have been identified in the progression of cancer, and for the majority of patients, the diagnostic stage is equivalent to approaching pain. The predominant feelings throughout this stage include anxiety, wrath, fear, denial, and despair (Ho et al. 2018). For many reasons, the early diagnosis of cancer is important (Chen et al. 2019). Delay might have a negative impact on the outcome of cancer treatment. In order to design effective, equitable, and cost-efficient cancer care systems, pathways, and models, we must first evaluate the effect of delay on mortality and other outcomes, such as recurrence or financial burden on patients (Hanna et al. 2020). As a result, it's crucial to get a cancer diagnosis early. Better alternatives are needed because traditional methods, such as complete blood counts, cytogenetic analyses, immune-phenotyping, liquid biopsies, tumor marker tests, urinalysis, urine cytology, biopsy, and imaging tests, have limitations such as radiation risk and poor selectivity (Nounou et al. 2015).

Microscopy is used in animal investigations, but it is labor- and cost-intensive. Microscopy is frequently utilized in animal investigations (Braissant et al. 2015). Owing to this, microcalorimetry is considered a preferable choice since it enables precise assessment of metabolic and motor activity with very little effort, thereby improving productivity and lowering laboratory expenses. Modern microcalorimeters can detect the heat produced by hepatocyte metabolism because they are more sensitive than earlier methods like spectrophotometry and enzyme tests. The approach is appealing as a bioactivity monitor for a variety of biomedical and

pharmaceutical applications because it also increases throughput procedures by enabling the measurement of multiple samples at once (Gros et al. 2019). Isothermal microcalorimetry, as opposed to more conventional methods like enzyme tests or spectrophotometry, can be used to measure the metabolic heat rate of hepatocytes (Braissant et al. 2015). There is also the benefit of the ability to track the metabolic activity of cells that are suspended, solid, in a gel, or adhering to a surface while under oxic or anoxic conditions in real time (Braissant et al. 2015). Isothermal microcalorimetry is therefore a good tool for examining intricate biological structures like tumor microtissues.

As regards cancer cells and viral infection mechanism/prognosis, identifying the fundamental mechanistic processes of human malignant cells and influenza virus is critical for creating viable therapies. The study by Oladejo and Adeboboye, (2022) on comprehending the preserved parts of the influenza viral genome that are less probable to elicit mutation, is connected to the metabolic processes of neoplastic cancerous cells which thereby shed light on cancer and influenza virus disease pathways which could inform prognosis.

Conclusions

The findings from the potential use of inhibitors as therapeutic targets for rare tumors are significant, providing a more effective and specific approach to cancer treatment, minimizing the side effects of traditional chemotherapy, and potentially leading to new therapeutic options for cancer patients in the future. To fully understand how fructose metabolism works in neuroblastoma and to figure out how well and safely fructose metabolism inhibitors work as a treatment, more research needs to be done on the metabolism gauge of human malignant neoplastic cells. The application of isothermal calorimetry calscreeners in cancer diagnostic strategies enables the future comparison of innovative treatment methods to established chemotherapy drugs. Hence, microcalorimetry offers a repeatable, reliable, and quick way to assess multiple medicinal responses simultaneously for cancer therapy. It will provide critical insights into the effect of the novel medicine on the unique patient's tumor, which will aid in the progression to a clinical trial and toward individualized tumor therapy.

Abbreviations

AQP1	Aquaporin 1
CAIX	Carbonic anhydrase IX
CT scan	Computerized tomography scan
DNA	Deoxyribose nucleic acid
ERK pathway	Extracellular signal-regulated kinase pathway
G1-phase	Growth 1 phase
MAPK pathway	Mitogen-activated protein kinase pathway
MCF-7 cells	Michigan cancer foundation cell line
MRI scan	Magnetic resonance imaging scan
PET scan	Positron emission tomography
PI3K/AKT/mTOR pathway	Phosphatidylinositol 3-kinase/protein kinase B/mammalian target of rapamycin
S-phase	Synthesis phase

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MTB conceptualized, investigate, draft outline and literature review of original draft. MAA, AFO, TAI, OYL performed the literature review of major aspects of the review draft. OJB, POA, GOA, OOA proofread and reviewed the edited draft. AEA performed the plagiarism check. All authors read and approved the final draft.

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