Technology in Cancer Research & Treatment
Volume 19: 1-2

DOI: 10.1177/1533033820943248
journals.sagepub.com/home/tct
SAGE

New Techniques in Understanding Cancer Biology and Metabolism

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Received: June 19, 2020; Accepted: June 25, 2020.

The challenges to understanding the biology of cancer lies in its heterogeneity that makes each type of cancer a cluster of different subtypes. This diversity not only increases the complexity of the disease but also makes every cancer unique in its composition. Over the past decades, researchers have amassed a tremendous understanding of a vast array of cancers driven by different mutations, responses of the immune system to tumors, symbiotic relationship of cancer cells with the tumor microenvironment, as well as reprogramming of various anabolic and catabolic processes.[1] The emergence of genetic technologies and structural biology approaches have allowed researchers to rapidly sequence and study cancer genomes and epigenomes, revealing genetic alterations.[2] Tremendous technological advances have enabled studying the whole proteome and/or metabolome that helps us to understand interactions with other proteins and effects on cellular behavior. Additionally, combination therapies targeting cancer stem cells have allowed for better treatment modalities for both chemoresistant solid tumors and hematologic cancers over the course of their progression.[3] Development of organoid cultures from patient tumors have helped analyze different yet concerted signaling cues in individual cells revealing how tumors respond to drugs. This has allowed for the development of more effective drugs and selection of the best course of treatment for individual patients; dawning in a new era of personalized precision medicine.[4] Some of these validated discoveries go on to identify clinically useful biological indicators or biomarkers or are developed into potential diagnostic techniques. Diagnostic, prognostic, or predictive biomarkers allows us to address the inherent complexity and the ever-shifting genetic landscape of cancer. There has been a significant advancement in the field that allows prediction, detection, location, as well as therapy monitoring of patients with cancer. Newer technologies are, however, required to address the challenges faced by existing diagnostic techniques to improve the sensitivity and specificity of detection as well as recurrence at an early stage.[5] This research topic is dedicated to articles (a) illustrating the identification of potential diagnostic indicators in cancer detection and prognosis, (b) highlighting novel technologies to further our understanding about cancer metabolism, and (c) evaluating applications of existing techniques and treatment modalities for cancer therapy.

Emerging evidences demonstrate the utility of noncoding RNAs (ncRNA) as a biological marker in different cancers.[6] Aberrant expression of the small nucleolar RNA (snoRNAs), a family of ncRNAs, and their association with the diagnosis as well as prognosis have been reported in distinct cancer types. Additionally, snoRNAs are reportedly stable and lie within detectable ranges in extracellular fluids, such as blood plasma, serum or urine; making it a potential candidate to become a cancer biomarker. In this research topic, Liu *et al*[7] report the role of snoRNA host gene 18 as a tumor suppressor in hepatocellular carcinoma (HCC) and its correlation with tumor grade. Furthermore, plasma snoRNA host gene 18 displayed a greater specificity and sensitivity in HCC patients with relatively lower levels of alpha fetoprotein levels when compared to patients with hepatitis B and cirrhosis. The robustness of both circulating and tissue specific snoRNA host gene 18 expression makes it a potential diagnostic indicator to distinguish HCC from cirrhosis and aid in early detection.

Detection and diagnosis by in situ tissue biopsies are challenged by (a) inaccessible anatomical location of the tissue, (b) safety risk and excruciating discomfort to the patients, (c)

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insufficient quantity or quality of the tissue acquired, (d) compromising the evaluation of genetic mutations throughout the tumor for highly precise methods (needle biopsies), (e) longer wait time for results, and (f) multiple invasive biopsies to assess the progression of cancer. The alternative mode of diagnosis is by liquid biopsy—a rapid, minimally invasive, low risk, high throughput technology. In this research topic, Lu *et al*[8] outline the latest advancement in liquid biopsy as an alternate means of precision therapy in non-small cell lung cancer (NSCLC), one of the most difficult cancers to diagnose. This review article focuses on the present advances and obstacles in employing droplet digital polymerase chain reaction and next-generation sequencing (NGS) techniques in detecting circulating tumor cells and cell-free DNA in NSCLC. Liquid biopsy using NGS allows detection of multiple gene mutations including those of drug resistance as well as tumor heterogeneity, although its sensitivity and specificity limits its use in the clinics. The authors also discuss the effectiveness and restrictions of using cell-free DNA and circulating tumor cells versus tissue biopsy in NSCLC.

The complex biological characteristics and pervasive heterogeneity of tumor cells complicates the process of distinguishing them into distinct morphological and phenotypic profiles. Single-cell technology has emerged as a powerful tool in addressing these difficulties in cancer research studies. In this research topic, Sengupta *et al*[9] illustrates the use of microfluidics for single cell analysis of the key glycolytic pathway metabolites in individual cells. Beyond different genetic or cellular markers, profiling of metabolites is a surrogate and promising diagnostic tool. However, the large cell to cell variability in a clinical setting only allows positron emission tomography measurements of an aggregate metabolic flux discounting tumor cell heterogeneity. The authors characterize a novel droplet microfluidic device for the multiplexed measurements of ^{18}F-fluorodeoxyglucose uptake and corresponding lactate release in single cells. The study underlines the reliance of individual cancer cells on multiple metabolic pathways, besides aerobic glycolysis, even under controlled culture conditions. This further highlights the multiformity of tumor cells and the need for single cell analyses to appreciate the complexity of cancer biology.

Application of stem cells as a cancer therapeutic is an attractive treatment modality that has emerged over the years. In their comprehensive review, Hawsawi *et al*[10] summarizes the mechanisms of various types of adult and pluripotent stem cells in treating different cancers. In addition, they also highlight the challenges, particularly durability, of using stem cells clinically. Although most cancer treatments can target the rapidly proliferating cells, they are unable to attack the slow cycling stem cells that can result in distal recurrences. The authors elaborate that combination therapies targeting both cancer stem cells and tumor mass will result in a more complete and durable response.

Authors' Note

Dipsikha Biswas and Md. Wasim Khan have contributed equally. Both authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication. D.B. is a NBHRF fellow at Dalhousie University and M.W.K. is a Researcher at UIC and funded by Department of Defense, USA (CA191042).

This is an editorial based on previously published work for the special collection. The manuscript did not involve human/animal subjects.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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References

1. Falzone L, Salomone S, Libra M. Evolution of cancer pharmacological treatments at the turn of the third millennium. *Front Pharmacol*. 2018;9:1300. doi:10.3389/fphar.2018.01300
2. Coyle KM, Boudreau JE, Marcato P. Genetic mutations and epigenetic modifications: driving cancer and informing precision medicine. *Biomed Res Int*. 2017;2017:9620870. doi:10.1155/2017/9620870
3. Bighetti-Trevisan RL, Sousa LO, Castilho RM, Almeida LO. Cancer stem cells: powerful targets to improve current anticancer therapeutics. *Stem Cells Int*. 2019;2019:9618065. doi:10.1155/2019/9618065
4. Qin X, Sufi J, Vlckova P, et al. Cell-type-specific signaling networks in heterocellular organoids. *Nat Methods*. 2020;17(3):335-342. doi:10.1038/s41592-020-0737-8
5. Gu H, Gowda GA, Raftery D. Metabolic profiling: are we en route to better diagnostic tests for cancer? *Future Oncol*. 2012;8(10):1207-1210. doi:10.2217/fon.12.113
6. Slack FJ, Chinnaiyan AM. The role of non-coding RNAs in oncology. *Cell*. 2019;179(5):1033-1055. doi:10.1016/j.cell.2019.10.017
7. Liu XF, Thin KZ, Ming XL, et al. Small nucleolar RNA host gene 18 acts as a tumor suppressor and a diagnostic indicator in hepatocellular carcinoma. *Technol Cancer Res Treat*. 2018;17:1533033818794494. doi:10.1177/1533033818794494
8. Lu J, Han B. Liquid biopsy promotes non-small cell lung cancer precision therapy. *Technol Cancer Res Treat*. 2018;17:1533033818801809. doi:10.1177/1533033818801809
9. Sengupta D, Mongersun A, Kim TJ, et al. Multiplexed single-cell measurements of FDG uptake and lactate release using droplet microfluidics. *Technol Cancer Res Treat*. 2019;18:1533033819841066. doi:10.1177/1533033819841066
10. Hawsawi YM, Al-Zahrani F, Mavromatis CH, Baghdadi MA, Saggu S, Oyouni AAA. Stem cell applications for treatment of cancer and autoimmune diseases: its promises, obstacles, and future perspectives. *Technol Cancer Res Treat*. 2018;17:1533033818806910. doi:10.1177/1533033818806910