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Editorial: Metabolic reprogramming and cancer progression

Metabolic reprogramming is a hallmark of malignancy first recognized a century ago, which is also known as the changes of tumor cellular bioenergetics. Compared with normal cells, cancer cells are surrounded by a different microenvironment. Thus, cancer cells exhibit rapidly adaptive responses to hypoxia and hypo-nutrient conditions. Recent work also demonstrates that cancer cells are able to obtain nutrients from a nutrient-deprived environment and to use them to sustain cancer progression, within crucial metabolic pathways, including altered metabolism of glucose, lipids, and amino acids. Also, it has been recognized that one of the major mechanisms of resistance to therapies is due to the altered metabolism. As our understanding of the complexity of tumor biology increases, metabolic heterogeneity among human tumors poses a challenge to developing therapies that exploit metabolic vulnerabilities. Therefore, there is a need to review emerging concepts about metabolic reprogramming in cancer, with particular attention on why metabolic properties evolve during cancer progression, and clearly understand the metabolic underpinnings of the different types of cancer as well as the role the therapies play in targeting the metabolic phenotype.

This Research topic consists of three reviews and eight original research articles. Three reviews focus on the major metabolically adapted pathways in cancer exploring either potential metabolic targets and corresponding agents for cancer treatment or how metabolic adaption influences cancer progression and resistance to therapies. Xiao et al. talked about cancer cells reprogramming into cancer steam cells (CSCs), metabolic reprogramming and microRNA (miRNA) medicated cancer cell reprogramming [1]. Fu et al. discussed mitogen-activated protein kinase (MAPK) pathway, Phosphatidylinositol-3-kinase (PI3K)/AKT/mammalian target of rapamycin (mTOR) signaling, and Wnt/β-catenin signaling pathway, which are altered in cancer cells, as the novel and promising therapeutic targets [2]. The review by Zheng et al. focused on understanding the metabolic mechanisms underlying the development of breast cancer (BC) to provide a druggable potential for BC treatment and drug discovery [3].

In those eight original research articles, as reported by Yan et al. mutation of nucleotide 125 from G to A in the CCN3 coding sequence resulted in differential glycosylated full-length CCN3 protein levels and altered the function of CCN3 protein in osteosarcoma cell invasion and differentiation [4]. In the study by Yang et al. long non-coding RNA (lncRNA) C9orf139 can regulate the progression of esophageal squamous carcinoma (ESCC) by mediating the miR-661/HDAC11 axis, and promoted potential therapeutic targets for ESCC [5]. Huang et al., determined that SULT2B1 may be a key target for reversing radio-resistance and increasing the radiosensitivity of colorectal cancer (CRC), and a potential drug target for treating radio-resistant CRC. Wogonin of *Scutellaria baicalensis* (SB) may be the core compound of SB for reversing radio-resistance in CRC [6]. Zeng et al. highlighted that lncRNA FAM201A accelerates the tumorigenesis and progression of CRC through miR-3163/MACC1 axis [7]. This is the first investigation to shed light on the potential and molecular mechanism of FAM201A in CRC and revealed that FAM201A might be a novel target for the treatment of CRC. Qiao et al. elucidated that KIAA1529 regulates RAD51 expression to confer PARP inhibitors (PARPi) resistance in ovarian cancer [8]. Therefore, targeting KIAA1529 may improve the sensitivity of ovarian cancer to PARPi. Xiong et al. indicated that lncRNA JPX modulates malignant progress of osteosarcoma (OS) through targeting the miR-33a-5p and PNMA1 regulatory loop [9]. These findings suggest that JPX may present a precise therapeutic target and provide a new research direction for OS treatment. Yang et al. revealed that Circular RNA 0010117 (circ-0001946) promotes aggressive glioblastoma behavior by regulating the miRNA-6779-5p/SPEN axis [10]. It provided the rationale for the use of circ-0001946 as a novel potential therapeutic target in glioblastoma. Du et al. discovered that human β-defensin-3 and nuclear factor-kappa B (NF-κB) p65 synergistically promoted the cell proliferation and invasion of oral squamous cell carcinoma (OSCC) [11].

This research topic brings witness that research on metabolic reprogramming is coming of age. It also will bring with exciting results to lay the bases for the development of new therapies. Those studies offer promise for better therapeutic strategies.

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