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Editorial

Cancer Onset and Treatment—From the Perspective of Alkalisation Therapy Based on Science-Based Medicine

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Mitochondria are the primary organs responsible for energy production (oxidative phosphorylation, OXPHOS) in eukaryotic cells and are also deeply involved in the induction of cell death (apoptosis).

In cancer cells, mitochondrial dysfunction triggers the 'Warburg effect' causing the primary energy production pathway to become dependent on glycolysis even in the presence of oxygen [1]. This metabolic reorganization allows cancer cells to maintain an alkaline intracellular environment and an acidic extracellular environment, enabling them to survive and proliferate under hypoxic conditions [2].

Otto Warburg reported in the 1950s that cancer cells rely on glycolytic energy metabolism (aerobic glycolysis) even in oxygen-rich environments, suggesting that this process may be deeply involved in the essence of cancer development [1,3]. Intermittent oxygen deprivation impairs mitochondrial OXPHOS function, halting ATP production and typically leading to cell death (apoptosis). However, some cells switch metabolic pathways via retrograde signals from mitochondria to the nucleus, adapting to oxygen-independent glycolytic metabolism and acquiring the potential to survive and become cancerous [3].

Abnormal glycolytic activity in cancer cells leads to the production of large amounts of protons (H^+), which are expelled from the cell via mechanisms such as sodium-hydrogen exchanger (NHE-1), causing strong acidification of the tumour microenvironment (TME) [2].

This acidic TME promotes the following cancer-specific malignant characteristics [4–8]:

- Promotion of invasion and metastasis
- Activation of the cell proliferation cycle
- Promotion of DNA synthesis and abnormal gene expression
- Induction of angiogenesis
- Activation of multidrug resistance genes
- Suppression of antitumour immunity (including dendritic cells, natural killer cells, and cytotoxic T cells)

The state in which various diseases, including cancer, occur is believed to be largely attributed to the fact that the human body is composed of a structure called a 'dissipative structure' [9]. That is, living organisms are viewed as non-equilibrium open systems that exchange energy and matter, i.e., dissipative structures. The onset of cancer may be closely associated with an increase in entropy within this dissipative structure, i.e., the collapse of internal order. Therapeutic strategies aimed at reducing entropy, i.e., 'reconstruction of order', such as alkalisation therapy, have been proposed. This new perspective redefines cancer not as a mere genetic abnormality, but as a systemic disorder caused by disturbances in the exchange of energy and matter.

Cancer cells maintain a higher alkaline intracellular pH (pHi: 7.2–7.7) than normal cells (pH 6.9–7.1), and the extracellular pH (pHe) is significantly acidified [10].

This acidic environment is maintained by proton efflux mechanisms (NHE-1 and monocarboxylate transporters) [11].

Alkalisation therapy (e.g., administration of baking soda, alkaline-rich diet) is believed to neutralise TME acidification, suppress malignant characteristics of cancer cells, and enhance treatment sensitivity. In particular, reduced NHE-1 activity has been proposed as a potential therapeutic target [12].

Regarding side effects, no serious adverse events were observed even with long-term administration of 0.17 g/kg/day of baking soda, suggesting safety [13].

The essence of cancer is believed to lie in avoiding irreversible damage to mitochondrial function and adapting to oxygen-independent metabolism [14–17]. Under oxygen-deprived conditions, when mitochondria are destroyed, some cells adapt to 'self-centred metabolism' forming an acidic TME while surviving and proliferating [18].

Alkalisation therapy may suppress cancer cell malignancy and improve treatment efficacy by reducing intracellular entropy and correcting the acidic TME. However, current evidence is primarily based on case reports and retrospective studies [19–25], and further validation through randomised controlled trials is necessary.

Cancer arises from metabolic abnormalities caused by localised and intermittent oxygen deprivation, promotes malignant transformation by forming an acidic TME, and acquires treatment resistance. Alkalisation therapy may inhibit cancer progression and improve treatment efficacy by neutralising the acidic TME. However, further prospective clinical trials are needed to establish its clinical efficacy.

Key points

- Mitochondrial abnormalities → Metabolic abnormalities → Carcinogenesis
- Formation of an acidic TME → Increased malignancy and treatment resistance
- Alkalisation therapy → Correction of the TME and potential for cancer suppression
- Further validation through randomised clinical trials is essential.

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