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MICROBIAL BASED THERAPY OF CANCER

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Relevance. Cancer is a leading cause of death worldwide, and traditional cancer therapies, such as chemotherapy and radiation, often have limited efficacy and can cause severe side effects. In recent years, there has been growing interest in using microbial-based therapy for cancer treatment. Microbial-based therapy includes the use of bacteria, viruses, and other microorganisms to selectively target cancer cells and trigger an immune response against the tumor.

Aim: this study will review the current status of microbial-based therapy for cancer treatment, including the types of microorganisms used, the mechanisms of action. It aims to use tumor-specific infectious microbes to fulfill the unmet medical needs for patients with difficult-to-treat malignancies.

Materials and methods. Genetically modified nontoxigenic *C. novyi*-NT, *C.histolyticum* and other clostridia., *S.typhimurium*, *L.monocytogenes*, *Bifidobacteria*, *E.coli*, *Lactobacilli*, etc.

Results and their discussion. Therapeutic approaches proposed include: direct damage of tumor cells by bacterial peptides (arenamides, halitoralins, idoglobomides, lucentamycins, etc), enzymes and toxins (toxin A, diphtheria toxin, verotoxin, C.difficile toxins etc.; immune system activation; tumor microenvironment modulation; bacteria can be used as delivery means for anticancer drugs, prodrug-to-drug-converting enzymes and coding or noncoding genes.

Bacteria used in the studies reviewed are mostly strict anaerobic and some facultative anaerobic species: Genetically modified nontoxigenic *C. novyi*-NT, *C.histolyticum* and other clostridia., *S.typhimurium*, *L.monocytogenes*, *Bifidobacteria*, *E.coli*, *Lactobacilli*, etc.

In principle, bacteria can be introduced into the host through different ways depending on therapeutic strategy and bacteria used, but usually by intratumoral injection. These bacteria disperse in various parts of the host after injection, including solid tumors, and normal organs. Their number and activity is controlled by innate and acquired immune system mechanisms, tumor microenvironment, antibiotics and other means.

More than 15 clinical trials (level I-III) have been conducted during recent 10 years.

Currently several potential advantages and disadvantages of bacteria based anticancer treatment may be considered: high potential for genetic engineering (attenuation, targeting, genes or drugs delivery etc.), high sensitivity of tumor cells to bacteria pathogenicity factors, capabilities of bacteria (anaerobic) to accumulate in ischemic and necrotic tumor core tissues and multiply in tissue, therapeutic bacteria are controllable by antibiotics. Among serious disadvantages are difficult introduction of bacteria into tumor, potential risk of septic complications (shock, tissue toxicity etc.), mutation and development unpredictable pathogenicity or resistance to control, inability to kill all tumor cells and metastases (additional therapy needed).

Conclusion: this study highlights the potential of bacteria based approaches to overcome the limitations of traditional cancer therapies and improve patient outcomes. The mentioned strategies need further research and development to optimize the efficacy and safety.