

## ABSTRACT

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Tumor treating fields: a comprehensive overview of the underlying molecular mechanism.

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**INTRODUCTION:** As a novel treatment modality, tumor treating fields (TTFields) exert low-intensity, medium-frequency electric fields on tumor cells. TTFields' effectiveness and safety have been demonstrated clinically and in the real world for treating glioblastoma, the most common and aggressive primary central nervous system tumor. TTFields therapy has also been approved for the management of malignant mesothelioma, and clinical trials are ongoing for NSCLC, gastric cancer, pancreatic cancer, and other solid tumors.

**AREAS COVERED:** This article comprehensively reviews the currently described evidence of TTFields' mechanism of action. TTFields' most evident therapeutic effect is to induce cell death by disrupting mitosis. Moreover, evidence suggests at additional mechanistic complexity, such as delayed DNA repair and heightened DNA replication stress, reversible increase in cell membrane and blood-brain barrier permeability, induction of immune response, and so on.

**EXPERT OPINION:** TTFields therapy has been arising as the fourth anti-tumor treatment besides surgery, radiotherapy, and antineoplastic agents in recent years. However, the precise molecular mechanisms underlying the effects of TTFields are not fully understood and some concepts remain controversial. An in-depth understanding of TTFields' effects on tumor cell and tumor microenvironment would be crucial for informing research aimed at further optimizing TTFields' efficacy and developing new combination therapies for clinical applications.

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