

UNDERSTANDING THE MECHANISMS OF ACTION OF TUMOR TREATING FIELDS (TTFIELDS) THERAPY



- TTFIELDS employ electric fields at a frequency of **100 kHz-500 kHz**
- They enter cancer cells and **disrupt processes critical to cell viability** with minimal stimulation or heating of the surrounding tissue
- TTFIELDS target and kill cancer cells, while sparing healthy cells and tissue
- Due to its multi-mechanistic actions, **TTFIELDS** demonstrate enhanced efficacy across solid tumour types when used concomitantly with:



Chemotherapy



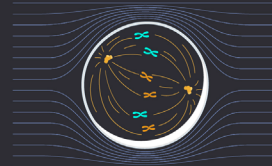
Targeted therapies



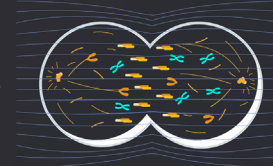
Radiation therapy



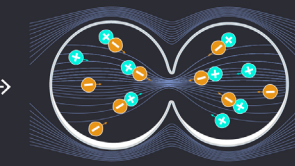
Immuno-oncology agents



Impair microtubule assembly in **METAPHASE**, of cancer cells



Disrupt septin arrangement in **ANAPHASE**, inducing mitotic failure



Push polar organelles and macromolecules at different intensities during **TELOPHASE**, inducing unequal division between parent and daughter cells leading to cell death



- Downregulate DNA replication and DNA damage response genes in cancer cells
- Disrupt DNA damage repair via downregulating the FA-BRCA pathway



Downregulation of DNA damage response



Disruption of mitosis

How TTFIELDS can Lead to Cancer Cell Death



Interference of cell movement and migration



Downstream enhancement of antitumour immunity



- Exert directional force on polar tubulins, aligning them in the direction of the field, reorganizing the microtubule network and leading to changes in the abundance of microtubules
- Initiate the GEF-H1/RhoA/ROCK signalling pathway, leading to increased actin bundling and the formation of focal adhesions, which disrupt cell polarity and migration directionality



Abbreviations
ATP: adenosine triphosphate;
DAMP: damage-associated molecular patterns; FA-BRCA: Fanconi anaemia/BRCA;
HMGB1: high mobility group box 1; TTFIELDS: tumor treating fields therapy.

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