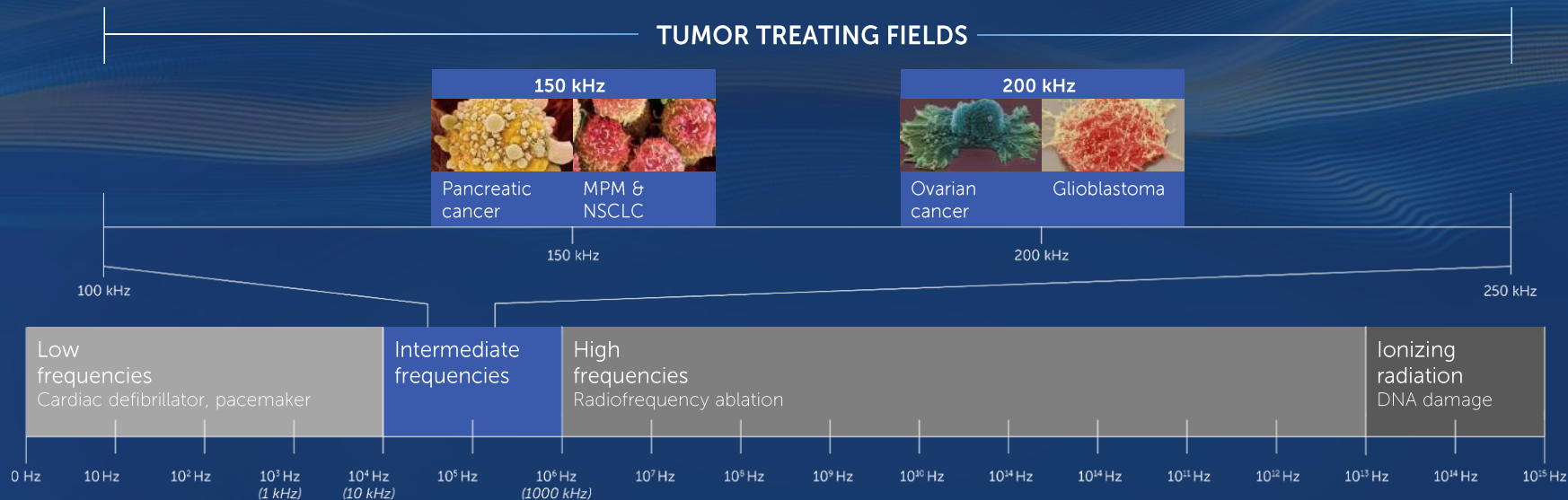


applying basic biology to address critical unmet needs

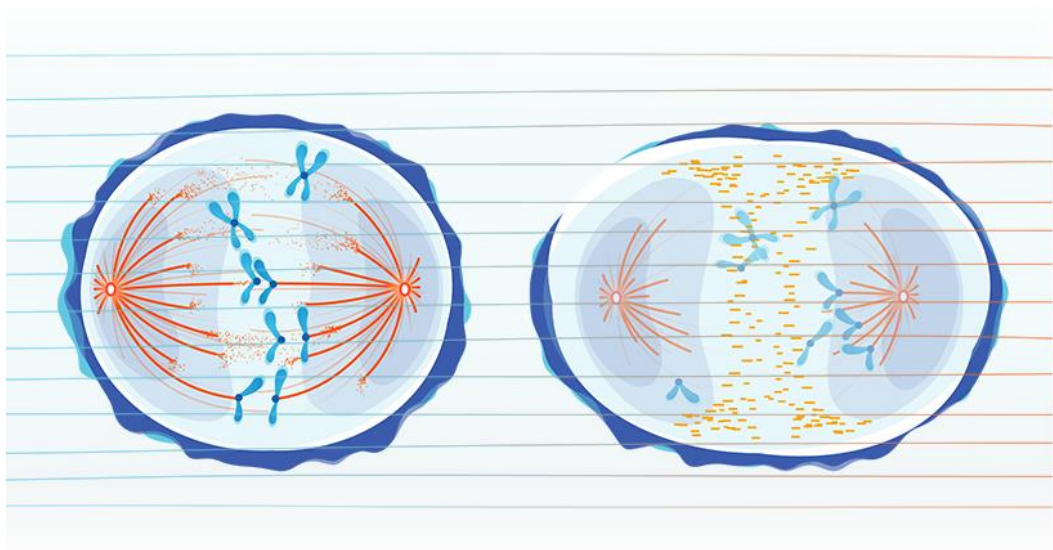
TRANSLATIONAL RESEARCH

Dr. Moshe Giladi
Director of Preclinical Research
Novocure

TTFields are unique in their frequency, intensity and mode of delivery



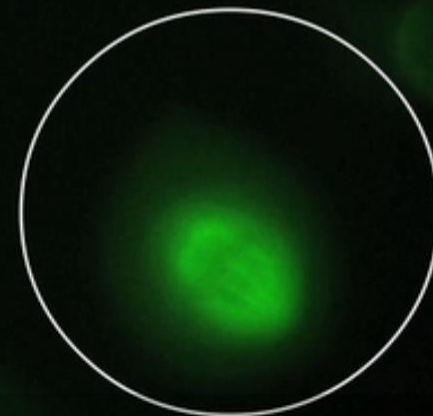
frequency tuning enables generation of electric field within cancer cells



Tumor Treating Fields are electric fields that disrupt cancer cell division

untreated cells

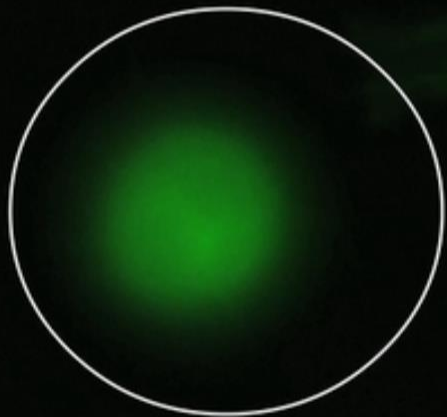
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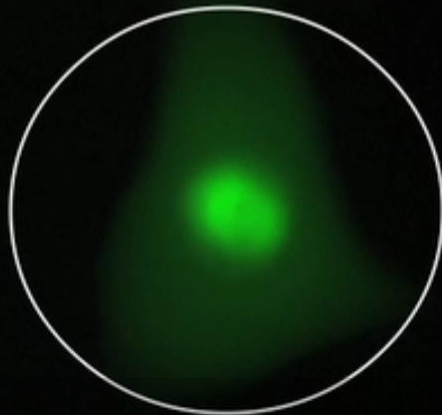
TTFields

disrupt key elements of mitosis

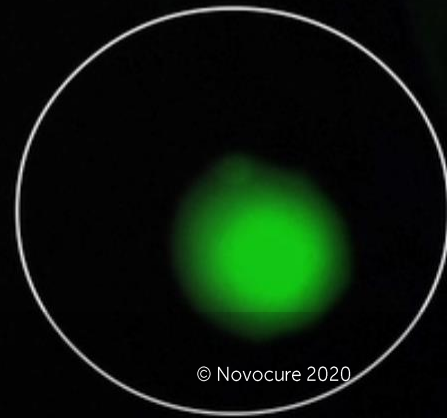
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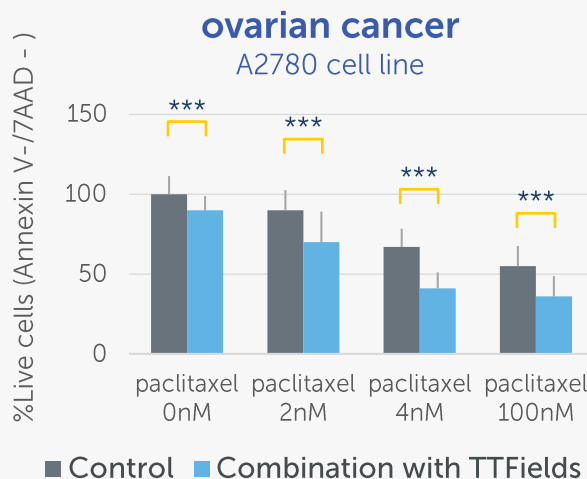
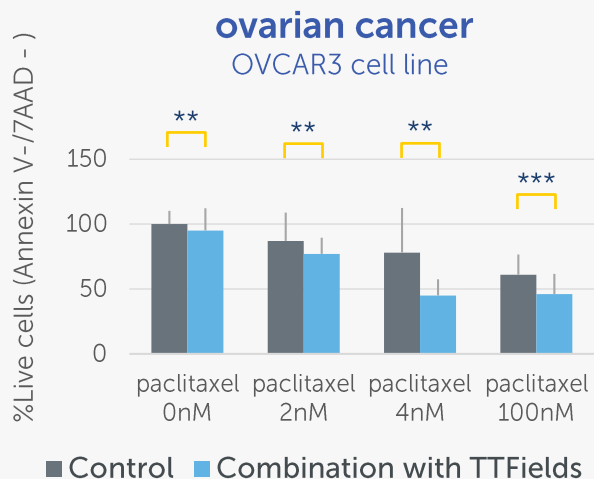
00:23:00



00:23:00



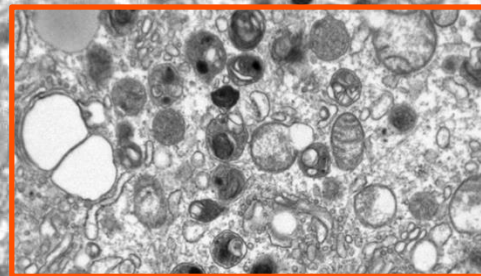
potential synergistic interactions of TTFields and anti-mitotic agents



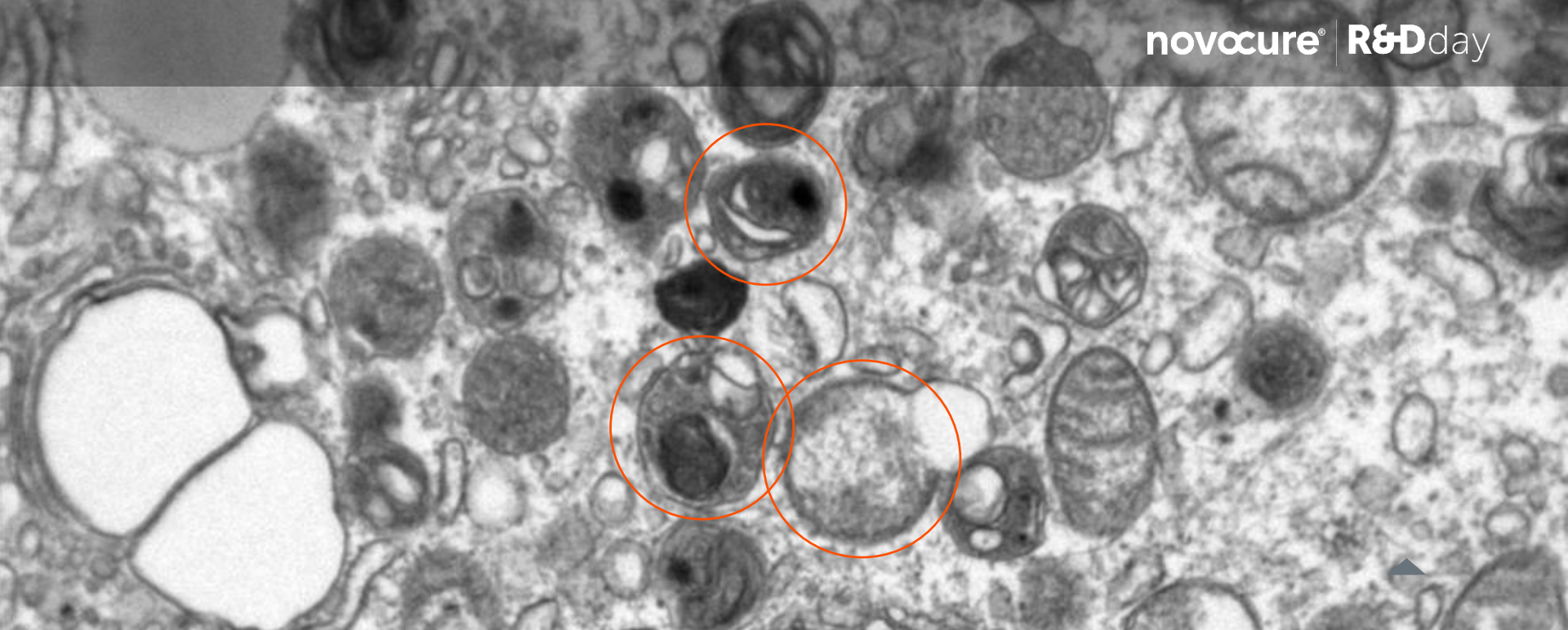
TTFields may synergize with anti-mitotic agents in multiple ovarian cancer cell lines

p < 0.01; * p < 0.001

TTFields' anti-mitotic effect is only the starting point for multiple other downstream outcomes

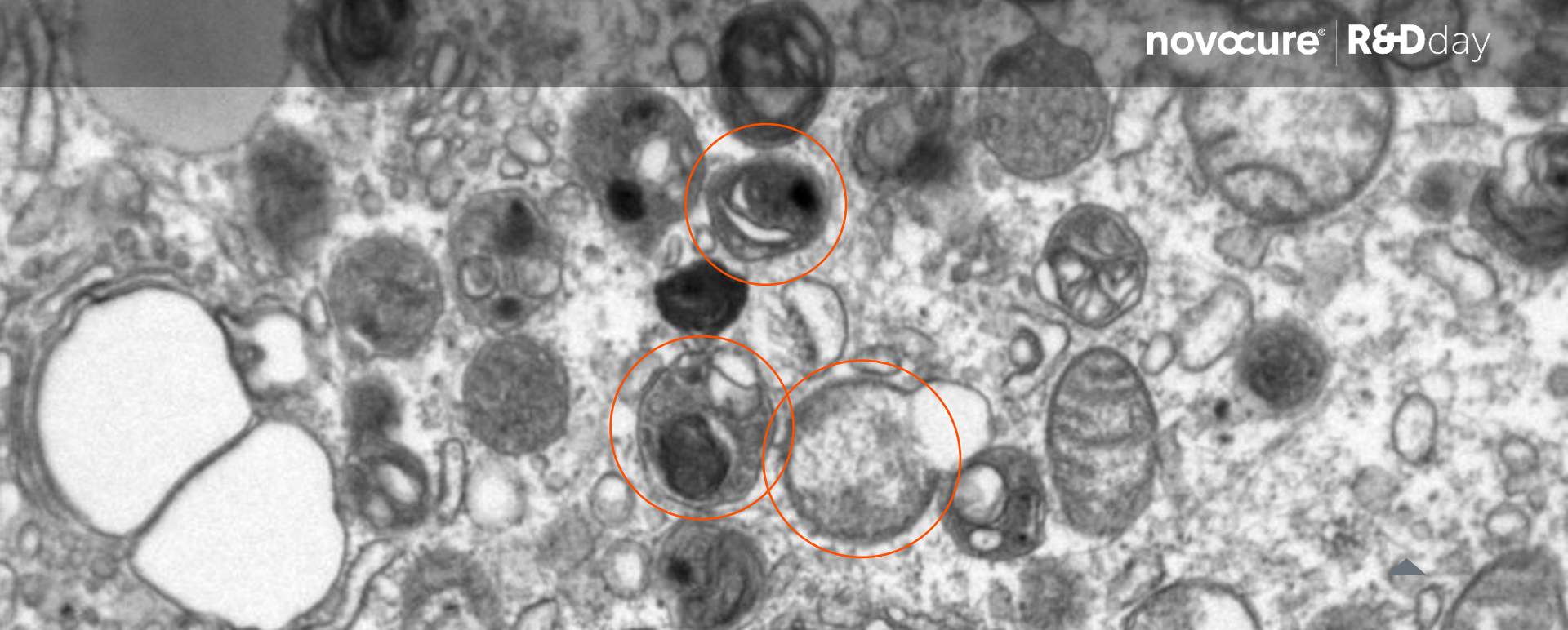


compromised cell functions



compromised cell functions

induction of autophagy and ER stress

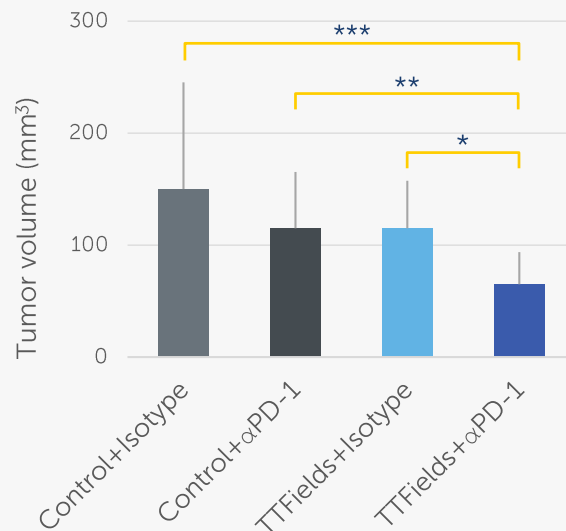


These are the key drivers for immunogenic cell death

TTFields enhanced efficacy of immune checkpoint inhibitors

combined TTFields and immune checkpoint inhibitors may enhance treatment efficacy

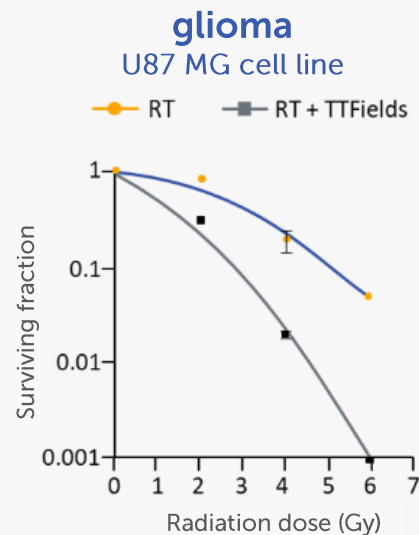
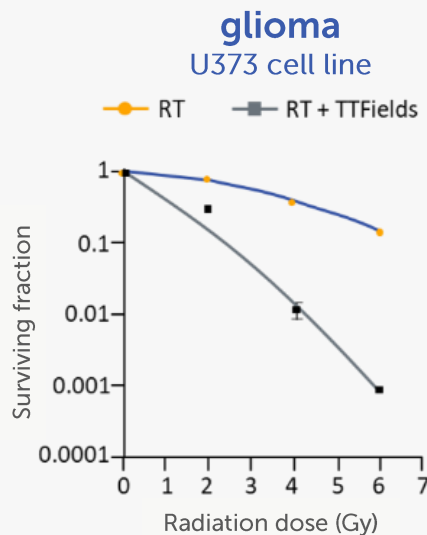
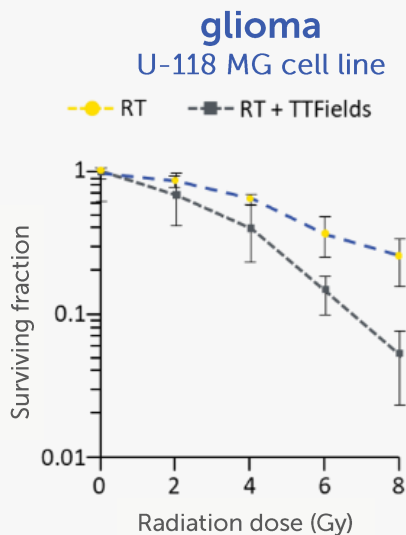
non-small cell lung cancer



* p < 0.05, ** p < 0.01, *** p < 0.001

TTFields interfered with DNA damage repair

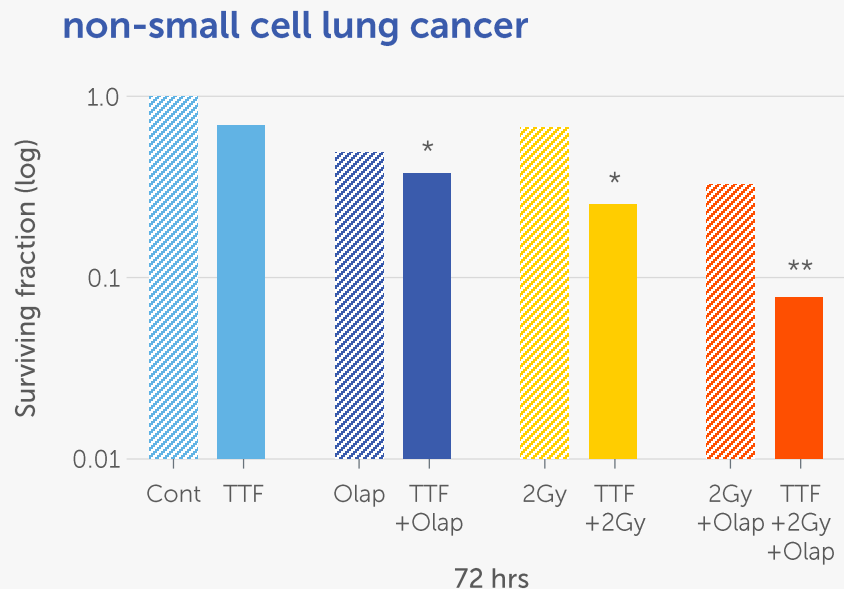
combination treatment may induce DNA damage



TTFields serves as a radiotherapy sensitizer and inhibits DNA damage repair mechanisms with outcomes repeated across multiple cell lines

Modified from:
<https://pubmed.ncbi.nlm.nih.gov/29284495/> and <https://pubmed.ncbi.nlm.nih.gov/27556699/>
 Tumor treating fields (TTFields) delay DNA damage repair following radiation treatment of glioma cells. Giladi M, Munster M, Schneiderman RS, Voloshin T, Porat Y, Blat R, Zielinska-Chomez K, Hääg P, Bornzon Z, Kirson ED, Weinberg U, Viktorsson K, Lewensohn R, Palti Y. *Radiat Oncol*. 2017 Dec 29;12(1):206. doi: 10.1186/s13014-017-0941-6.PMID: 29284495
 Biological effect of an alternating electric field on cell proliferation and synergistic antimitotic effect in combination with ionizing radiation.
 Kim EH, Kim YH, Song HS, Jeong YK, Lee JY, Sung J, Yoo SH, Yoon M. *Oncotarget*. 2016 Sep 20;7(38):62267-62279. doi: 10.18632/oncotarget.11407.PMID: 27556699

predictable & synergistic deterioration of cell lines



combination strategies may further enhance TTFIELDS efficacy

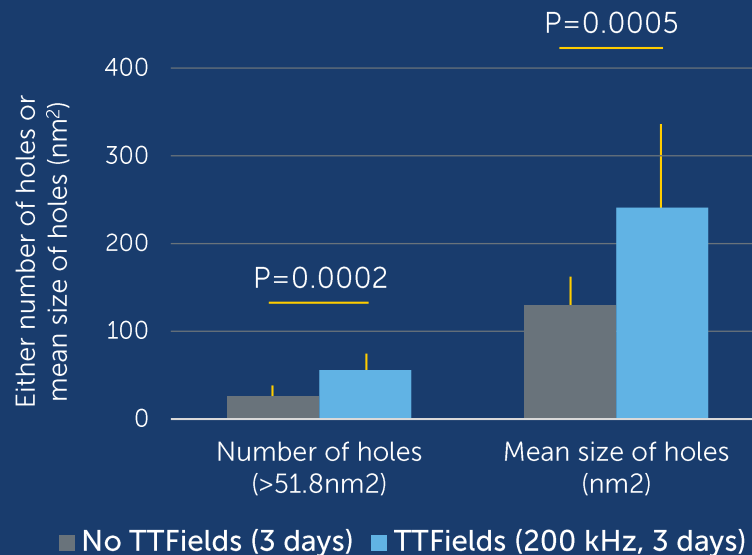
*p < 0.05; ** p < 0.01

TTFields' effects on cell membrane permeability

60,000x
(200nm)

Control

TTFields



<https://pubmed.ncbi.nlm.nih.gov/30534421/>
 Tumor treating fields increases membrane permeability in glioblastoma cells.
 Chang E, Patel CB, Pohling C, Young C, Song J, Flores TA, Zeng Y, Joubert LM, Arami H, Natarajan A, Sinclair R,
 Gambhir SS. Cell Death Discov. 2018 Dec 5; 4:113. doi: 10.1038/s41420-018-0130-x. eCollection 2018. PMID: 30534421

Continuous investment in R&D driving new research outcomes

3 years
of AACR-Novocure
research grants program



44

projects studying TTFields
preclinically in leading
institutes worldwide

20x

preclinical research scientists