cancers

Supplementary Materials: Modulated Electro-Hyperthermia Induces a Prominent Local Stress Response and Growth Inhibition in Mouse Breast Cancer Isografts

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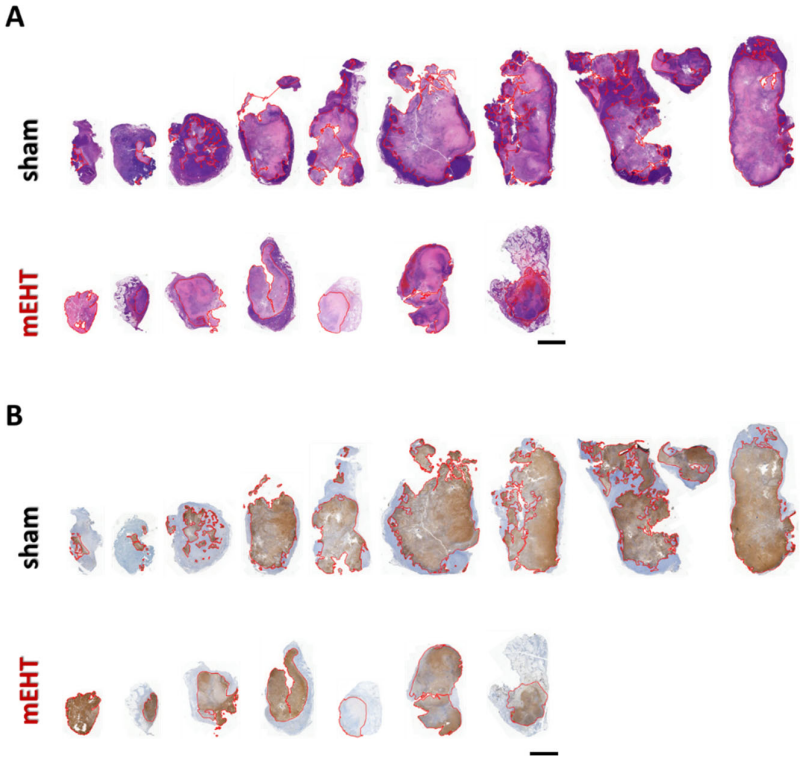

Figure S1. Hematoxylin-eosin (HE) (A) and cleaved caspase-3 (cC3) (B) immunohistochemistry stained sections of all tumors by groups, 24h after the fifth mEHT treatment. Destructed area is annotated (red) for calculation of TDR. ($n_{(sham)}$ = 9, $n_{(mEHT)}$ =7. Scale bar: 2000 μm).

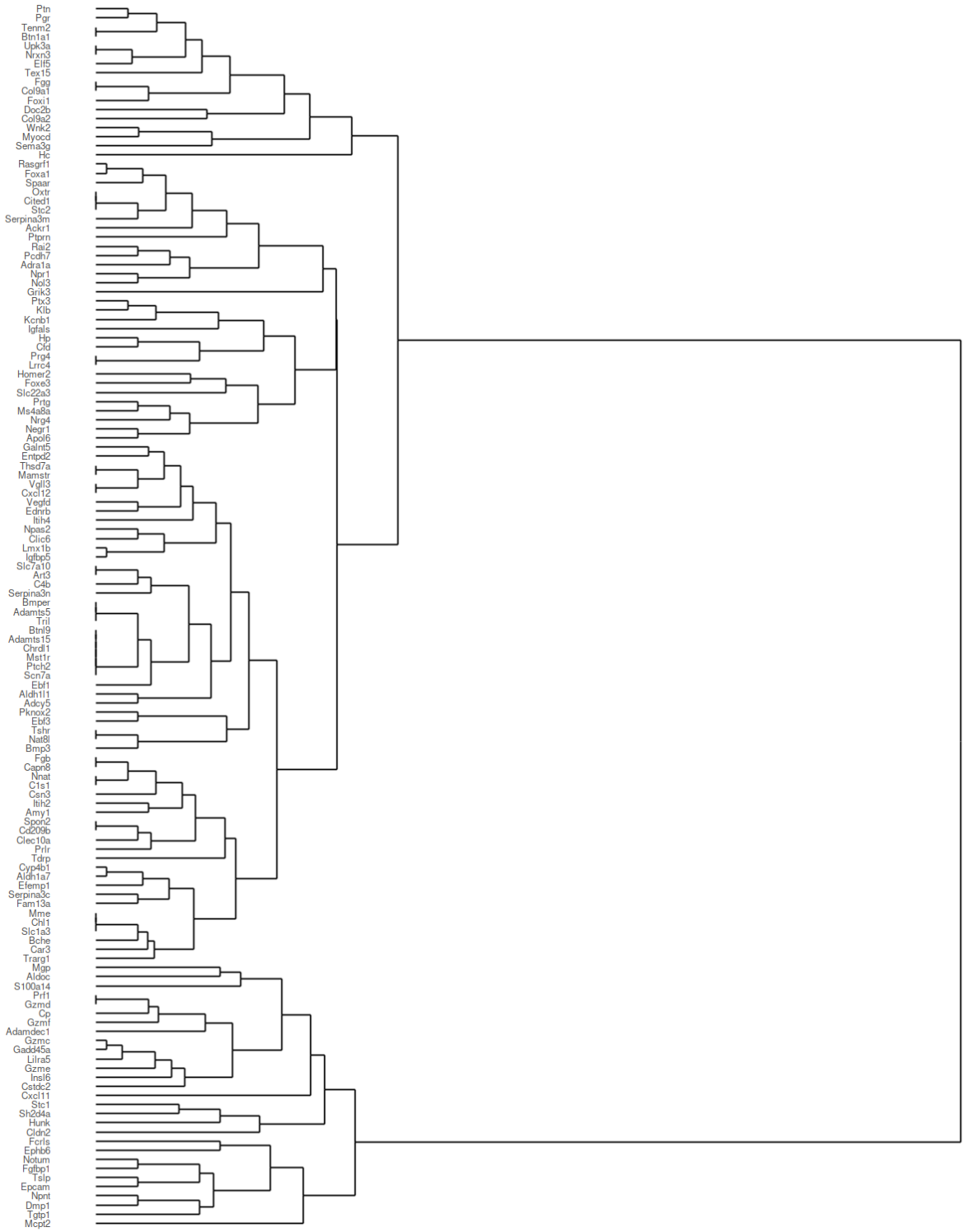

Figure S2. Heat map dendogram of the differentially expressed (DE) genes with labels after 3 mEHT treatments.

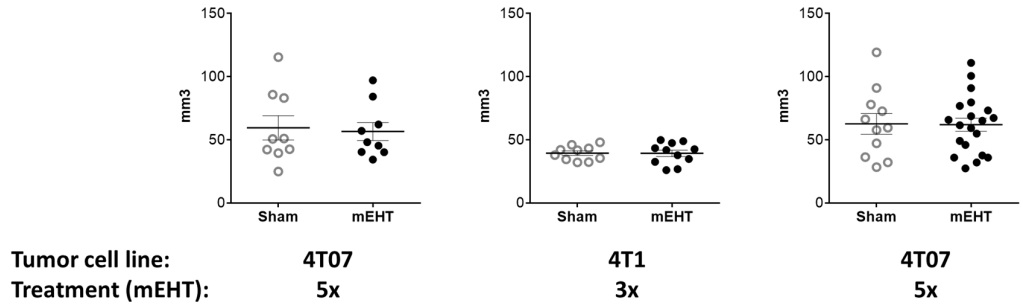

Figure S3. Tumor volumes measured by ultrasound at randomization (day 6 after inoculation). Treatment interval: 48h, harvest: 24h after last treatment.

Table S1. Tabular display of Figure 6.: upregulated genes in the response to stimulus pathway as identified by the gene ontology (GO) analysis.

Gene Name	Description	*p*	FC
Fgb	fibrinogen beta chain	2.1E-04	28.4
Itih4	inter alpha-trypsin inhibitor, heavy chain 4	2.7E-04	22.7
Klb	klotho beta	1.5E-03	17.7
Car3	carbonic anhydrase 3	3.5E-04	16.9
Nnat	neuronati	2.3E-03	15.8
Bmper	BMP-binding endothelial regulator	4.3E-03	15.6
Fgg	fibrinogen gamma chain	5.9E-03	15.0
Prlr	prolactin receptor	9.3E-04	14.9
Slc7a10	solute carrier family 7 (cationic amino acid transporter, y+ system), member 10	2.0E-03	13.6
Cited1	Cbp/p300-interacting transactivator with Glu/Asp-rich carboxy-terminal domain 1	1.3E-04	12.9
Foxa1	forkhead box A1	2.8E-03	12.0
Oxtr	oxytocin receptor	5.7E-04	11.5
Tshr	thyroid stimulating hormone receptor	4.4E-03	11.5
Bche	butyrylcholinesterase	1.8E-03	11.3
Igfals	insulin-like growth factor binding protein, acid labile subunit	4.7E-03	11.0
Gpr182	G protein-coupled receptor 182	8.0E-04	10.3
Cfd	complement factor D (adipsin)	1.2E-03	10.0
Amy1	amylase 1, salivary	2.1E-03	9.7
Hp	haptoglobin	7.4E-04	9.7
Lmx1b	LIM homeobox transcription factor 1 beta	4.0E-03	9.5
Slc36a2	solute carrier family 36 (proton/amino acid symporter), member 2	1.8E-03	9.3
Nat8l	N-acetyltransferase 8-like	7.8E-03	9.2
Grik3	glutamate receptor, ionotropic, kainate 3	1.0E-03	8.4
Slc1a3	solute carrier family 1 (glial high affinity glutamate transporter), member 3	3.3E-03	8.4
Serpina3n	serine (or cysteine) peptidase inhibitor, clade A, member 3N	6.8E-04	8.4
Slc22a3	solute carrier family 22 (organic cation transporter), member 3	1.0E-03	7.5
Rasgrf1	RAS protein-specific guanine nucleotide-releasing factor 1	6.3E-03	7.4
Igfbp5	insulin-like growth factor binding protein 5	2.8E-03	6.9
Cxcl12	chemokine (C-X-C motif) ligand 12	5.4E-03	6.8
Slc25a23	solute carrier family 25 (mitochondrial carrier; phosphate carrier), member 23	4.3E-03	6.7
Dpyd	dihydropyrimidine dehydrogenase	6.9E-03	6.5
Serpina3m	serine (or cysteine) peptidase inhibitor, clade A, member 3M	1.1E-03	6.4
Stc2	stanniocalcin 2	3.2E-03	6.1
Trarg1	trafficking regulator of GLUT4 (SLC2A4) 1	8.9E-03	5.3
Adamts3	a disintegrin-like and metallopeptidase (reprolysin type) with thrombospondin type 1 motif, 3	3.7E-03	5.2
Draxin	dorsal inhibitory axon guidance protein	6.6E-03	5.1
Cyp4b1	cytochrome P450, family 4, subfamily b, polypeptide 1	7.1E-03	5.1
Zfp423	zinc finger protein 423	4.8E-03	3.9
response to stimulus, GO:0050896			

p = 0.00012, genes: 38

Top row: GO identification number and p-value of the pathway, and the number of genes upregulated by modulated electro-hyperthermia (mEHT) in the pathway. Table: gene descriptions, and individual p and FC values of the genes.

Table S2. Upregulated genes in stress response related pathways as identified by the gene ontology (GO) analysis.

Gene Name	***p***	**FC**	**Gene Name**	***p***	**FC**	**Gene Name**	***p***	**FC**	**Gene Name**	***p***	**FC**
Fgb	2.1E-04	28.4	Itih2	2.1E-05	31.1	Ptx3	4.6E-02	5.6	Fgb	2.1E-04	28.4
Cd5l	1.6E-01	19.6	Itih4	2.7E-04	22.7	C4b	3.0E-02	4.6	Bmper	4.3E-03	15.6
Spon2	1.3E-02	15.5	Serpina3n	6.8E-04	8.4	Vsig4	2.0E-01	3.5	Fgg	5.9E-03	15.0
Cfd	1.2E-03	10.0	Serpina3c	1.1E-02	7.0	Serping1	1.1E-01	2.6	Dmbt1	5.1E-02	12.1
Reg3g	1.3E-01	4.6	Serpina3m	1.1E-03	6.4	Cd93	3.0E-01	2.3	Col9a2	2.5E-03	11.6
C4b	3.0E-02	4.6	Serpinb2	2.5E-01	4.0	C5ar1	3.7E-01	2.3	Col9a1	2.9E-02	8.0
Hc	4.0E-02	3.9	Col28a1	1.2E-01	3.1	Cfh	4.6E-01	2.1	Ogn	7.9E-02	8.0
Cd37	1.1E-01	3.7	Serping1	1.1E-01	2.6	Cd59a	5.0E-01	2.0	Efemp1	3.8E-02	7.3
Ppbp	3.5E-01	3.6	Wfdc17	3.9E-01	2.4	-	-	-	Col6a6	9.9E-02	5.1
Pf4	2.1E-01	3.6	Serpina1b	3.0E-01	2.4	-	-	-	Vtn	1.1E-01	5.0
Vsig4	2.0E-01	3.5	-	-	-	-	-	-	Prelp	4.5E-02	4.0
Hpx	2.3E-01	3.5	-	-	-	-	-	-	Spock2	9.8E-02	3.9
C1s1	4.9E-02	3.4	-	-	-	-	-	-	Col17a1	9.1E-02	3.8
Ltf	2.7E-01	3.0	-	-	-	-	-	-	Matn4	1.4E-01	3.8
Cd55	2.6E-01	2.9	-	-	-	-	-	-	Col28a1	1.2E-01	3.1
Cfi	3.3E-01	2.9	-	-	-	-	-	-	Dcn	6.8E-02	3.1
Cxcl3	3.8E-01	2.7	-	-	-	-	-	-	Vcan	9.0E-02	3.1
C2	1.7E-01	2.6	-	-	-	-	-	-	Dpt	2.3E-01	3.0
Serping1	1.1E-01	2.6	-	-	-	-	-	-	Lama2	1.2E-01	2.9
Col20a1	3.4E-01	2.4	-	-	-	-	-	-	Col14a1	2.6E-01	2.7
C1rb	3.5E-01	2.3	-	-	-	-	-	-	Col3a1	1.8E-01	2.6
-	-	-	-	-	-	-	-	-	Comp	2.8E-01	2.6
-	-	-	-	-	-	-	-	-	Fbln1	1.4E-01	2.6
-	-	-	-	-	-	-	-	-	Hmcn2	2.0E-01	2.6
-	-	-	-	-	-	-	-	-	Col5a3	5.3E-02	2.5
-	-	-	-	-	-	-	-	-	Col9a3	3.3E-01	2.4
-	-	-	-	-	-	-	-	-	Fbn2	2.6E-01	2.4
-	-	-	-	-	-	-	-	-	Slit2	2.8E-01	2.4
-	-	-	-	-	-	-	-	-	Fbn1	2.5E-01	2.3
-	-	-	-	-	-	-	-	-	Col6a5	4.6E-01	2.2
-	-	-	-	-	-	-	-	-	Mmrn2	3.5E-01	2.2
-	-	-	-	-	-	-	-	-	Emilin2	3.9E-01	2.2
-	-	-	-	-	-	-	-	-	Hmcn1	4.3E-01	2.1
-	-	-	-	-	-	-	-	-	Bgn	3.8E-01	2.1
-	-	-	-	-	-	-	-	-	Col1a1	4.3E-01	2.1
-	-	-	-	-	-	-	-	-	Col15a1	4.6E-01	2.1
-	-	-	-	-	-	-	-	-	Nid1	4.8E-01	2.0
-	-	-	-	-	-	-	-	-	Col27a1	4.9E-01	2.0
-	-	-	-	-	-	-	-	-	Fras1	6.6E-01	1.7
humoral immune response GO:0006959			**serine-type endopeptidase inhibitor activity GO:0004867**			**complement binding GO:0001848**			**extracellular matrix structural constituent binding GO:0005201**		
***p* = 1.38e-05, genes: 21**			***p* = 1.9e-05, genes: 10**			***p* = 0.000241, genes: 8**			***p* = 4.9e-11, genes: 39**		

Top row: GO identification numbers and p-values of the pathways, and the number of genes upregulated by modulated electrohyperthermia (mEHT) in the pathways. Table: gene descriptions, and individual p and FC values of the genes.