

Local oncothermia treatment fights against systemic malignancy

Prof. Dr. Andras Szasz

Professor of physics & biophysics

Chair, Department of Biotechnics, St. Istvan University, Hungary &

Visiting professor (bioelectromagnetics) in Pazmany P. Catholic University, Hungary &

Visiting professor (fractal physiology) in Chiba University, Japan &

Chief Scientific Officer (CSO), Oncotherm GmbH, Troisdorf, Germany

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Clifford Hospital, Ghuangzhou, China

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Outline

☐ **Historical challenge**

☐ **Concept – integrative medicine**

☐ **Oncothermia – integrative therapy**

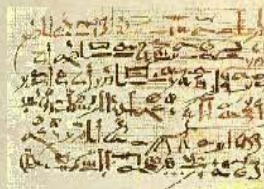
☐ **Results and perspectives**

Western pages

Eastern pages

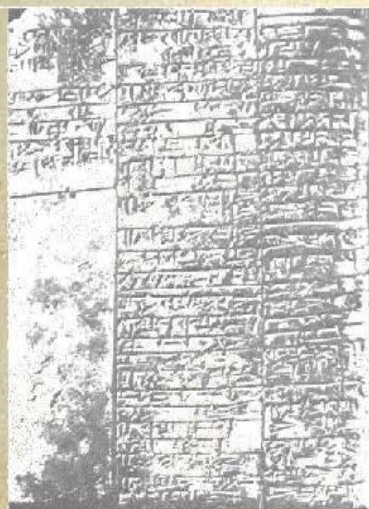
First written summary on medicine (3000 BC)
(Edwin Smith Surgical *Papyrus*)

First written summary on medicine (3000 BC)
(Huang Ti, "The Yellow Emperor")



Western pages

Eastern pages



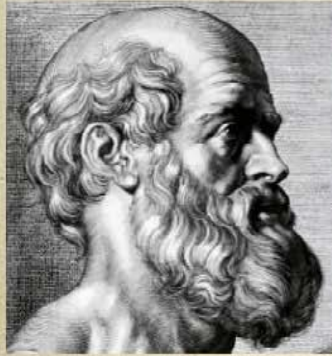
THE OLDEST MEDICAL "HANDBOOK"
Clay tablet with pharmaceutical inscription from Nippur, Late 3rd millennium B.C.
National Museum, University of Pennsylvania, Philadelphia

Medical philosophy

**Philosophy of Western medicine -
Hippocrates (400 BC)**

**Philosophy of Eastern medicine -
Lao Zi (500 BC)**

Western pages



"Nil Nocere"
- Help the nature -

Oncology: hyperthermia

Eastern pages



"Be harmonic"
- Nature is harmonic -

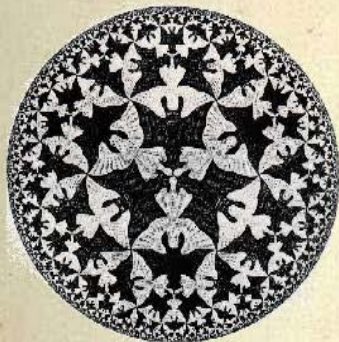
Oncology: herbal medicine

The symbols and philosophy

Western symbol of complexity

Eastern symbol of complexity

Western pages

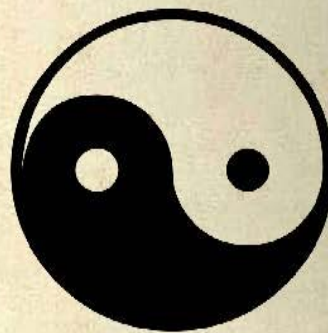


Plato &
Aristotle

ideal
↕
material



Eastern pages



Confucius & Lao-zi

social ↔ **individual**



Measurements (laboratory, imaging, ECG, etc.)

Registers the measurements in values (cm, g, s, ...)

Diagnosis is based on the **physiological, anatomical system**

Questioning based on data of the patient (ECG, Laboratory, ergometry, etc.):

“organ failure?”

Medication:
mostly **artificial** industry products



Observations (smelling, hearing, touching, asking, etc.)

Evaluates the observations (yin-yang, five-phases, etc.)

Diagnosis is based on the **human energy system**

Questioning based on actual state of the patient (nutrition, emotion, social, etc):

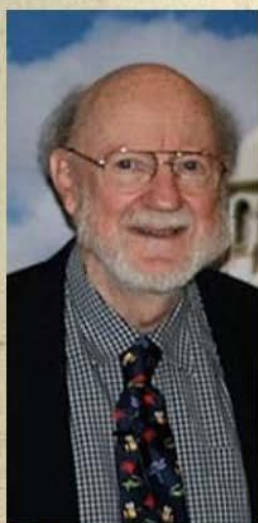
“energetic failure?”

Medication:
mostly **natural** TCM products

Western pages

Eastern pages

The 2015 Nobel Prize in Physiology or Medicine
has been jointly awarded for their discoveries of the
natural products



Dr. William C. Campbell



Dr. Satoshi Ōmura



Dr. You You Tu

The 2015 Nobel Prize in Physiology or Medicine



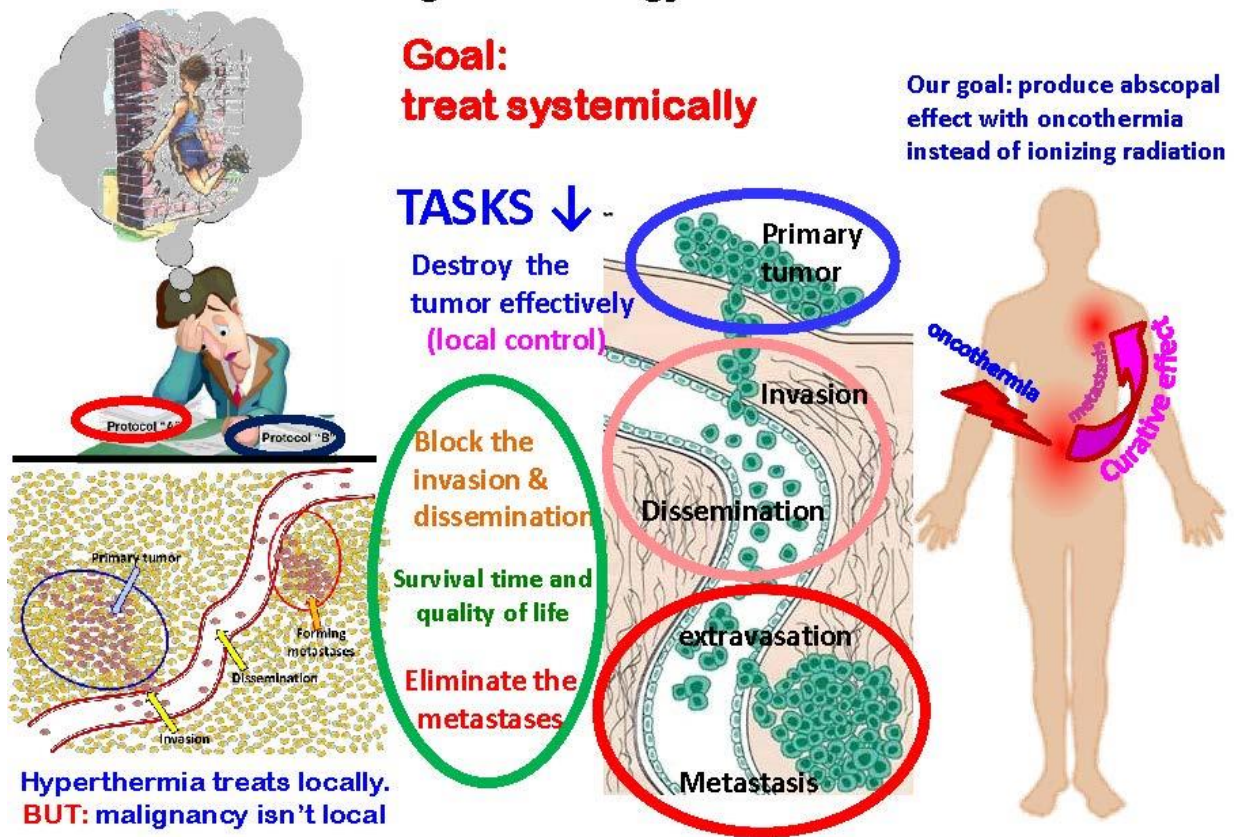
Dr. You You Tu

Dr. Tu received the award for her work on **artemisinin**, an anti-malarial agent **from *Artemisia annua***, a plant that has been used in reducing fevers for centuries and is well documented in **traditional Chinese medicine**.

Outline

- ☐ Historical challenge
- ☐ Concept – integrative medicine
- ☐ Oncothermia – integrative therapy
- ☐ Results and perspectives

Challenge in oncology – what to treat?



Integrative thinking is necessary

Cancer is not cellular disease!

Cancer is systemic, it is a loss of complexity!



Bruce West
Chief scientist for the
Army Research Office at
the U.S. Army Laboratory

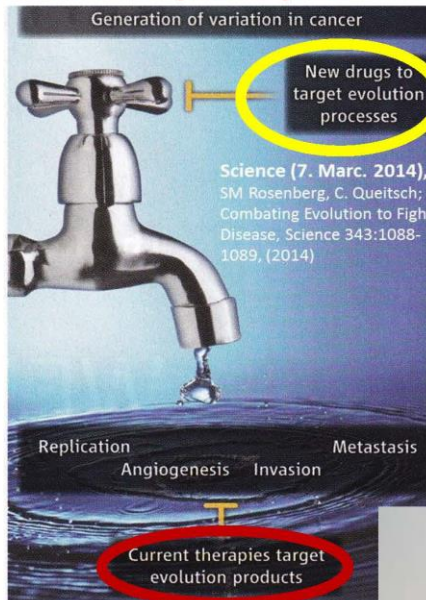


**TCM is not
alternative medicine
It is integrative!**

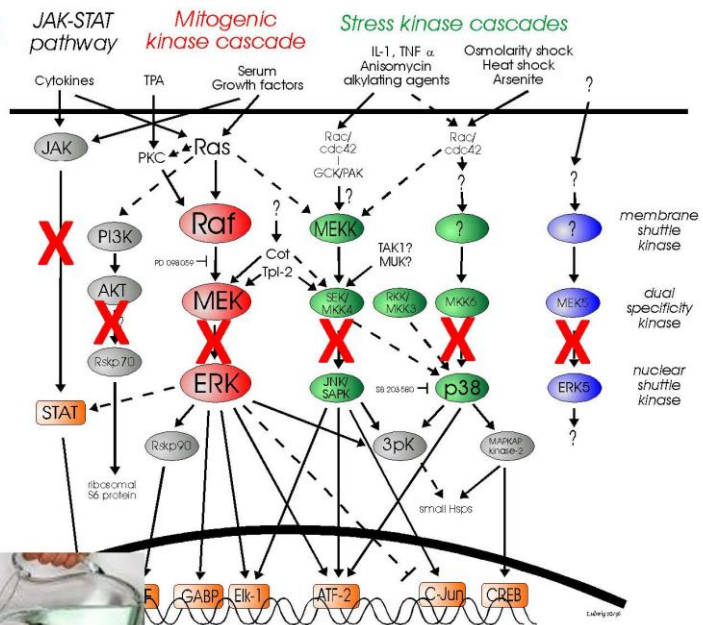
Recovering the Path to Complexity

What's Wrong?

Critics of the present pharma-concepts



Example:



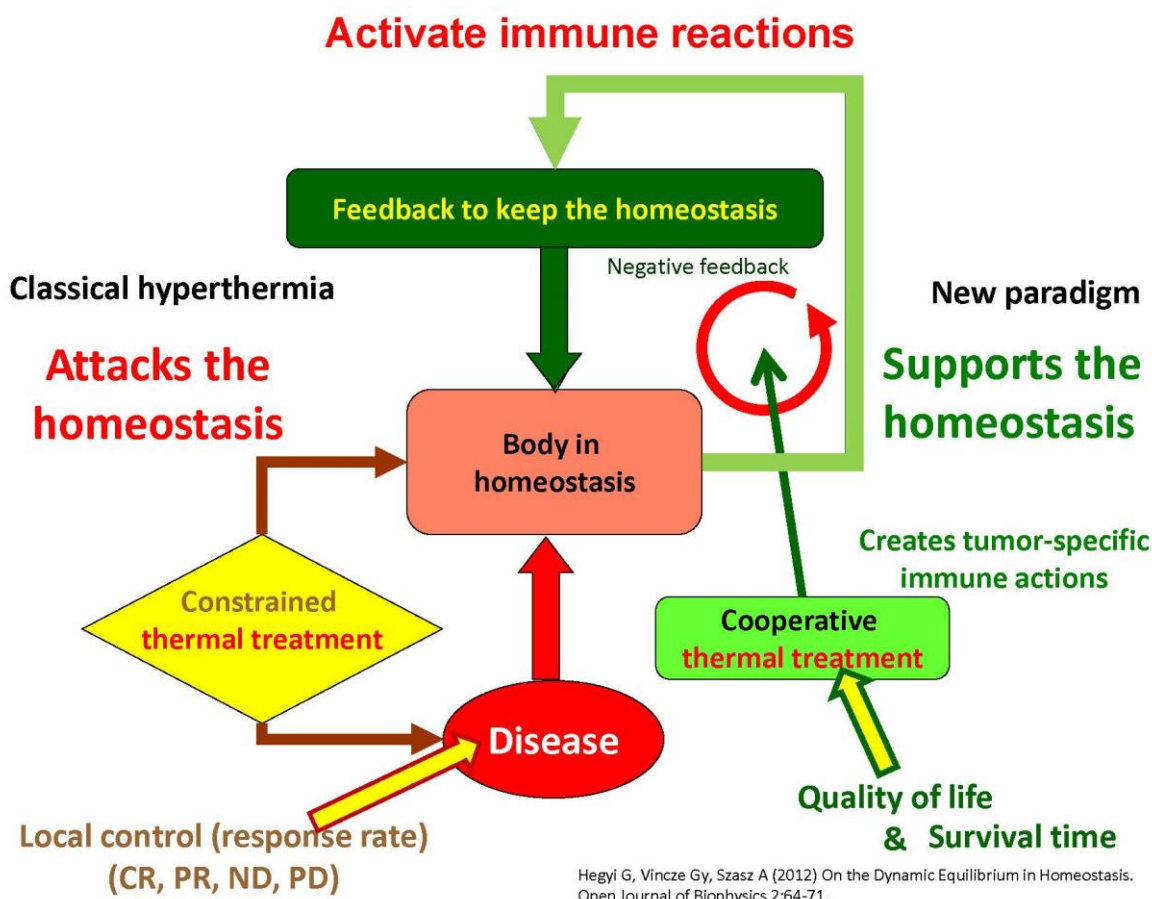
No feedback mechanisms

The above processes are not realistic

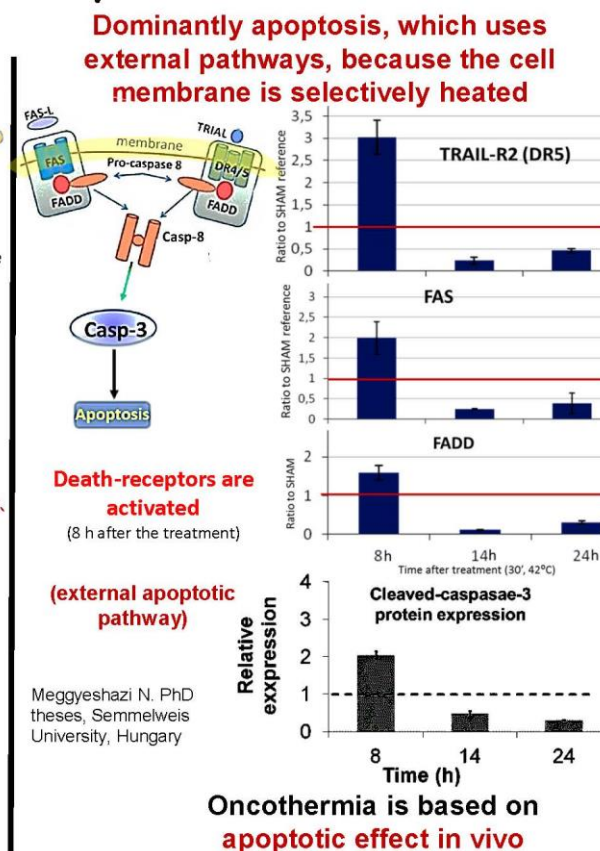
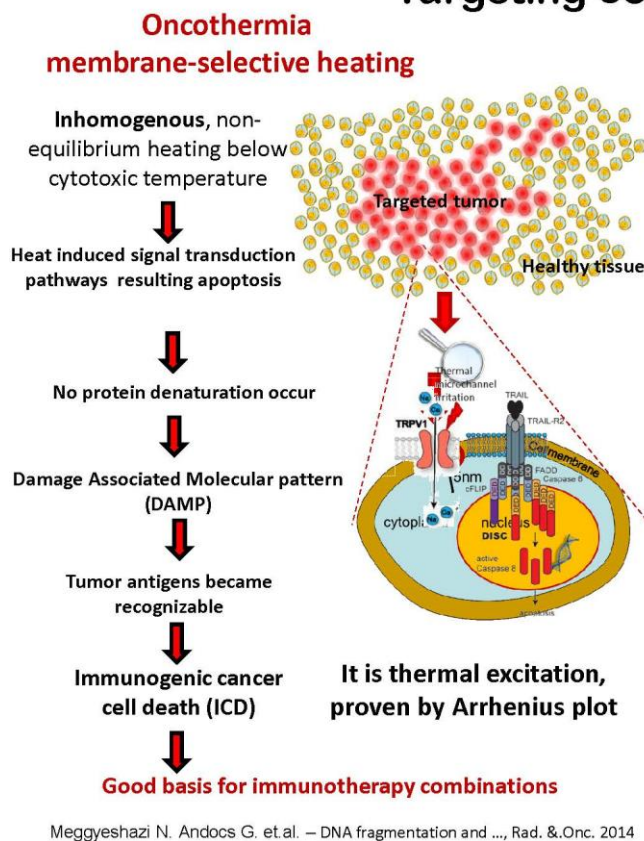
Integrative medicine concentrates on the processes and cares on the balances!

Outline

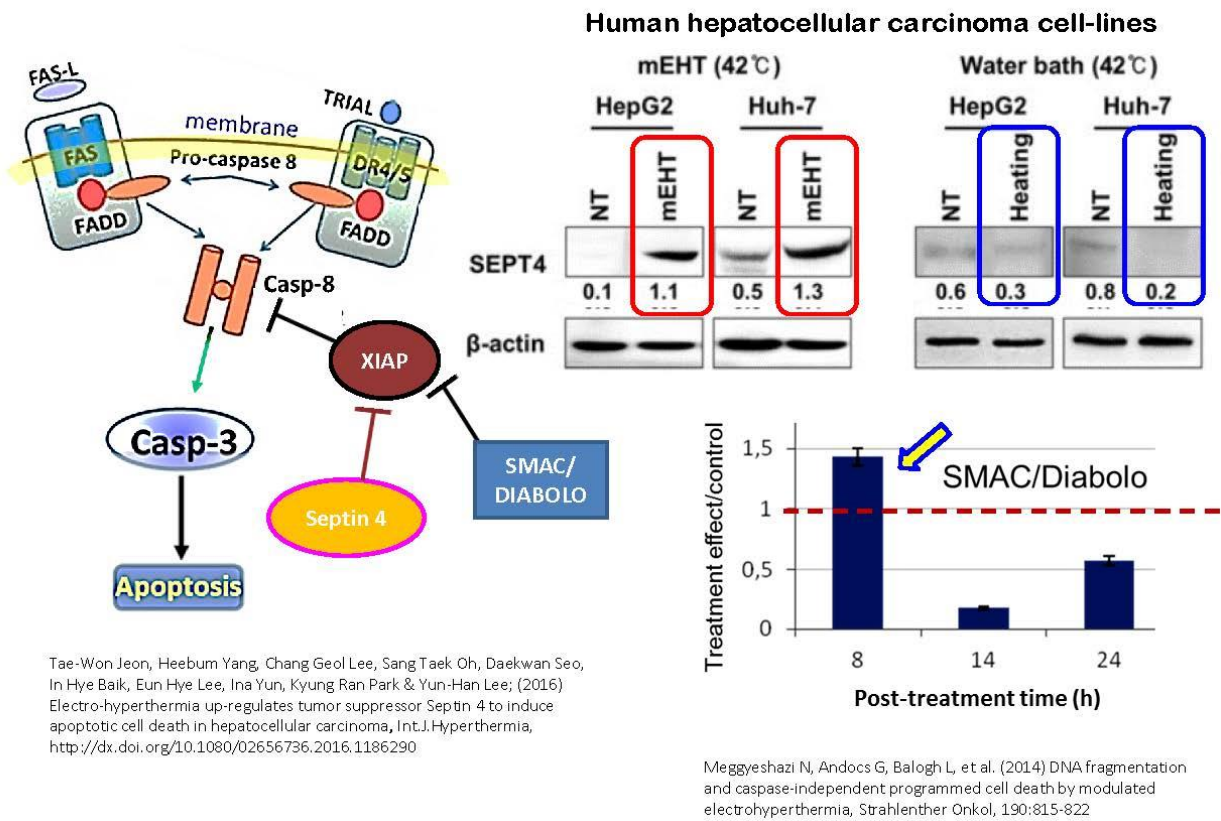
- ☐ Historical challenge
- ☐ Concept – integrative medicine
- ☐ Oncothermia – integrative therapy
- ☐ Results and perspectives



Targeting consequences



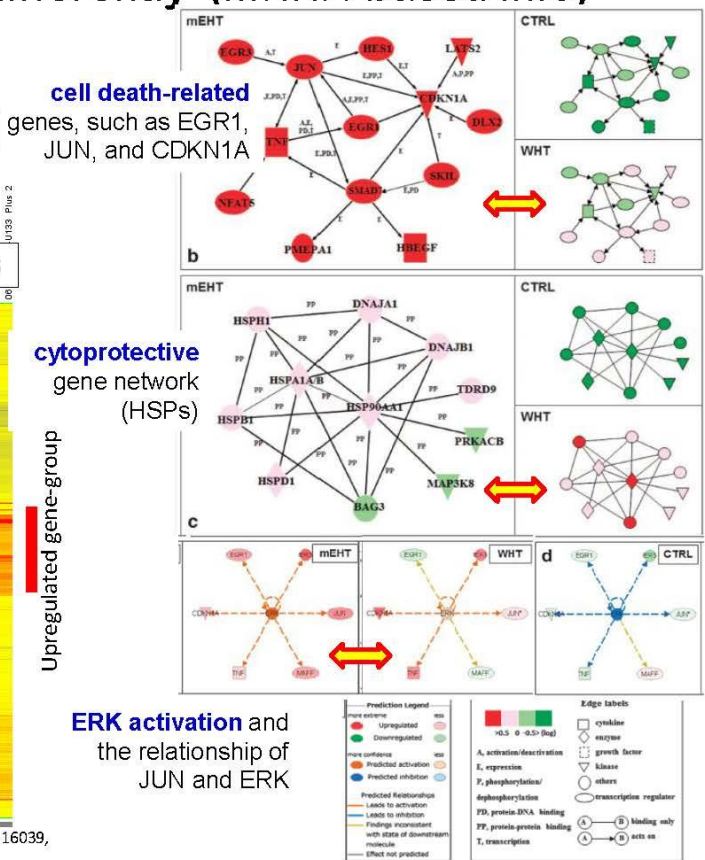
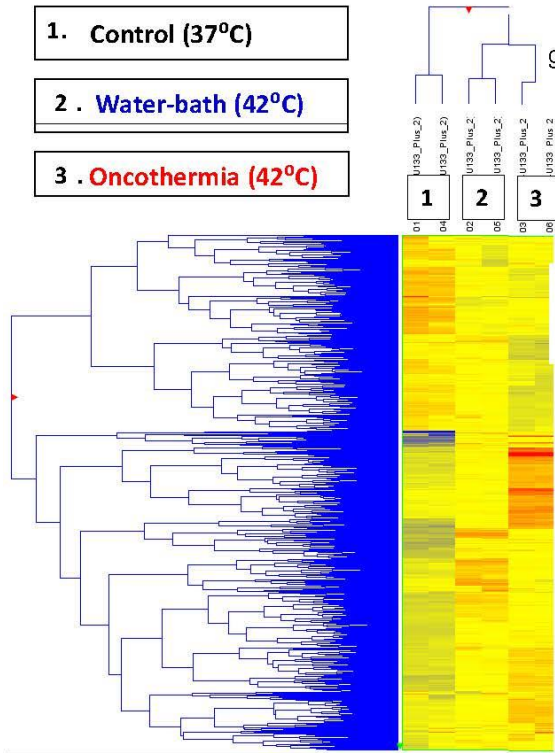
The enemy of my enemy is my friend



Oncothermia heats differently (mRNA-based info)

Human lymphoma U937 cell (in-vitro)

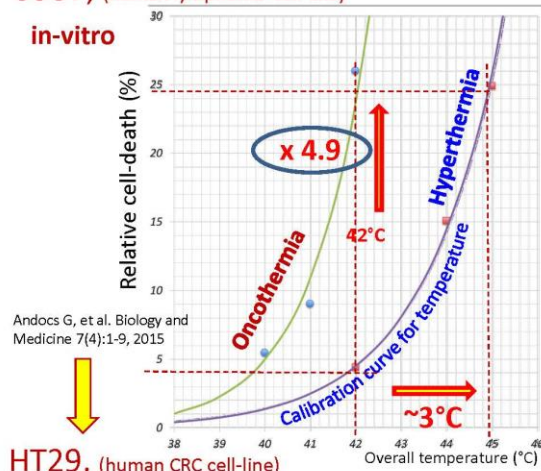
1. Control (37°C)
2. Water-bath (42°C)
3. Oncothermia (42°C)



Oncothermia heats the cell-membrane rafts

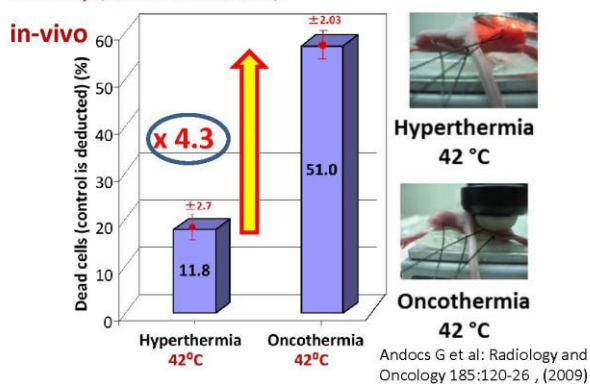
U937, (human lymphoma cell-line)

in-vitro



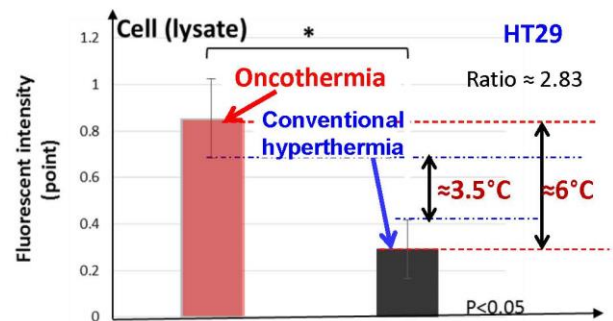
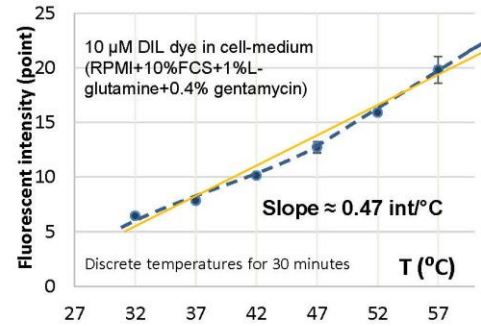
HT29, (human CRC cell-line)

in-vivo

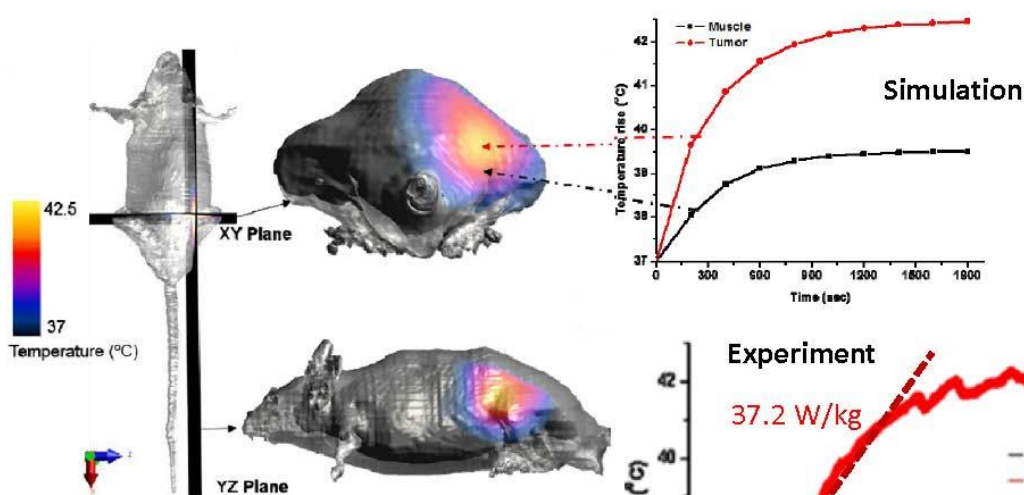


HT29, (human CRC cell-line); in vitro

Vancsik T et al; 33rd annual Conference of International Clinical Hyperthermia Society (ICHS), Bad Salzhausen, Germany, July 11-13, 2015



Temperature mapping



Jung Kyung Kim, Bibin Prasad, Suzy Kim; (2017) Temperature mapping and thermal dose calculation in combined radiation therapy and 13.56 MHz radiofrequency hyperthermia for tumor treatment, Proc. of SPIE Vol. 10047 1004718-1; Optical Methods for Tumor Treatment and Detection: Mechanisms and Techniques in Photodynamic Therapy XXVI, edited by David H. Kessel, Tayyaba Hasan, Proc. of SPIE Vol. 10047, 1004718 © 2017 SPIE · CCC code: 1605-7422/17/\$18 · doi: 10.1117/12.2253163

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- ❑ Results and perspectives

SCLC double arm prospective study

Investigator: Professor DY Lee, Kagnam Severance Hospital, Yonsei University, Seoul, S.Korea

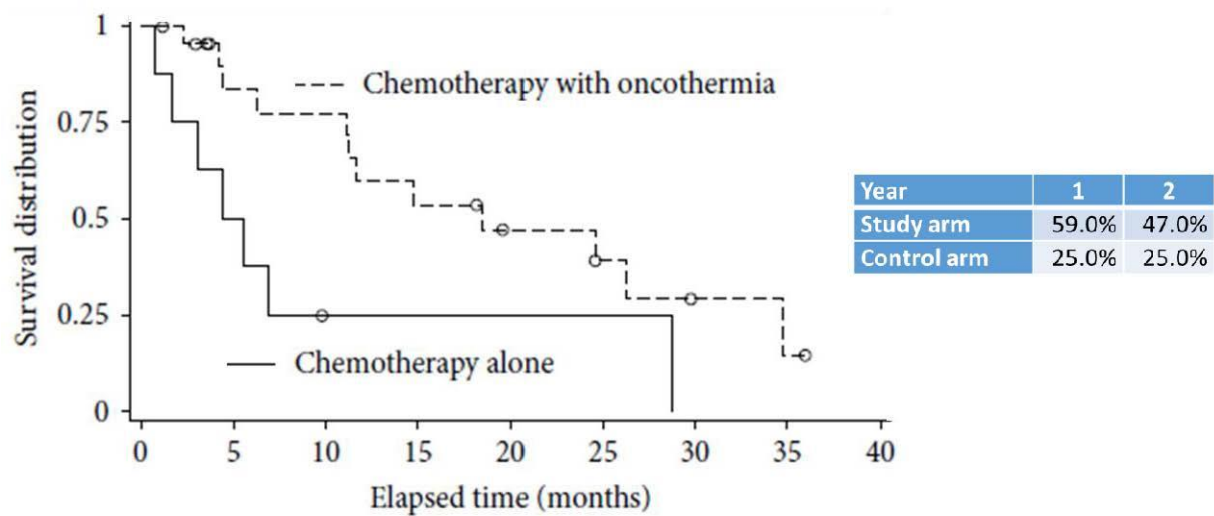
Published: Lee DY, Haam SJ, Kim TH, Lim JY, Kim EJ, Kim NY (2013) Oncothermia with Chemotherapy in the patients with Small Cell Lung Cancer; Conference Papers in Medicine, Vol.2013, Article ID 910363, pp.7

Prospective, monocenter, cohort double-arm study of chemotherapy with and without complementary oncothermia

Chemotherapy 1st line (n=28): Irinotecan (60 mg/m²), Cisplatin (60 mg/m²) three times.

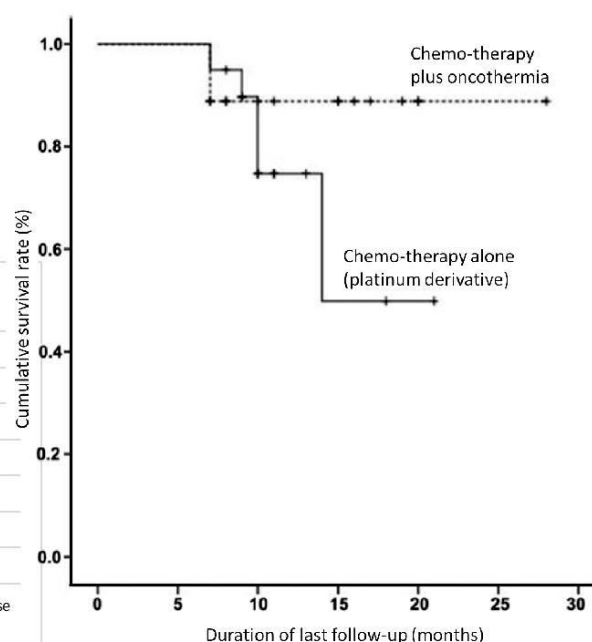
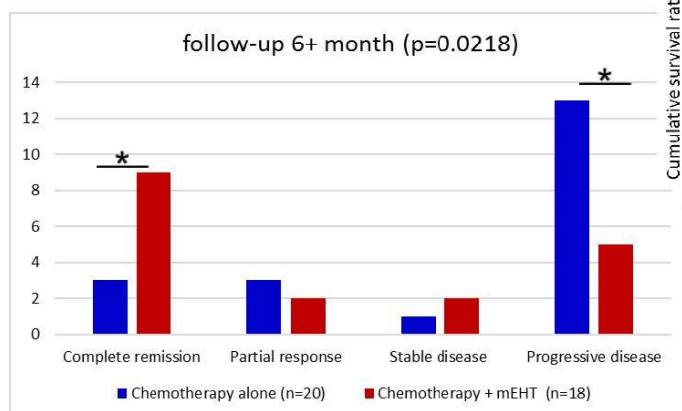
Chemotherapy 2nd line (n=19): Etoposide, (110 mg/m²) Cisplatin (70 mg/m²)

Additional oncothermia in 2nd line combination (n=9): 150 Watt, 1,490.5 kJ, 60 min, every second day, with rise in temperature to 38.5°C–42.5°C. Electrode 30 cm diameter at least 12 sessions were in 1 cycle.

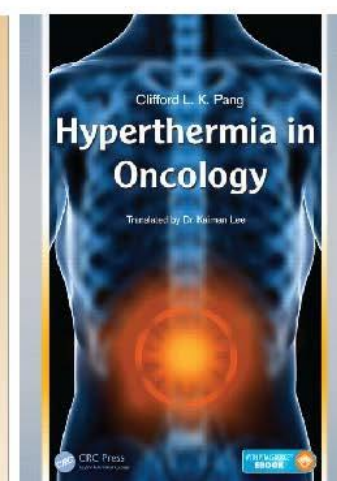
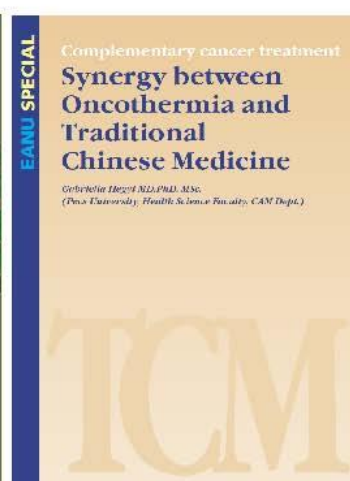
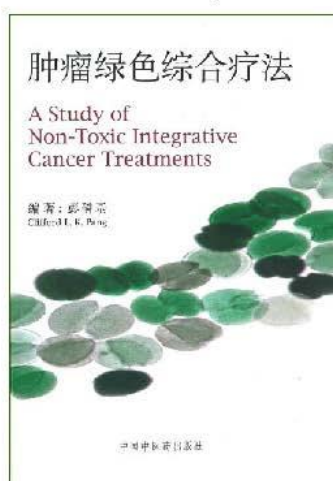


Recurrent cervix double arm, randomized study

Lee SY, Lee NR, Cho D-H, Kim JS; (2017) Treatment outcome analysis of chemotherapy combined with modulated electro-hyperthermia compared with chemotherapy alone for recurrent cervical cancer, following irradiation, *Oncology Letters*, <https://doi.org/10.3892/ol.2017.6117>



Valuable publications for oncothermia with TCM



MOLECULAR AND CLINICAL ONCOLOGY 6: 723-732, 2017

Local modulated electro-hyperthermia in combination with traditional Chinese medicine vs. intraperitoneal chemoinfusion for the treatment of peritoneal carcinomatosis with malignant ascites: A phase II randomized trial

CLIFFORD L.K. PANG¹, XINTING ZHANG¹, ZHEN WANG², JUNWEN OU³, YIMIN LU⁴, PENGFEI CHEN⁵, CHANGLIN ZHAO⁵, XIAOPU WANG⁵, HONGYU ZHANG⁵ and SERGEY V. ROUSSAKOW⁶

Journal of Complementary Medicine & Alternative Healthcare
Research Article
Volume 16, Number 1, 2019
DOI: 10.1089/jcm.2018.0001

Oncothermia-Booster (Targeted Radiofrequency) Treatment -in Some Non- Oncological Diseases as Special Physiotherapy

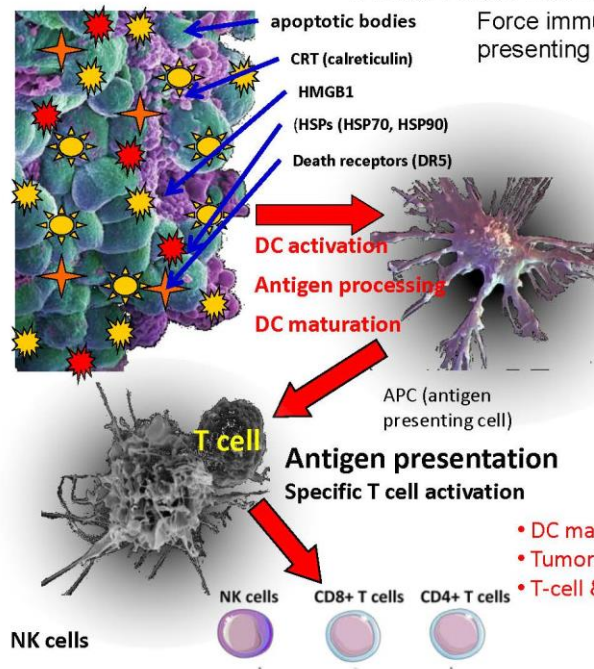
Agnes Miki, Istvan Molnar, Gaber Petrovic and Gabriella Hegyi

ACUPUNCTURE & ELECTRO-THERAPEUTICS RES., INT. J., Vol. 36, pp. 161-197, 2013
Copyright ©2013 Cognizant Communication Corp. Printed in the USA.
0360-1293/13 \$60.00 + .00
<http://dx.doi.org/10.3727/036012913X13831832269243>

ONCOTHERMIA: A NEW PARADIGM AND PROMISING METHOD IN CANCER THERAPIES

Gabriella Hegyi MD, MSc, PhD.

Activate immune reactions



NK cells

CD8+ T cell
(killer T-cells)

CD4+ T cell
(helper T-cells)

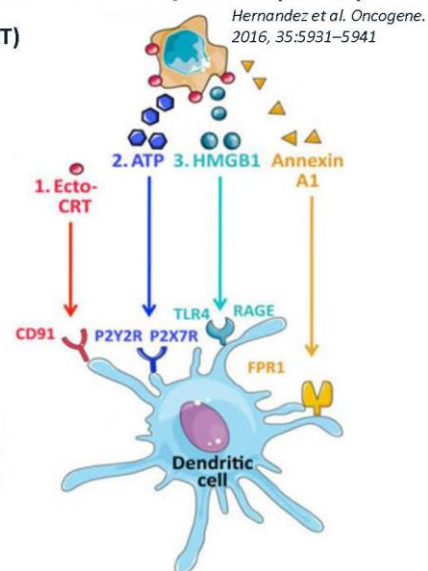
Antitumor immune response

Specific cytotoxic lysis of tumor

Force immunogenic cell-death with DAMP. Develop antigen presenting cells, produce CD4+ & CD8+ T-cells suppress T_{reg}.

Damage associated molecular patterns (DAMP)

- Calreticulin (CRT)
„eat me” signal
- ATP
„find me” signal
- HMGB1
„danger” signal
- HSP70
genetic info

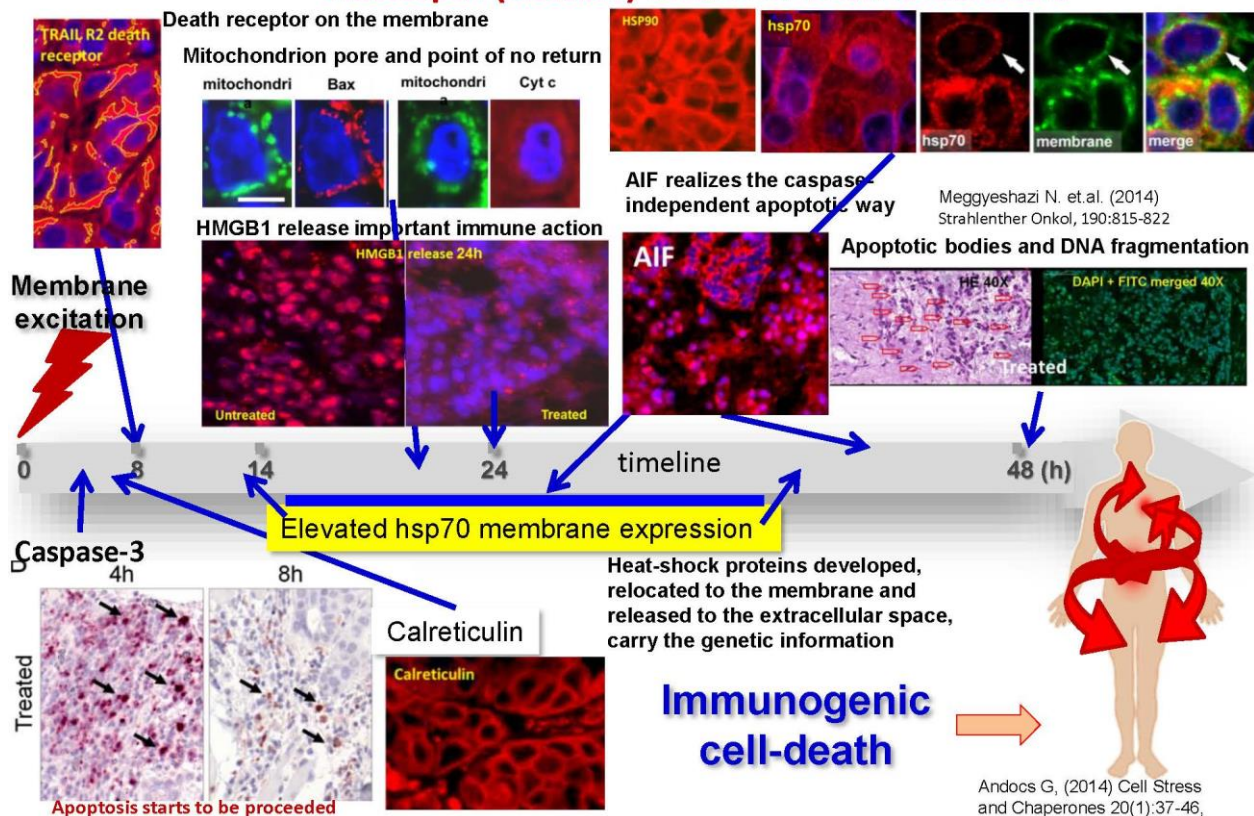


One of the anti-tumor immune responses is the **immunogenic cell death (ICD)**, which needs **spacio-temporal DAMP**

Szasz et al. (2014) Tumor-vaccination, Patent USA

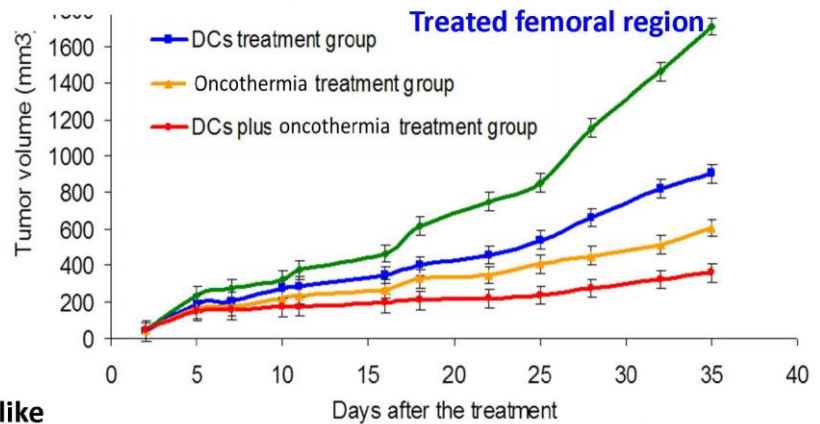
DAMP production → Immunogenic cell-death HT29 in-vivo

Abscopal (distant) effect of local treatment

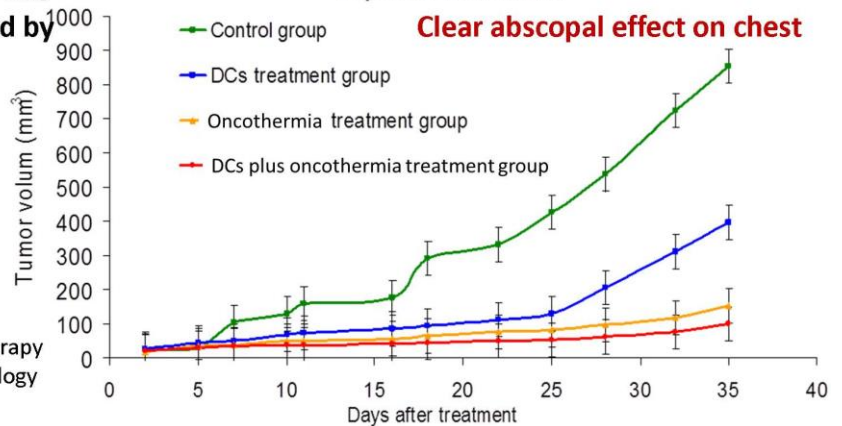


Oncothermia + DC therapy combination

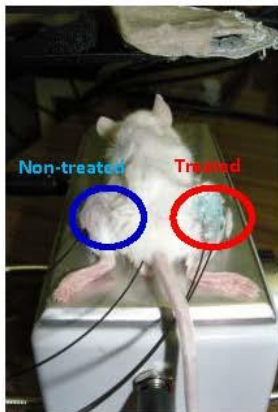
Tumor induced on femoral region (treated by oncothermia)



Tumor induced on chest region like model of metastasis, not treated by oncothermia

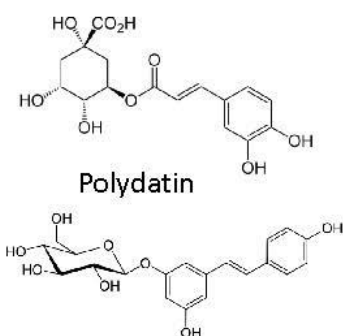


Wei Quin et.al; Modulated electro-hyperthermia enhances dendritic cell therapy through an abscopal effect in mice; Oncology Reports 32: 2373-2379, 2014

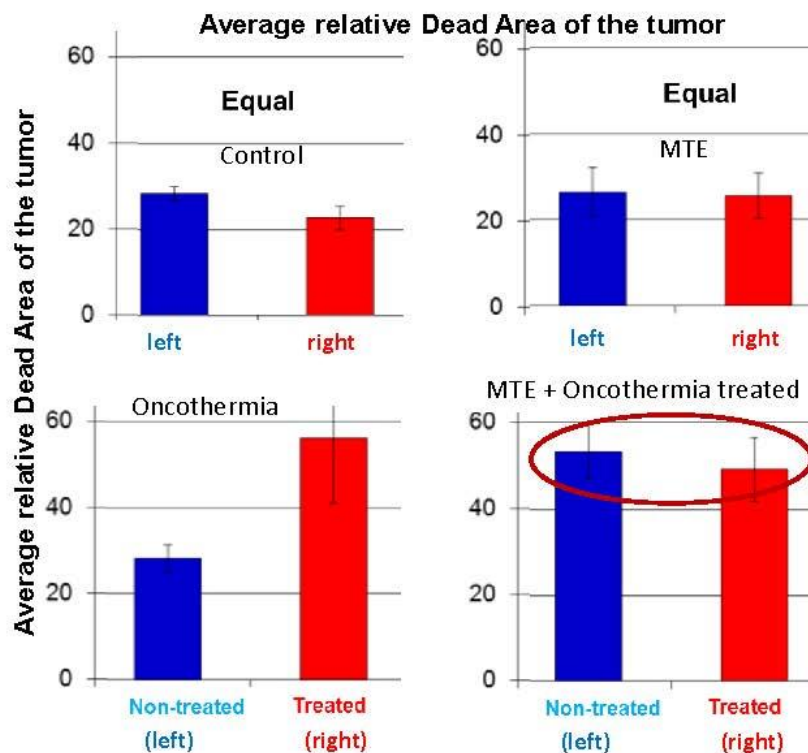


Marsdenia tenacissima (MTE, Xiao-aiping) injection before Oncothermia

Chlorogenic-acid (11 mg/ml)

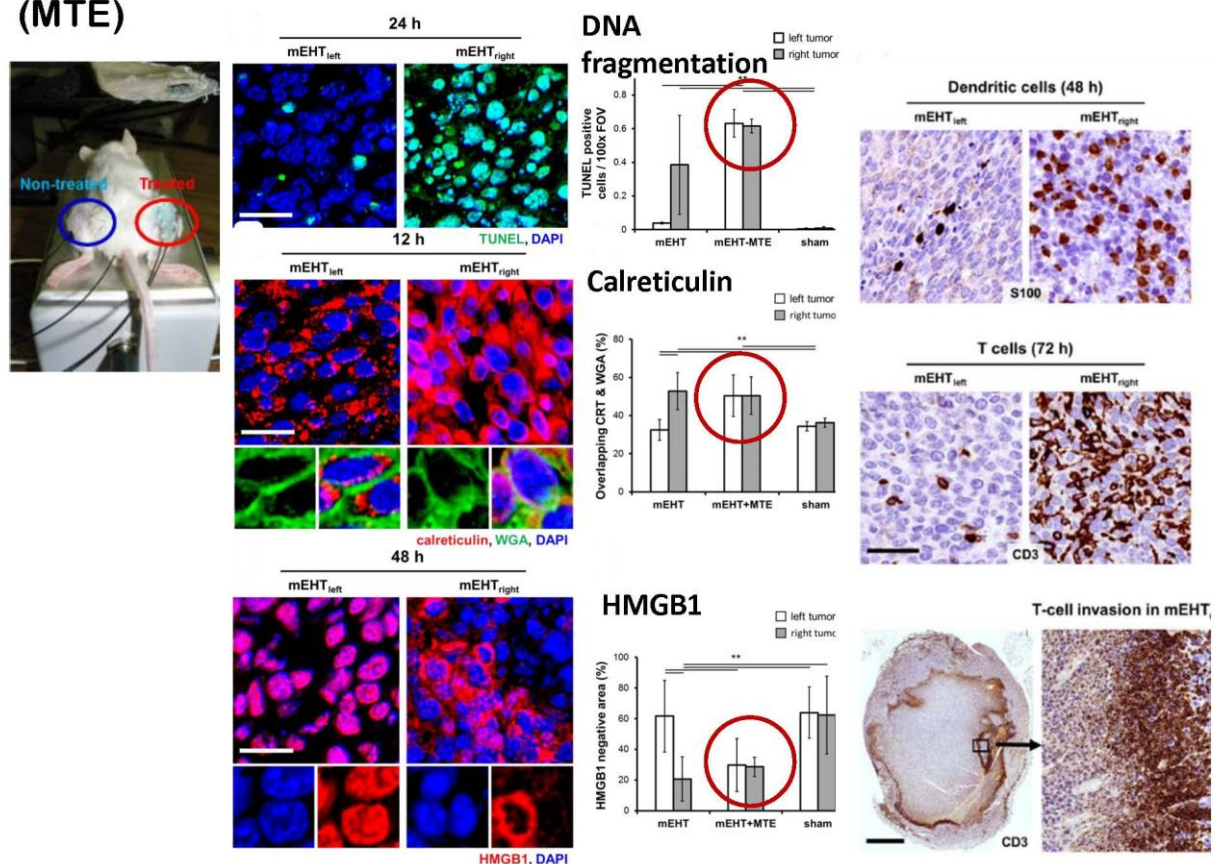


Abscopal effect by Xiao-aiping (MTE)



The abscopal effect is clearly proven

Abscopal effect by Xiao-ai-ping (MTE)

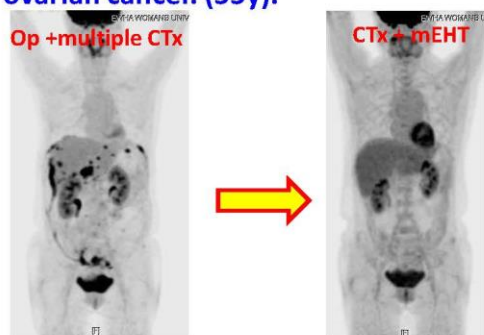


Abscopal effect

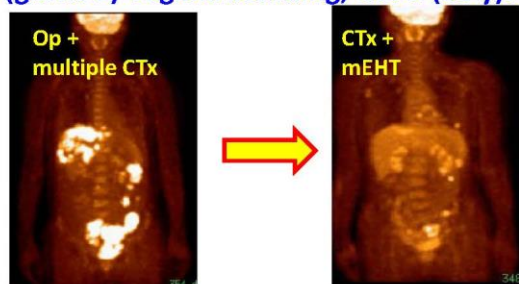
Investigator: Prof. Dr. YH Kim; Ewha Womans University Mokdong Hospital, Seoul, Korea

Recurrent refractory progressive ovarian cancer. (55y).

Op + multiple CTx



Invasive adenocarcinoma of ovary (grade 2) Vaginal bleeding; G5P2 (33 y).



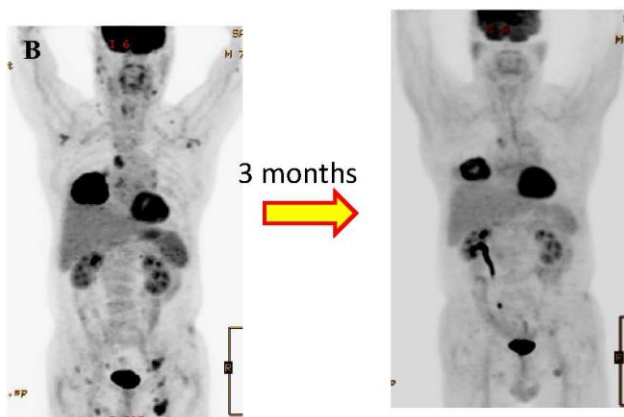
Metastatic non-small-cell lung cancer (55y).

Investigator: Prof. Dr. Seong Min Yoon, Division of Hematology-Oncology, Department of Internal Medicine, Samsung Changwon Hospital, Sungkyunkwan University, Korea

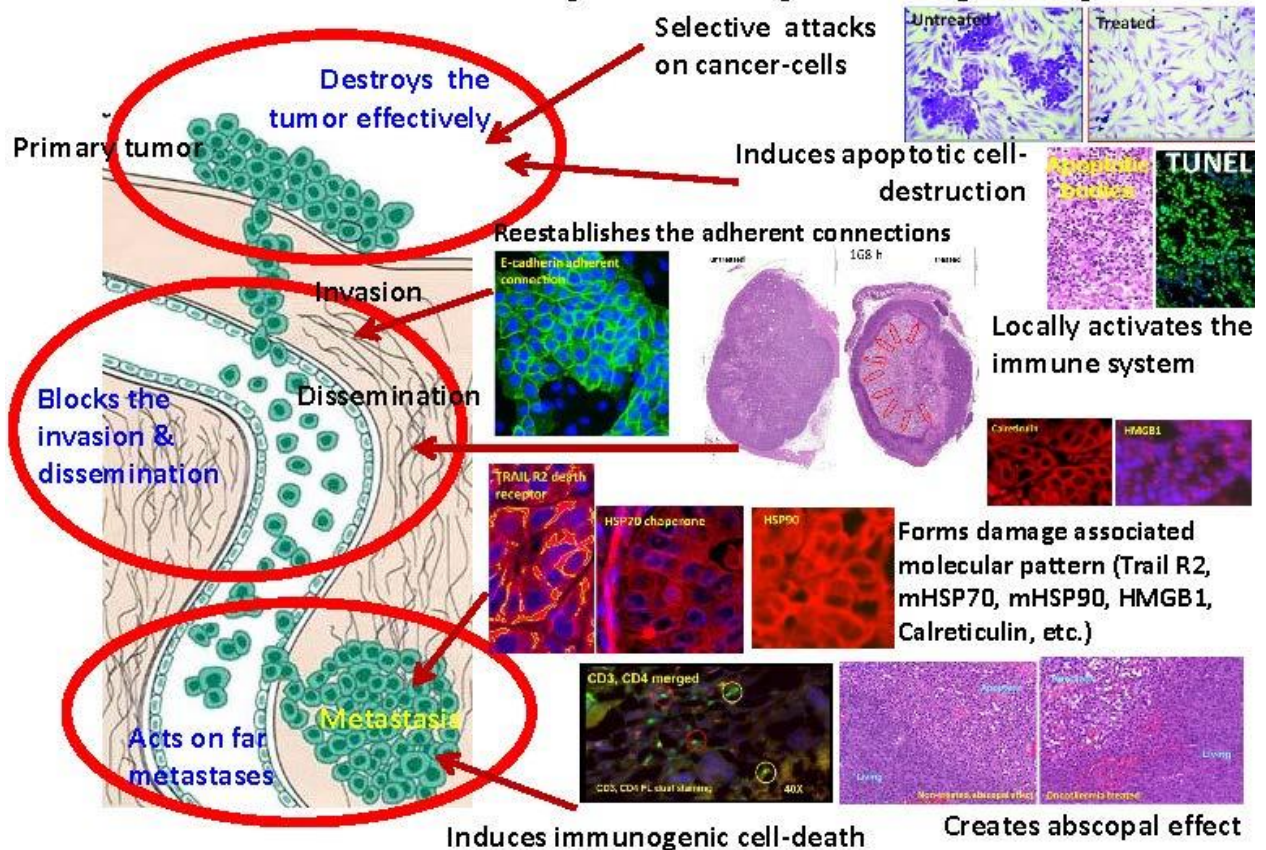
Patient: SAsc, 72 y, male, Primer-tumor: Non-small cell lung cancer; Size: 9.5 cm right middle lobe; Metastases: in sentinel and distant lymph-nodes;

Tumor-classification: cT2 cN2 Mx, stage IIIB

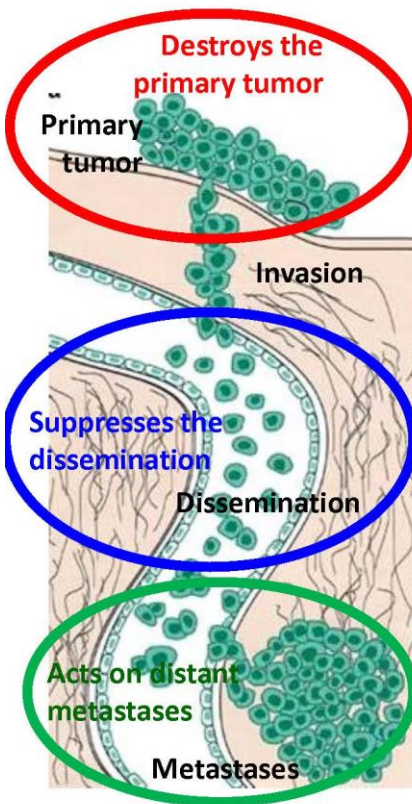
Treatment: 28x1.7 Gy; support: **250 microgram Leukine (GM-CSF) and Oncothermia 6x**



Oncothermia acts systemically in malignancy



Oncothermia results/hot-topic



Selectively destroys the malignant cells with high metabolic rate

Szasz A, et al. (2003) Magneto- and electro-biology 22(2):103–115

Induces massive apoptosis (produces apoptotic bodies)

Meggyeshazi N, et al. (2014) Strahlenther Onkol 190:815–822

Apoptotic signal starts from the cell-membrane

Andocs G, et al. (2015) Biology and Medicine 7(4):1–9

Expression of: mHSP70, mHSP90, Trail-R2, CRT, Cyt-C, HMGB1

Andocs G, et al. (2014) Cell Stress and Chaperones 20(1):37–46

Regulates different genes than the same temperature heating

Andocs G, et al. (2016) Cell Death Discovery (Nature Publishing Group), 2, 16039

Produces immunogenic cell-death (ICD)

Andocs G, et al. (2014) Cell Stress and Chaperones 20(1):37–46

Forms APC with ICD process

Meggyeshazi N, et al. (2013) Hindawi, Conference Papers in Medicine, Volume 2013, Article ID 187835

Reestablishes the cellular connections (E-cadherin)

Yang K-L, et al. (2016) Oncotarget, oi: 10.18632/oncotarget.11444

Forms bonding connections (β-catenin)

Szasz A (2013) Thermal Med 29(1):1–23

The primary tumor is enveloped by lymphocytes

Szasz A, et al. (2013) A chapter in book Ed: Huilgol N, ISBN 980-953-307-019-8, InTech,

Activates the neutrophils in the envelop

Szasz A, et al. (2010) Springer Science, Heidelberg

Creates abscopal effect

Qin W, et al. (2014) Oncol Rep 32(6):2373–2379

The rechallenge could not be forced

Yuk-Wah Tsang, et al. (2015) BMC Cancer 15:708

Immune (and/or small-vehicles) actions

Kleef R, et al. (2012) Case Rep Oncol 5:212–215; SchrmacherV, et al. (2015) Immunotherapy 7: 855–860

Volker S, et al. (2014) Oncology Letters 8:2403–2406

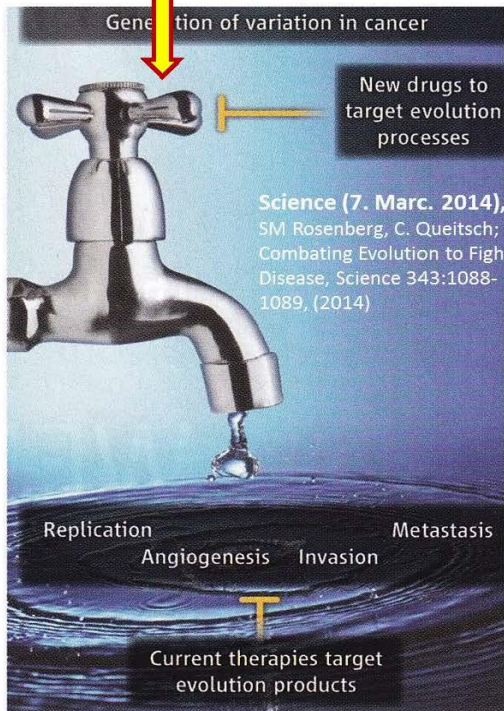
Tumor-specific immune-reactions (vaccination)

Patent (EU) <http://www.google.com/patents/EP2703001A1?cl=en>,

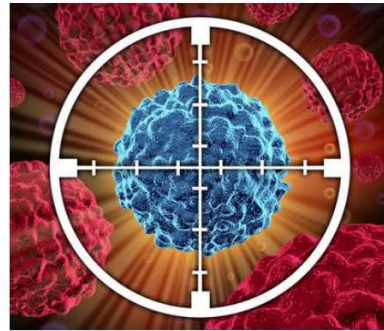
Patent (USA) <http://www.freepatentsonline.com/20150217099.pdf>

Oncothermia fits well to the modern oncology

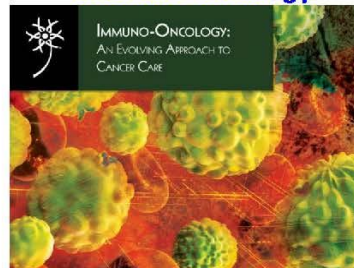
Oncothermia targets the malignant processes, controls the evolution



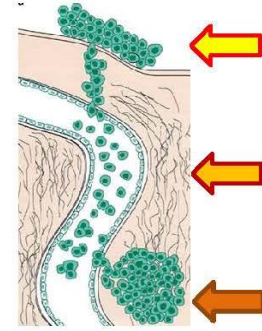
Targeted therapy to malignant cells



Direct and effective way to immuno-oncology



Complex therapy to system



New kind of hyperthermia

Heats selectively
Physiology compatible

Applicable dose
Precise electronics

Thank you for your attention