COST 281Seminar **"Subtle Temperature Effects of RF-EMF“**
November 12-13, 2002, London UK

INDIRECT EVIDENCE OF NON-THERMAL BIOLOGICAL EFFECTS INDUCED BY MOBILE PHONE RADIATION IN VITRO

Dariusz Leszczynski

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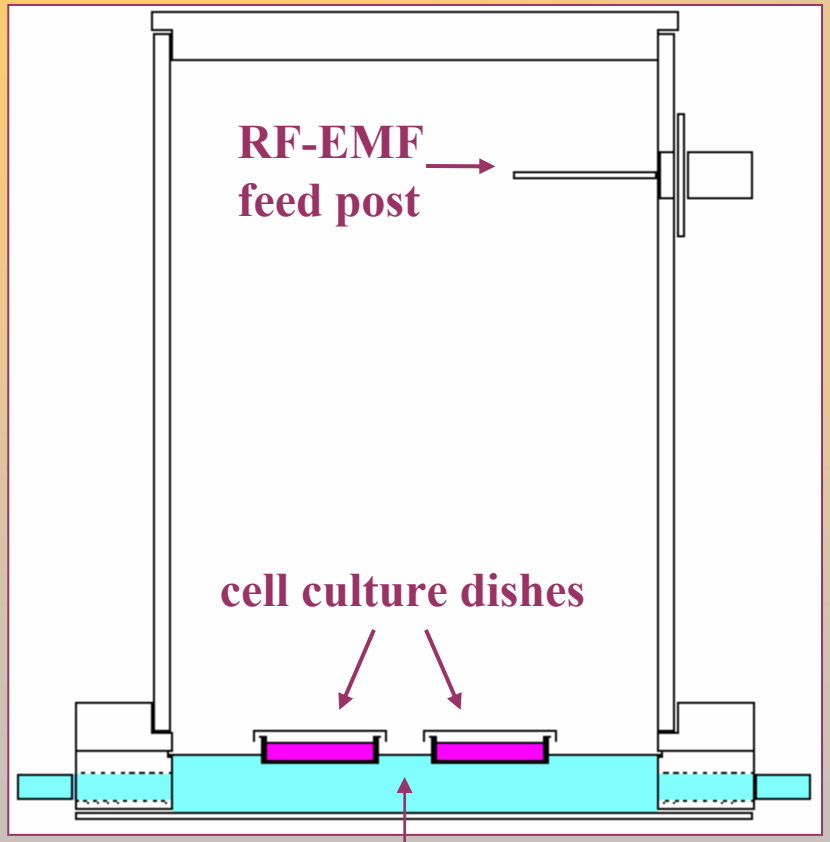
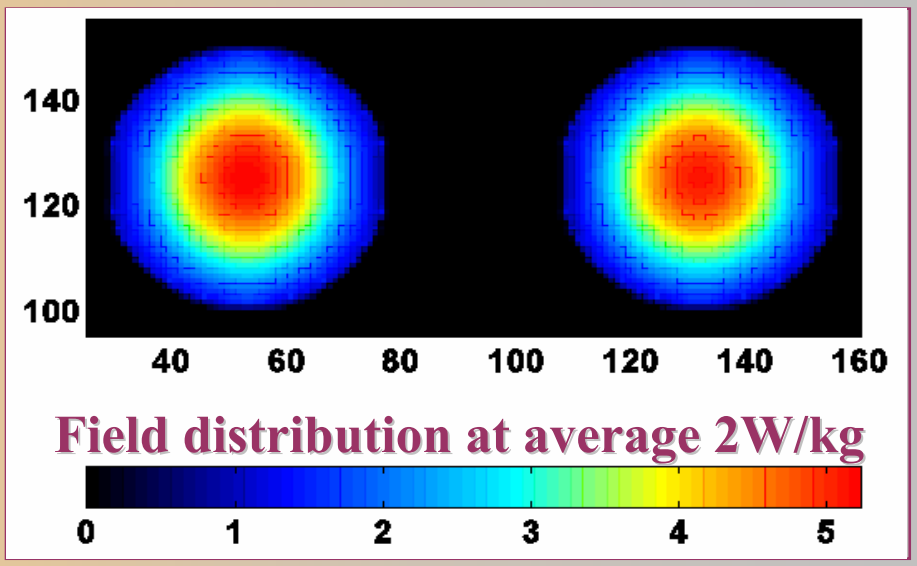
Radiation and Nuclear Safety Authority, Helsinki, Finland

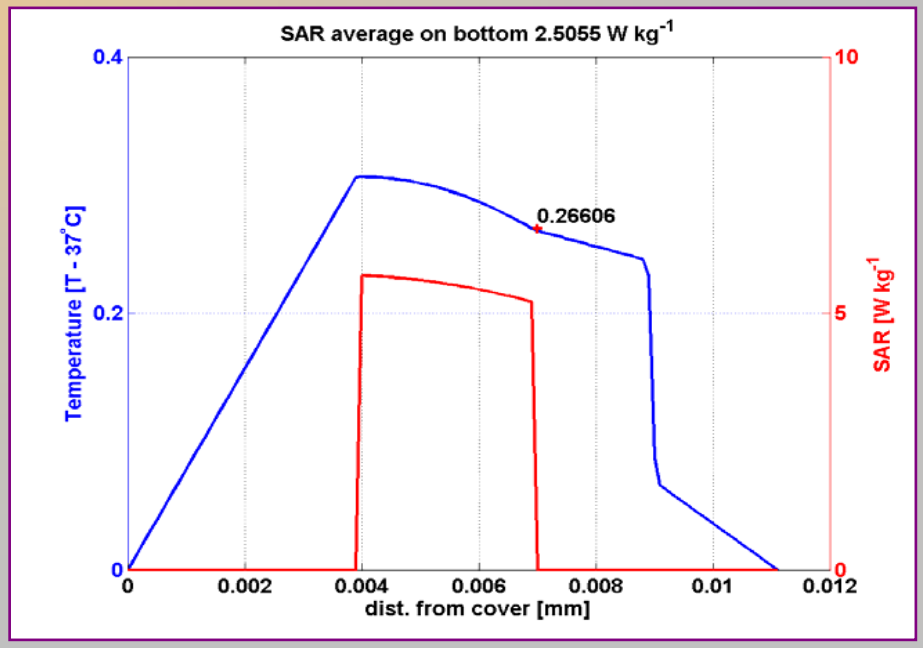
- Jokela's chamber
- Kuster's chamber
- Heat stress
- What are thermal/non-thermal effects?

Jokela's chamber

Jokela's chamber



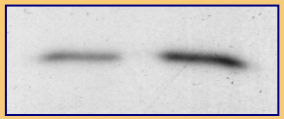




hsp27 phosphorylation in SAR dose-dependent manner

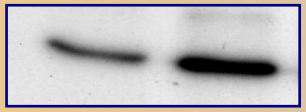
^{32}P-labeling + immunoprecipitation

sham 1.2SAR



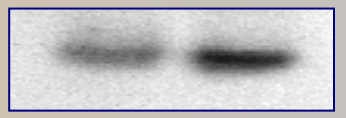
<2-folds up

sham 1.8SAR



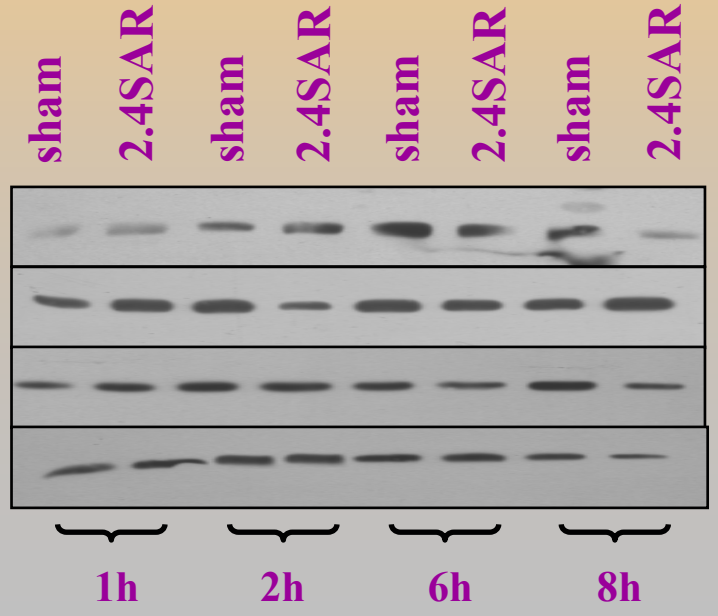
>2-folds up

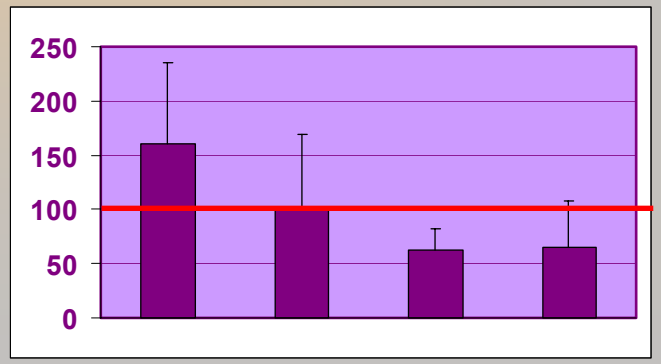
sham 2.4SAR



3-4-folds up

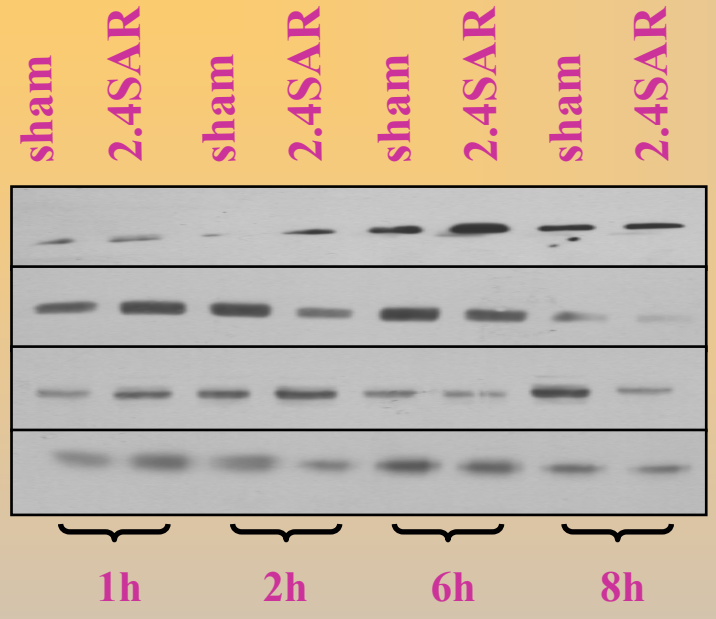
hsp27 expression in time-dependent manner

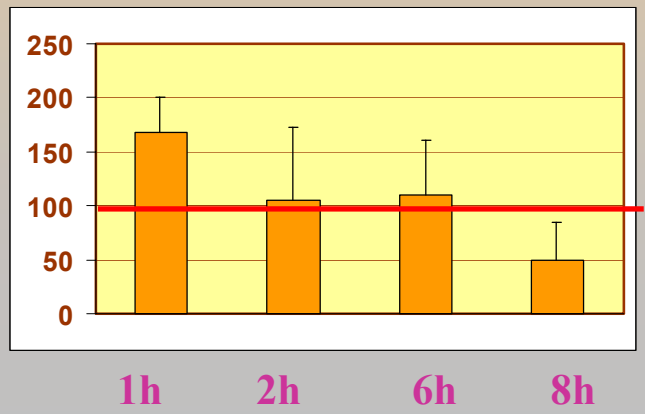




p38 MAP kinase

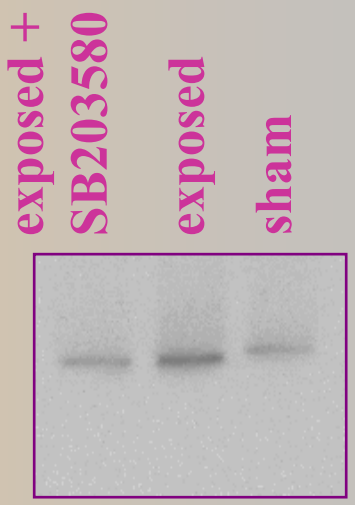
expression





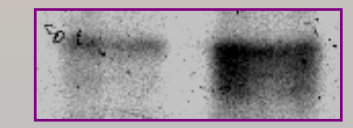
activity

inhibitor prevents ^{32}P-hsp27

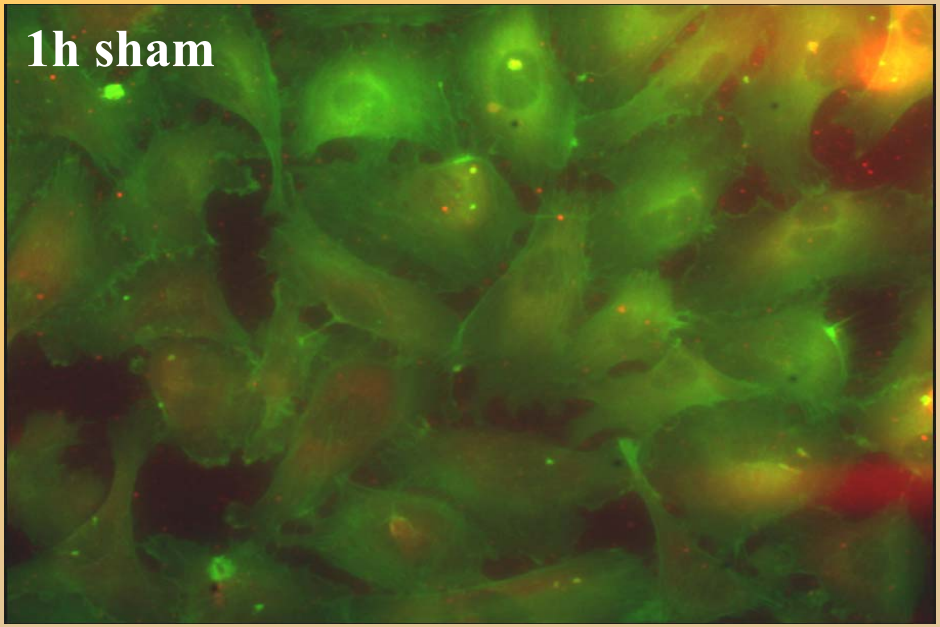


RF-EMF causes activation

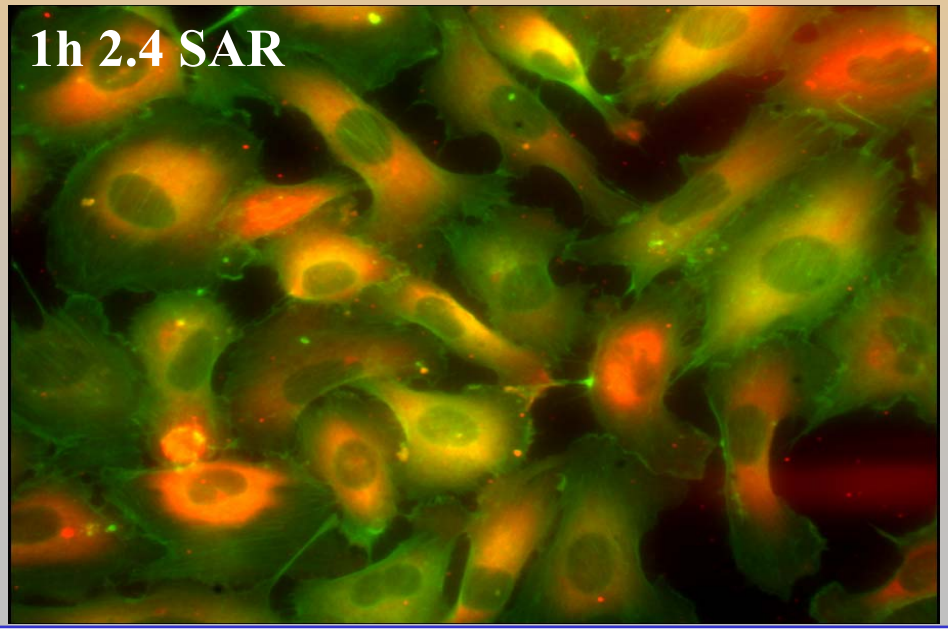
sham 2.4SAR

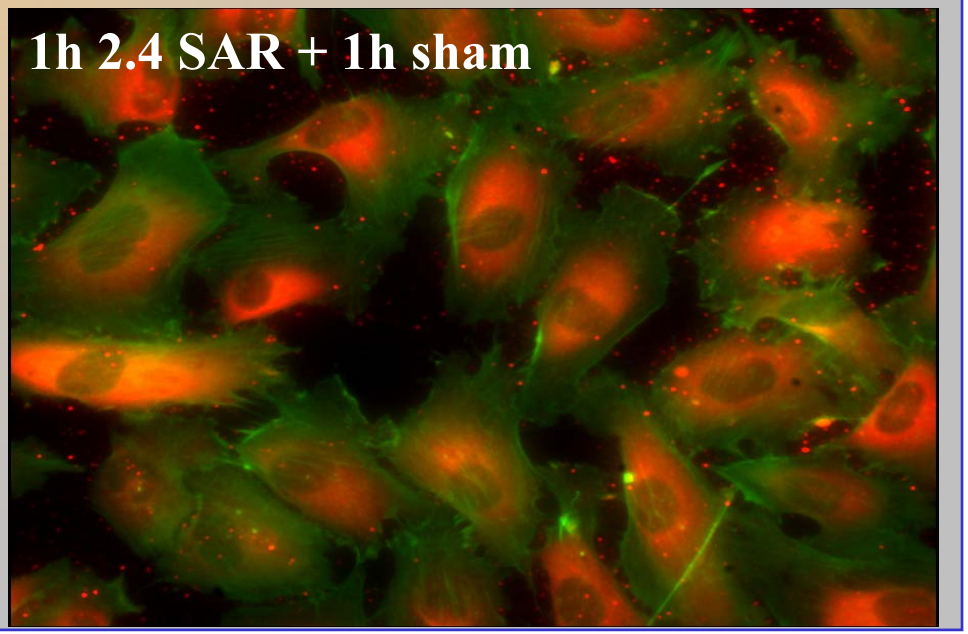


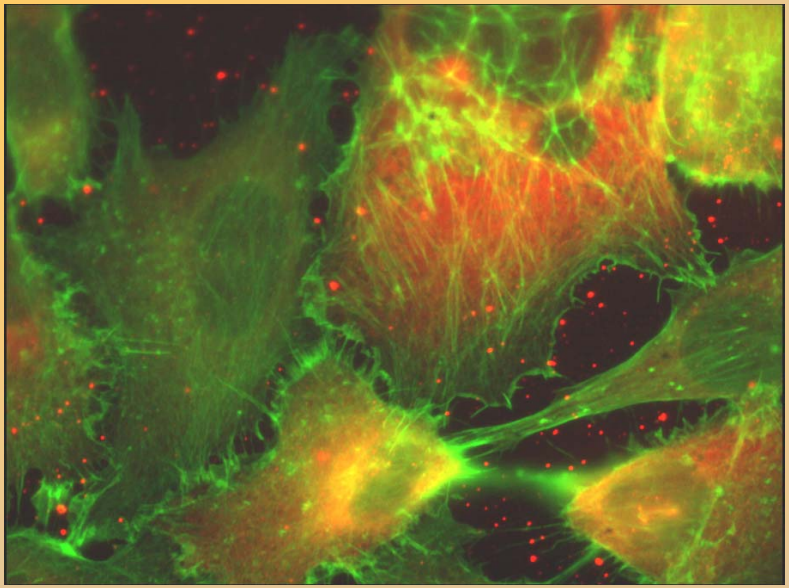
<2-folds up



hsp27
&
stress fibers



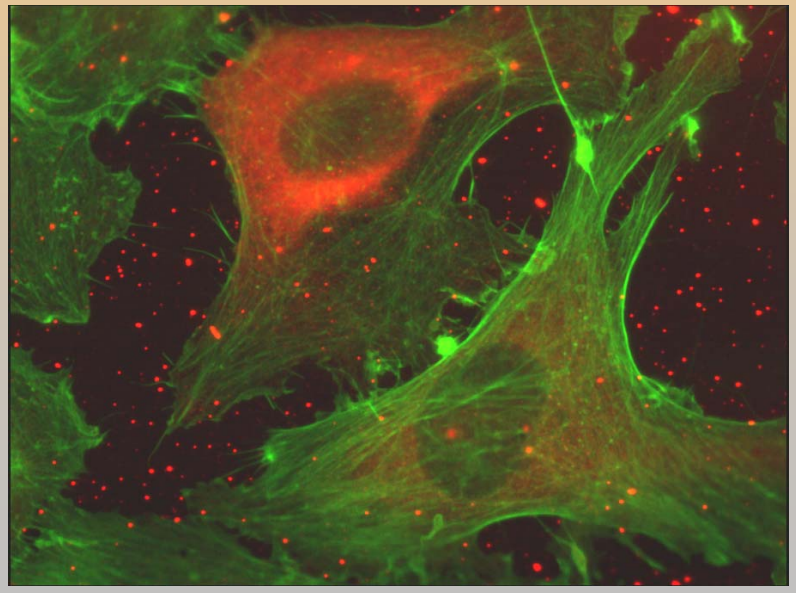


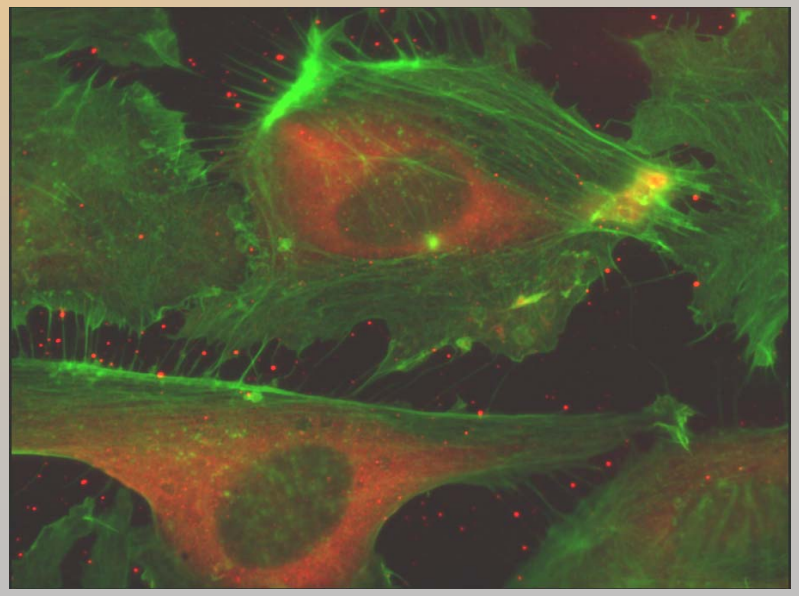


cells with high expression of hsp27 (red color) have prominent stress fibers-network (green color) and stress fiber components are present also in the ruffles (edges) of the cells

…

combined effect of the increased expression and increased phosphorylation of hsp27

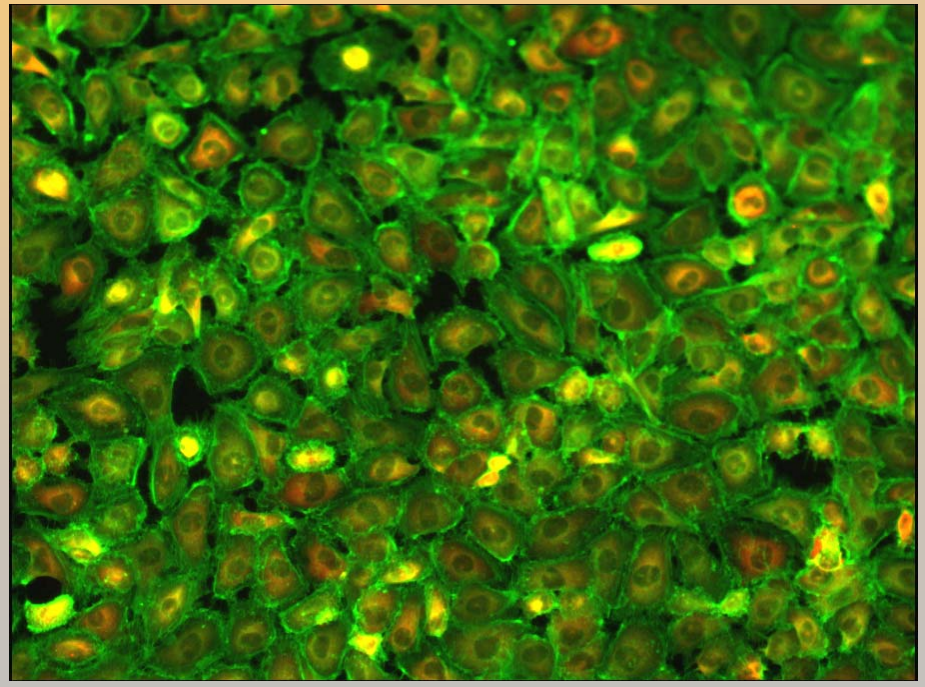




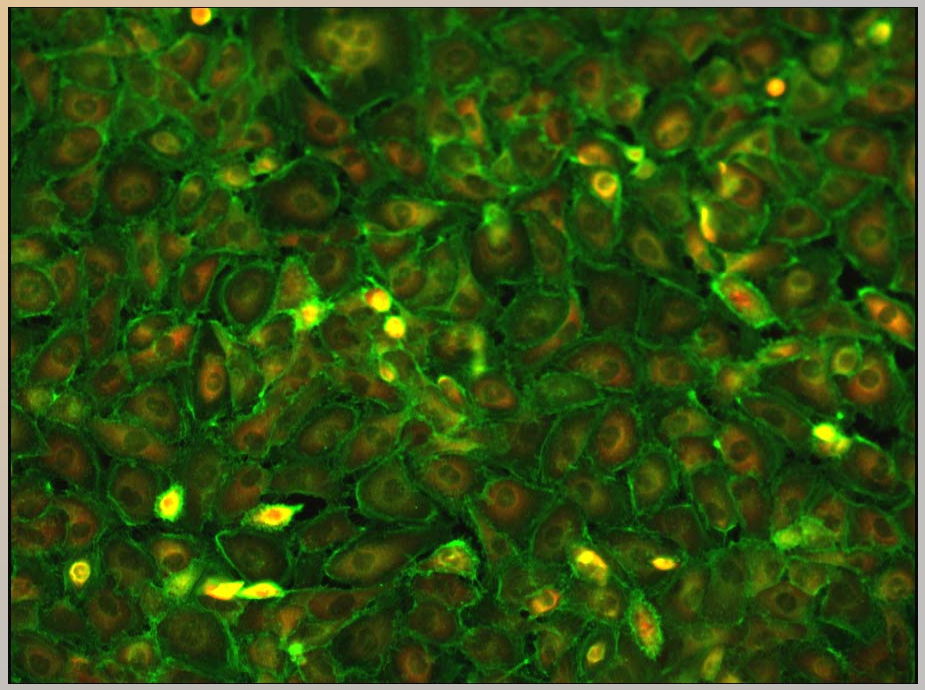
Active hsp27 regulates stability of stress fibers in EA.hy926

SB203580 – inhibitor of p38MAP kinase

1h 2SAR without SB203580



1h 2SAR with SB203580



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Jacques Landry (Laval University, Quebec, Canada)

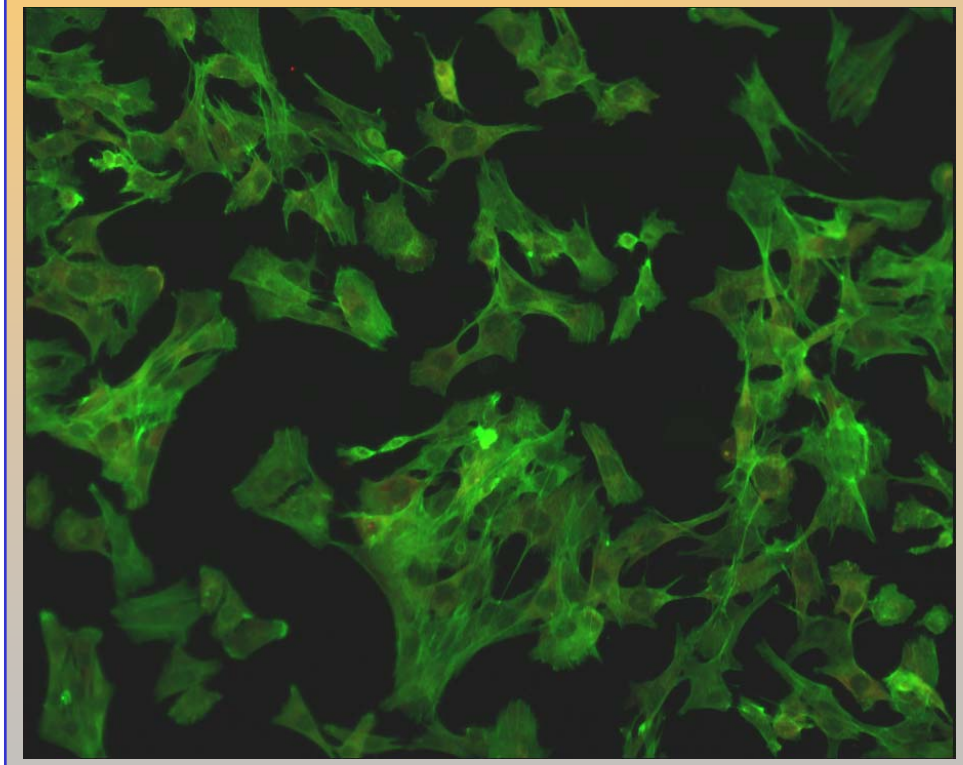
Chinese hamster cell lines (fibroblasts):

- **CCL39 - control cell line (hamster hsp27)**
- **CCL39 - over-expressing human wild-hsp27**
  - 3 phosphorylation sites are active
- **CCL39 - over-expressing human mutant-hsp27**
  - 3 phosphorylation sites are inactivated

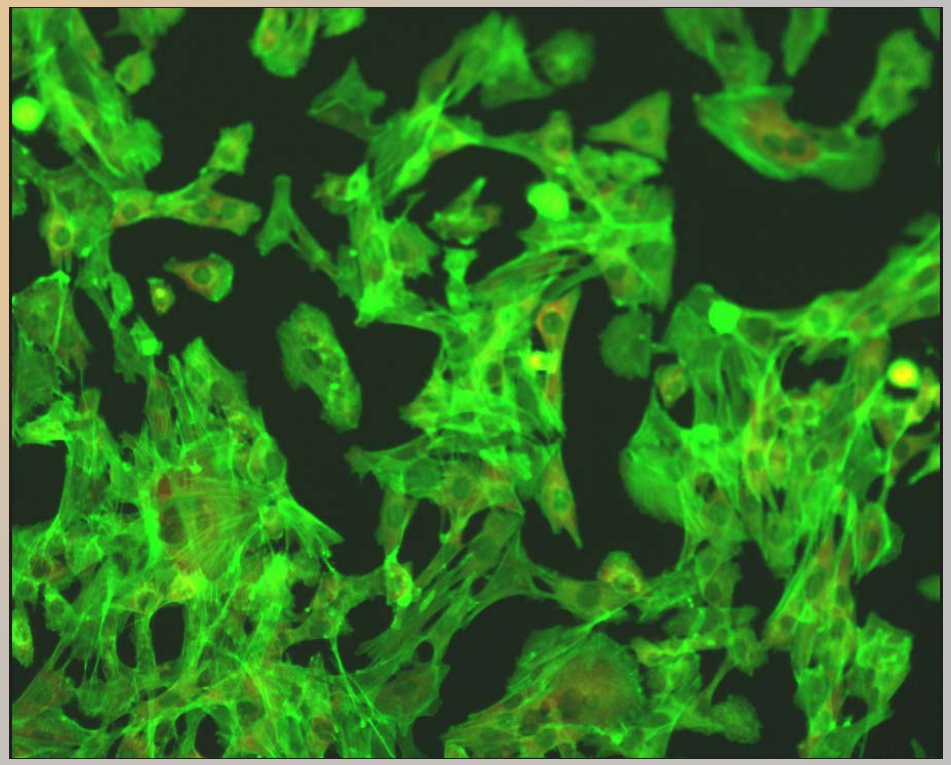
Cells were exposed to 900GSM for 1h at 2SAR

hamster cell line CCL39
over-expressing human wild-hsp27

sham



1h 2SAR



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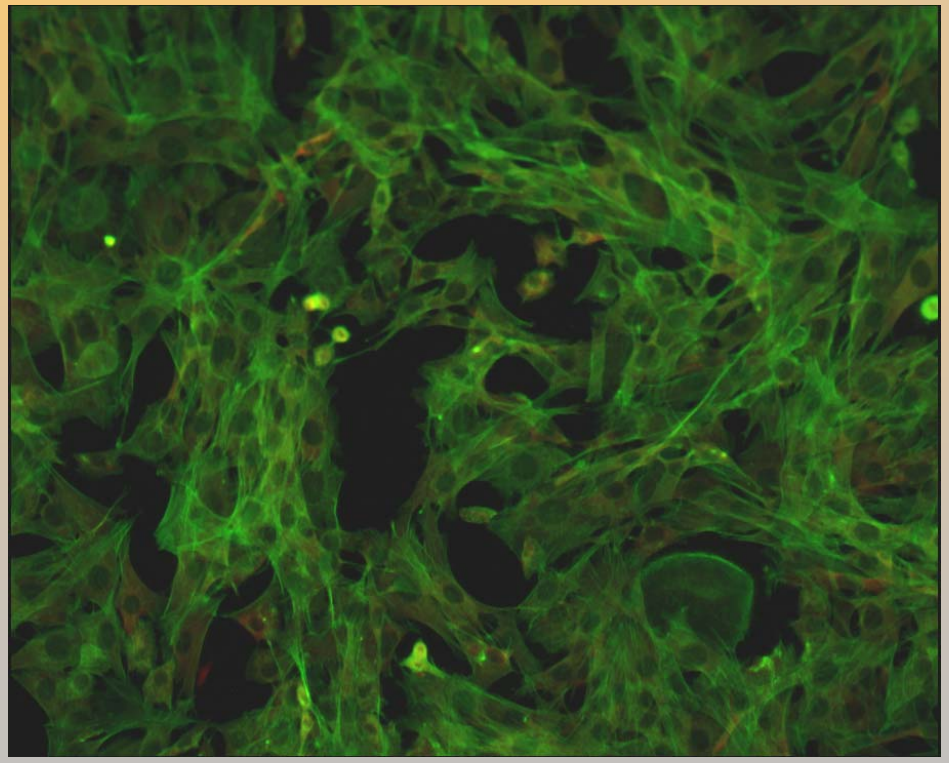
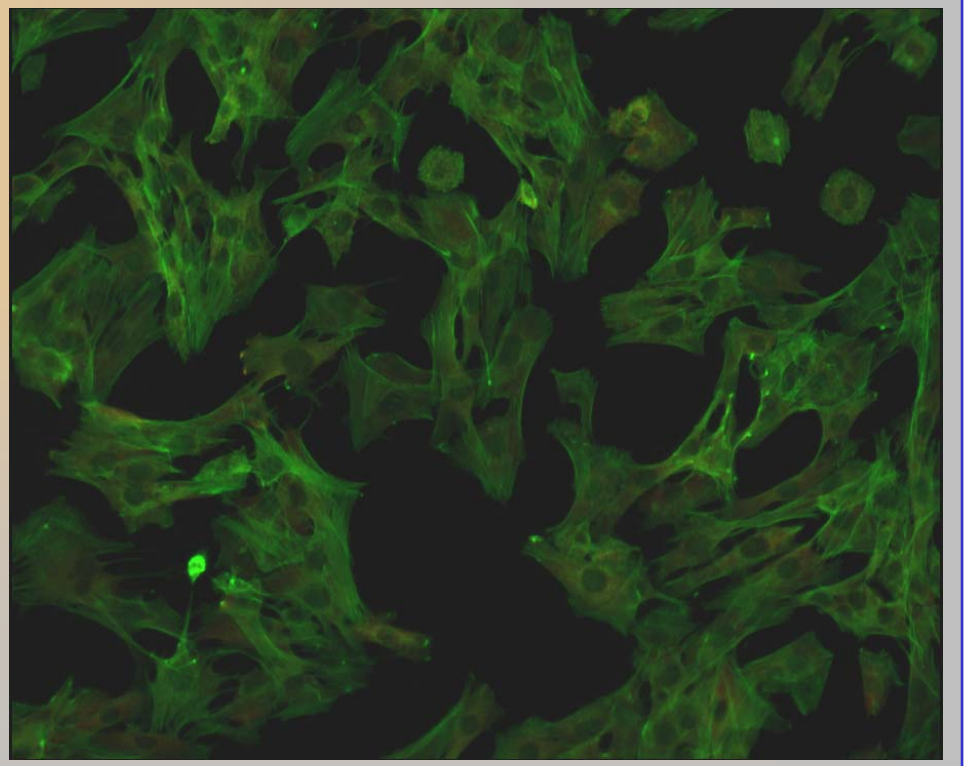
hamster cell line CCL39
over-expressing human mutant-hsp27

sham

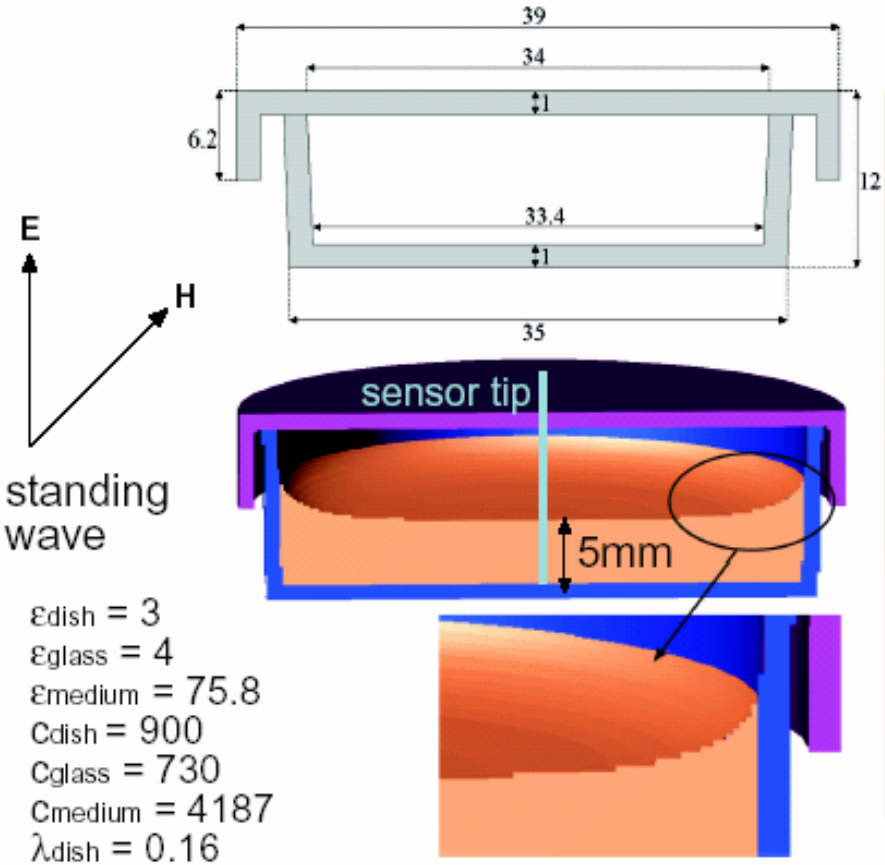


1h 2SAR



Kuster's chamber

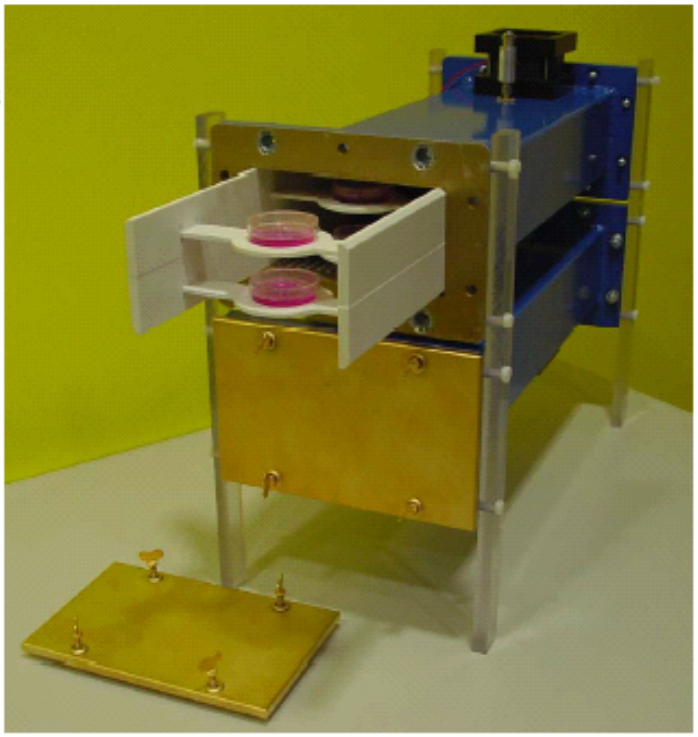
Exposure Setup & Numerical Modelling



standing wave

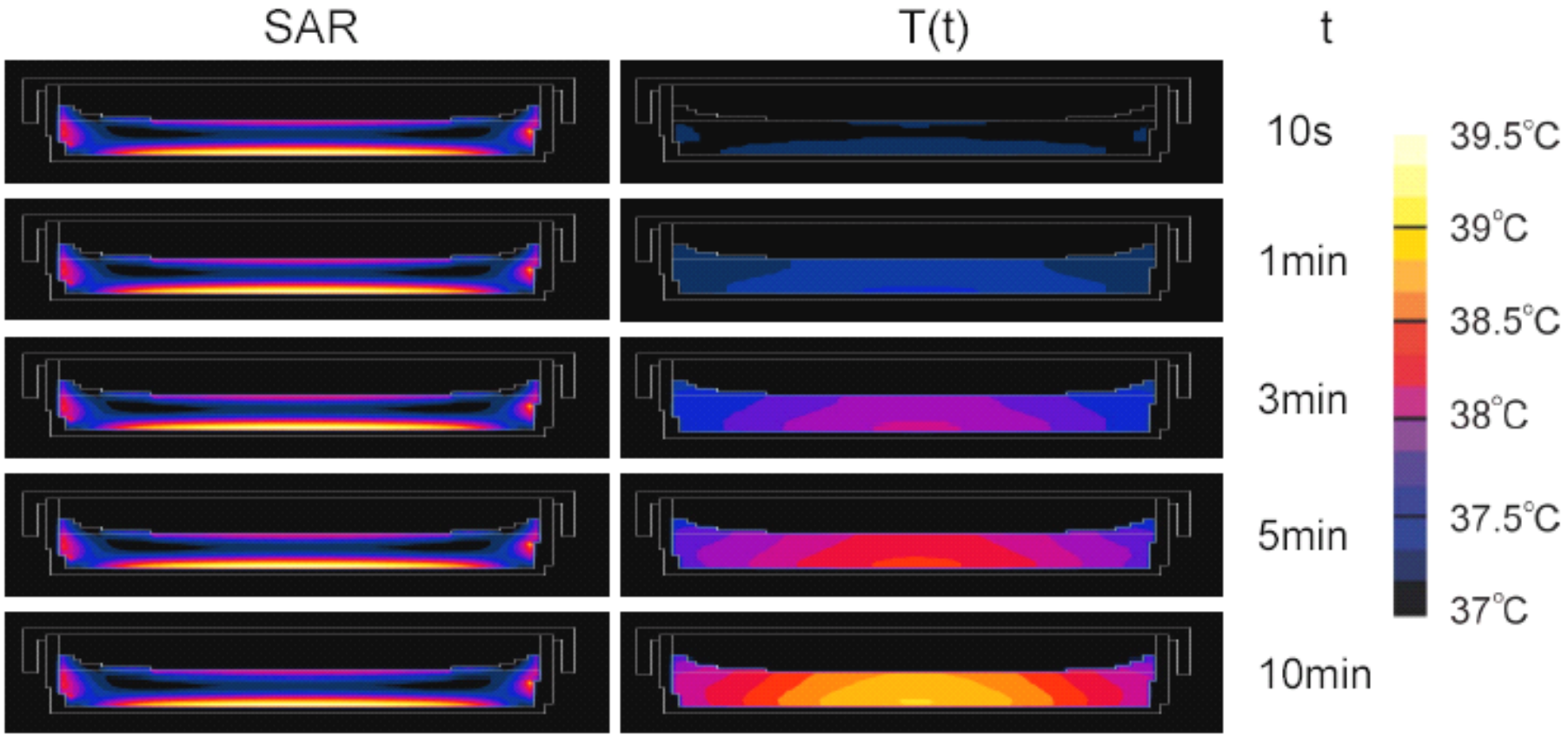
$\varepsilon_{dish} = 3$
$\varepsilon_{glass} = 4$
$\varepsilon_{medium} = 75.8$
$C_{dish} = 900$
$C_{glass} = 730$
$C_{medium} = 4187$
$\lambda_{dish} = 0.16$
$\lambda_{glass} = 0.81$
$\lambda_{medium} = 0.6$

waveguide resontor, 1800MHz



Thermal Analysis of In Vitro Exposure

Temperature distribution

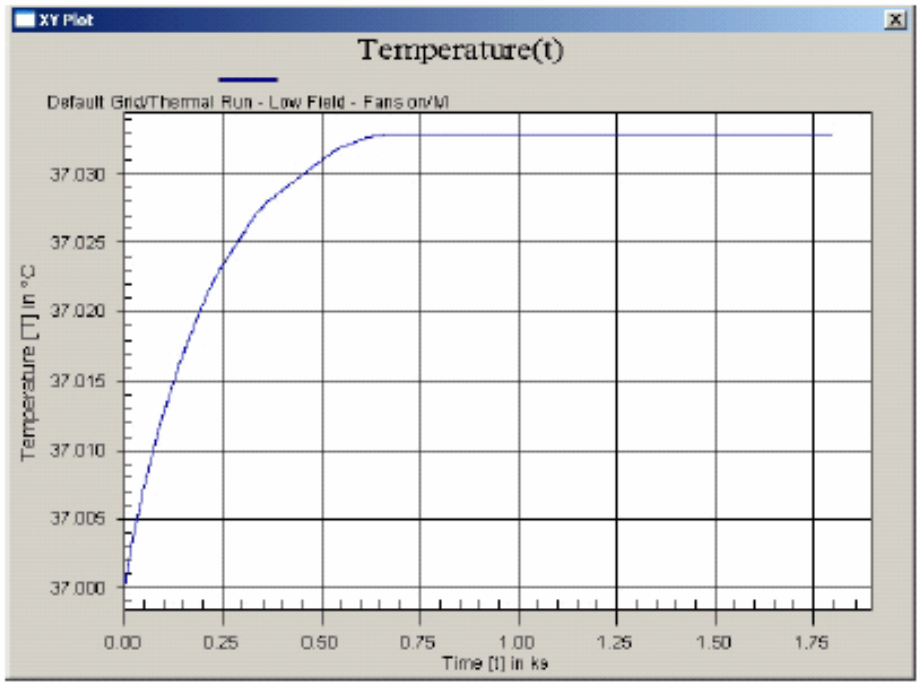


linear scale, liquid 5mm, normalization:
(i) SAR to slice maximum, (ii) temperature to global maximum

Thermal Analysis of In Vitro Exposure

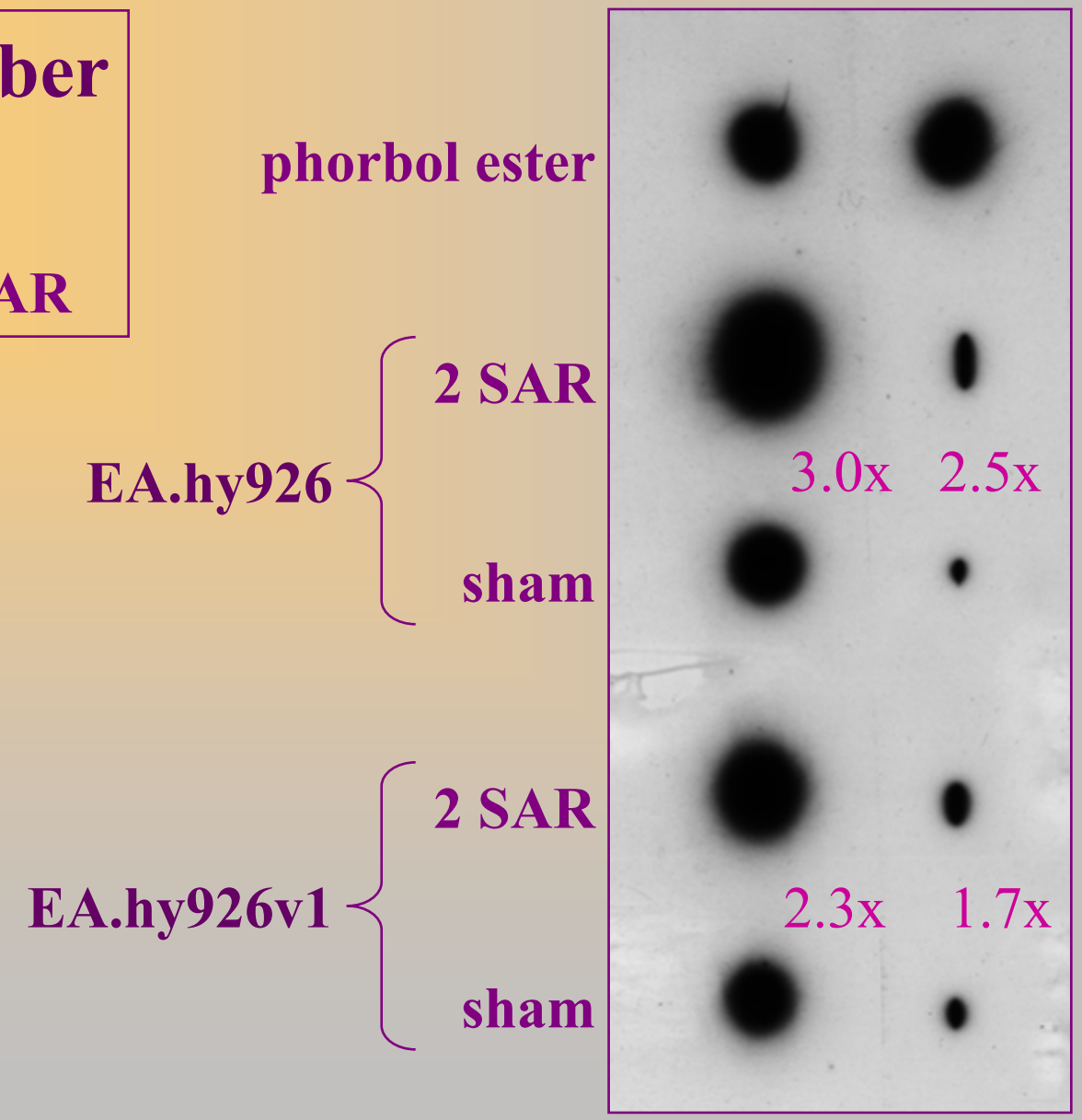
Experimental conditions

SAR_{max} = 2W/kg, ΔT_{max} =0.033°C, $\Delta T_{ave} \approx$ 0.026°C



Kuster's chamber

1800 GSM
talk signal
1h exposure at 2SAR



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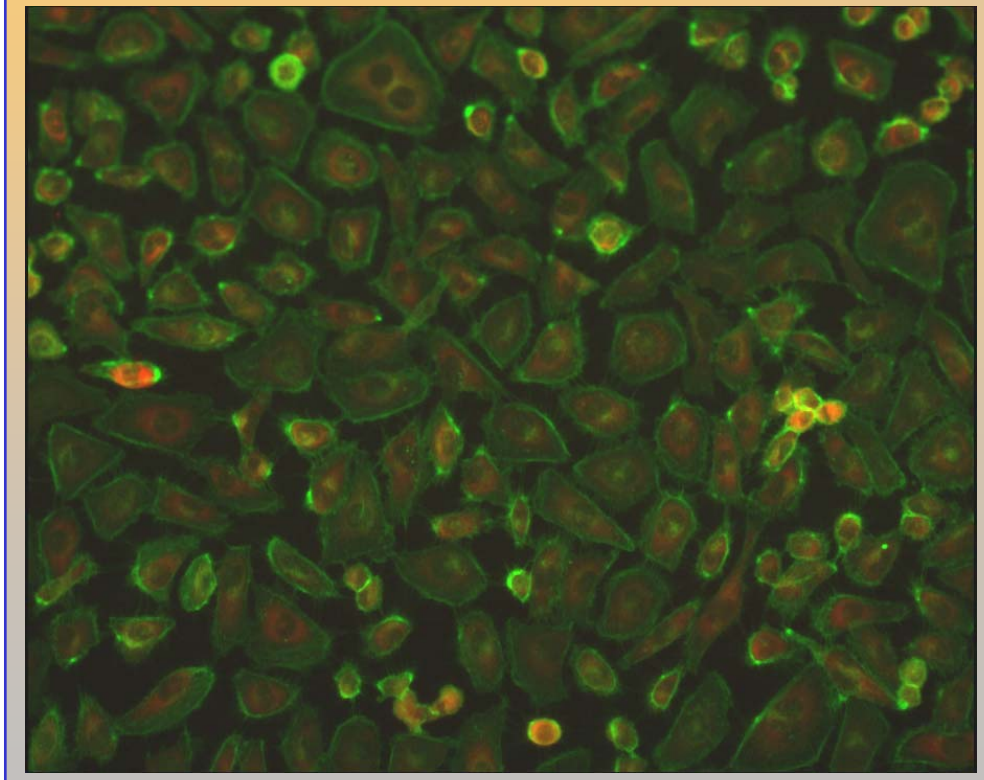
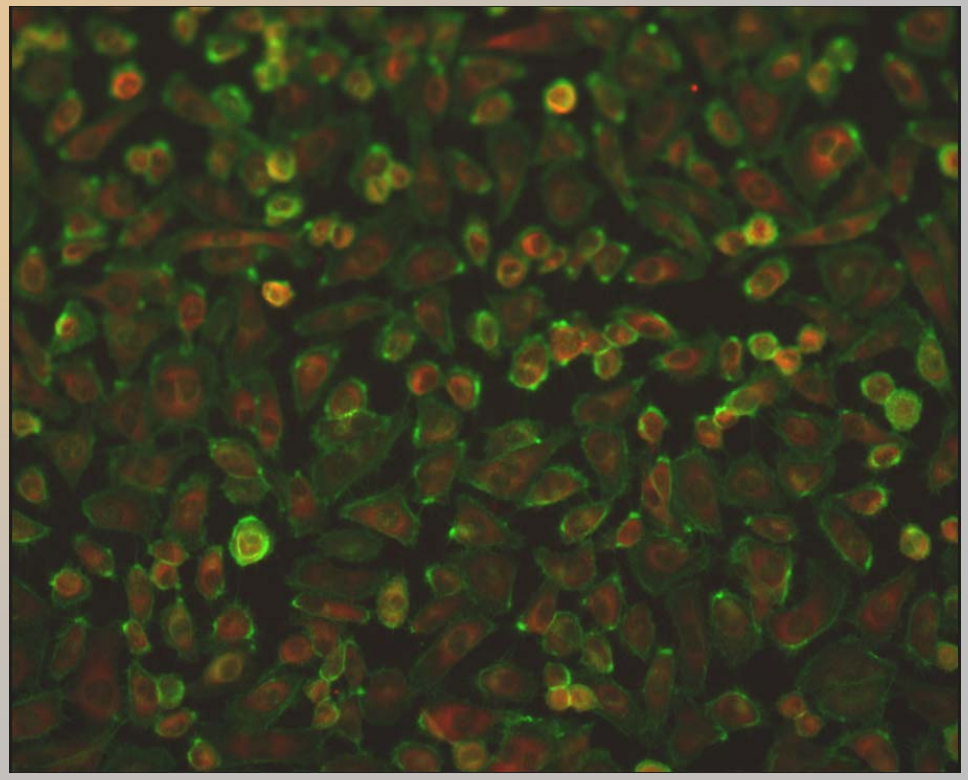
hsp27 & stress fibers

Kuster's chamber

1h sham



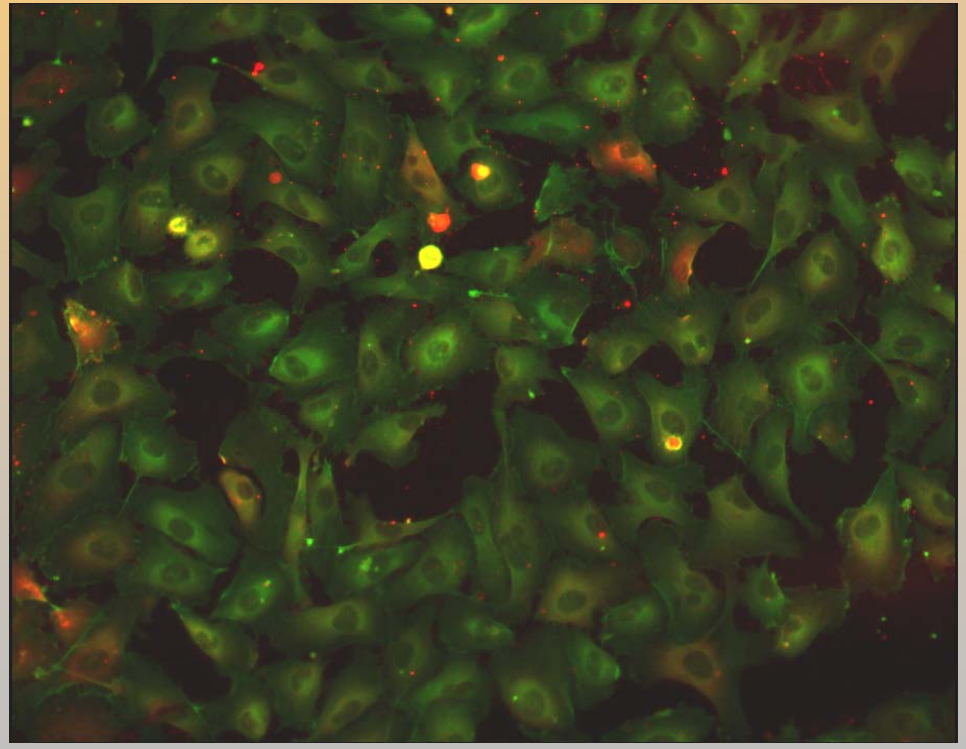
1h 2.0 W/kg



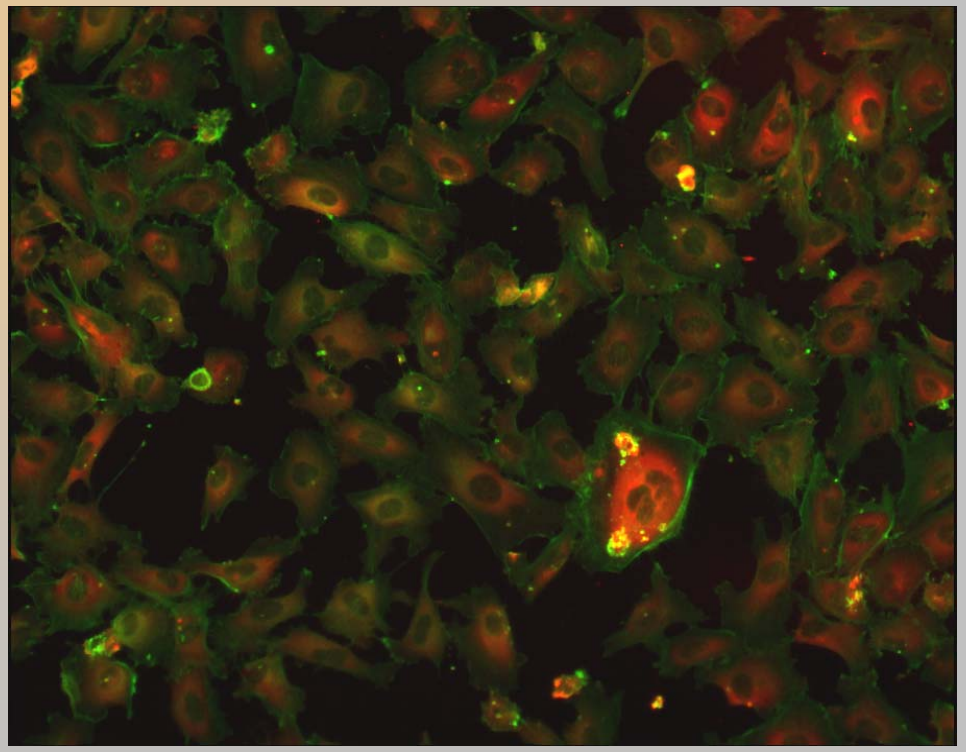
hsp27 & stress fibers

Jokela's chamber

1h sham



1h 2.4 SAR



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Summary of hsp27-effects

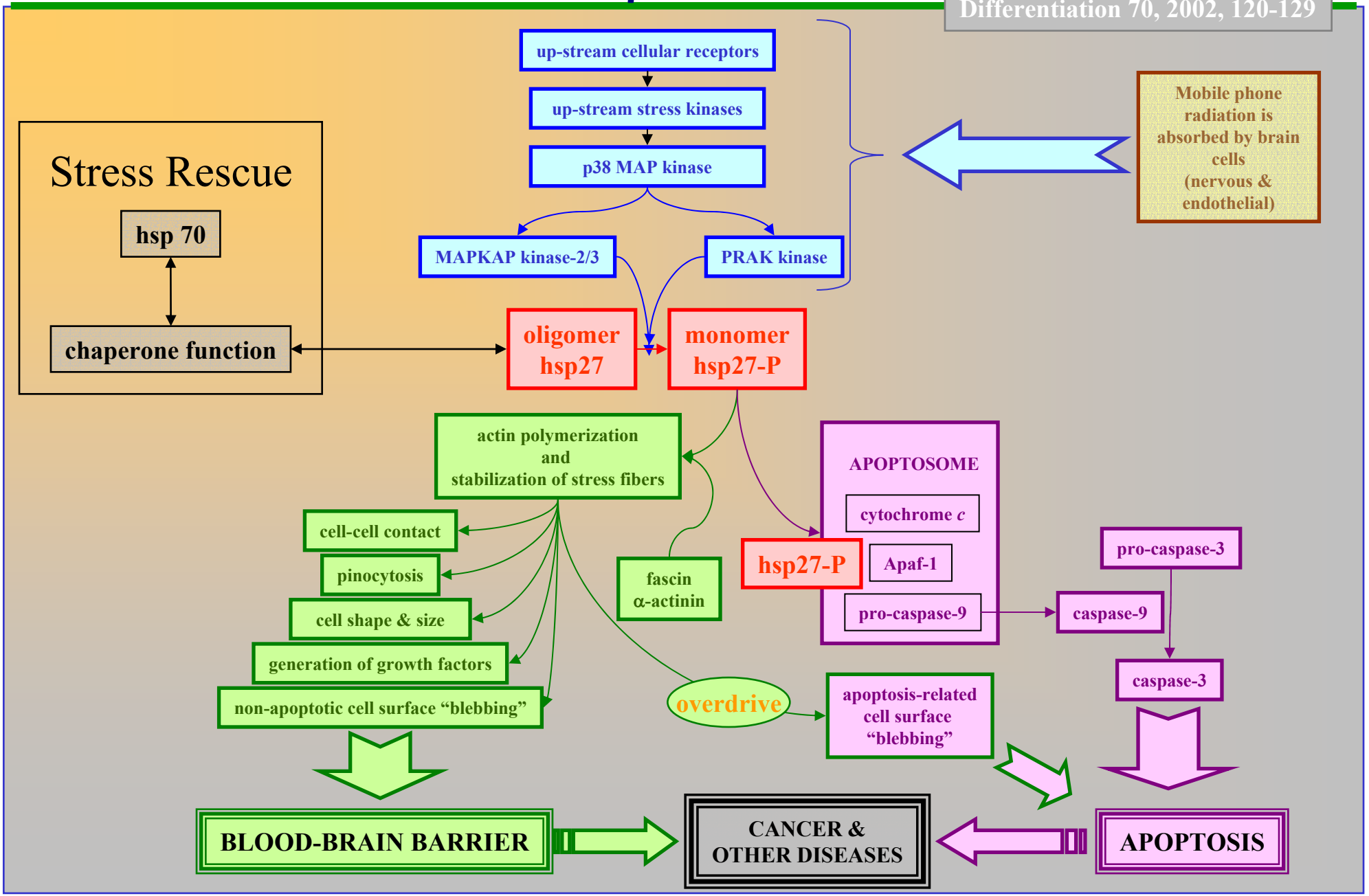
- Jokela's 1.2 SAR - <2 fold
- Kuster's 2.0 SAR - 2-3 fold
- Jokela's 2.4 SAR - >3-fold

Molecular event:
activation of p38MAPK/hsp27 pathway

Physiological event:
hsp27-P alters stability and distribution of stress fibers

Observed in:
- human endothelial cell line
- hamster cell line
- hamster cell line transfected with human hsp27

modified from Leszczynski et al.
Differentiation 70, 2002, 120-129



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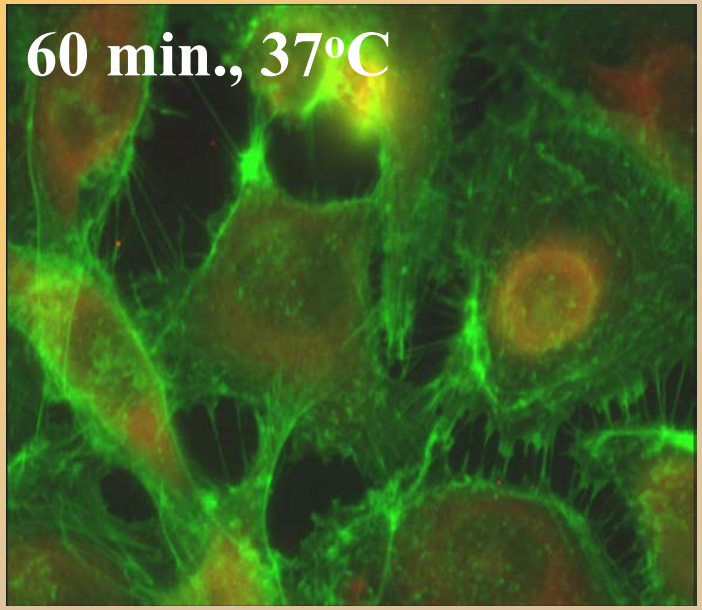
We see effects but are these effects thermal or non thermal?

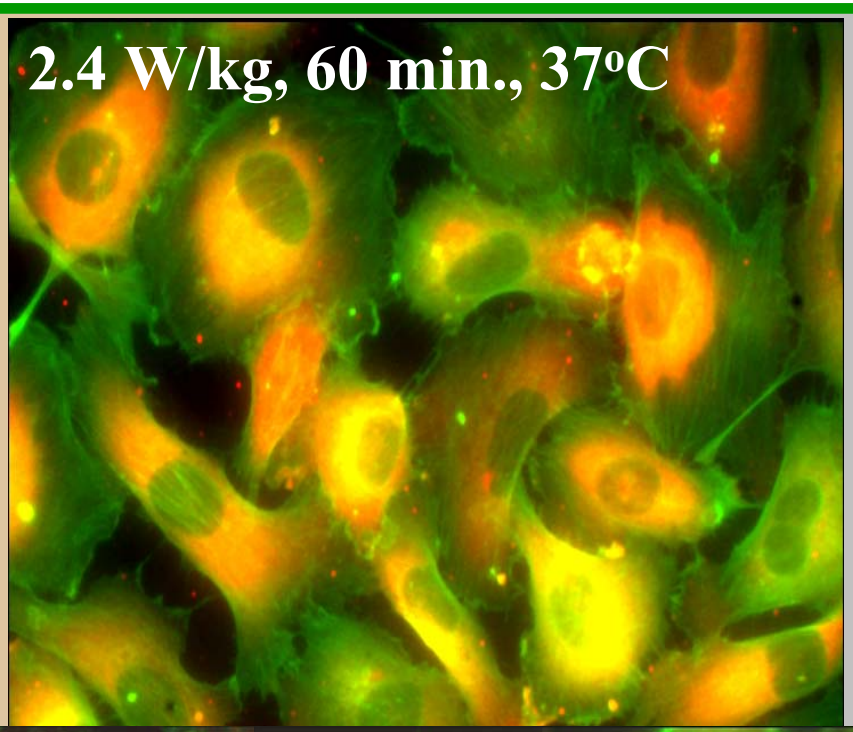
Temperature increases are

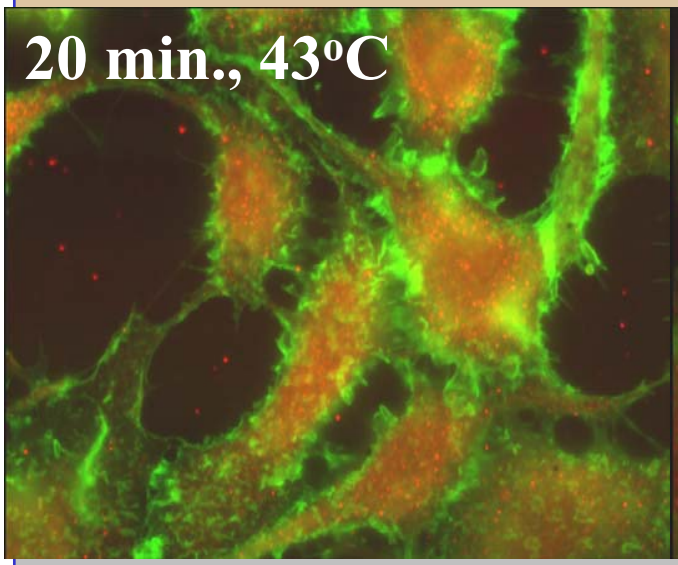
- **<0.3°C in Jokela's chamber**
- **<0.1°C in Kuster's chamber**

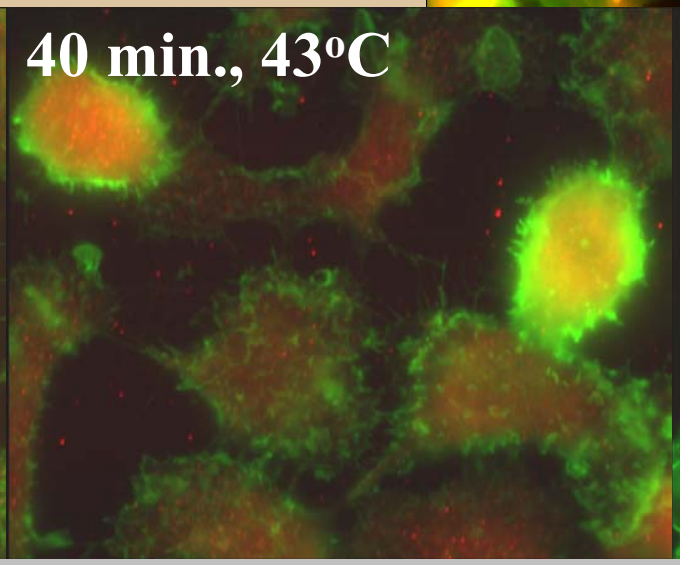
Thermal regulation of hsp27

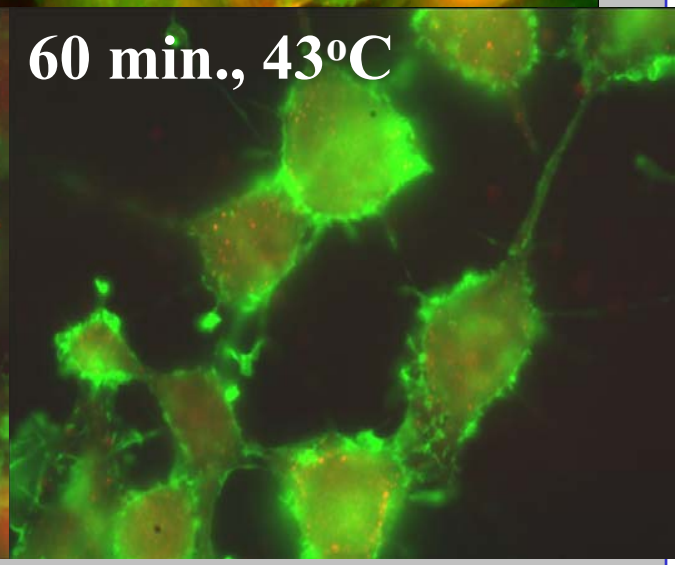
Heat stress effect (water bath)











Cells exposed in cell culture incubator on copper plate for 60 min.

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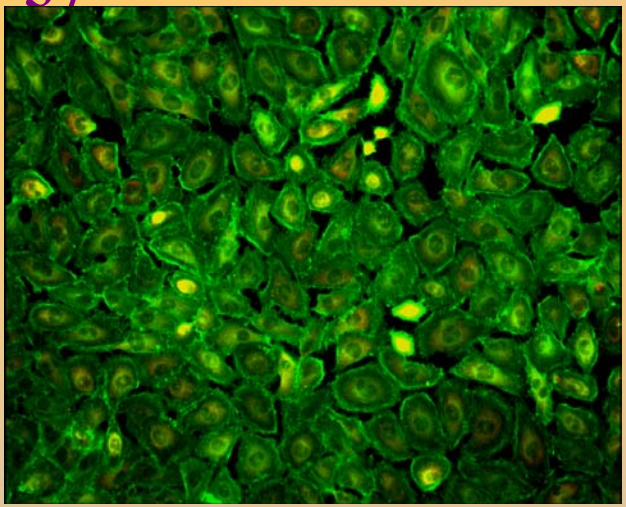

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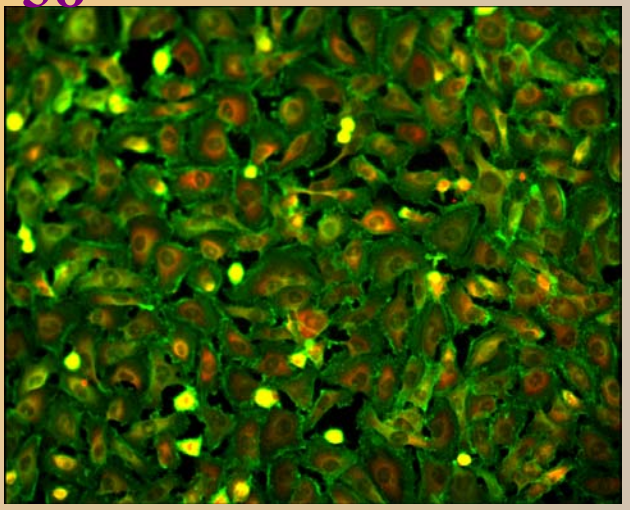

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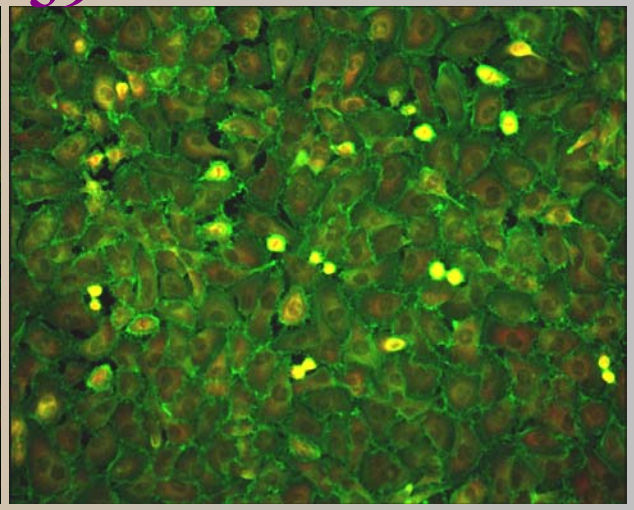

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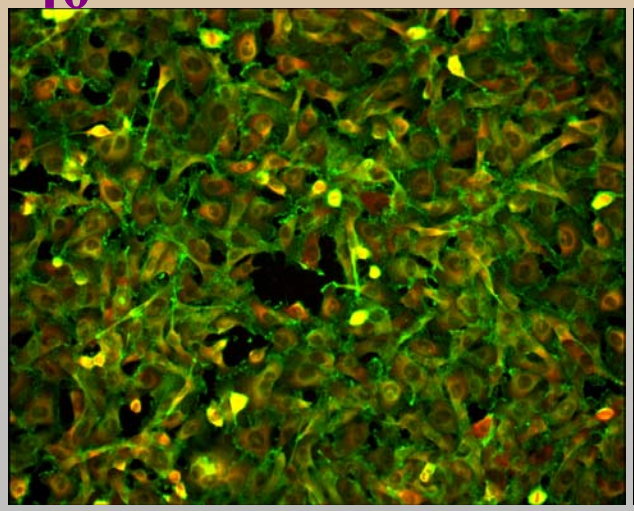

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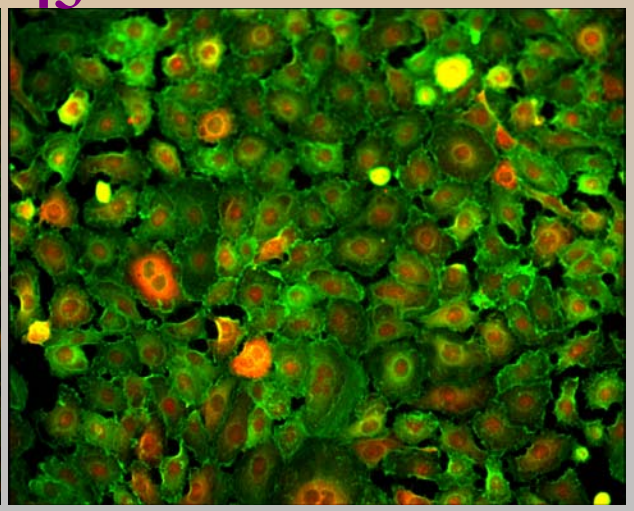
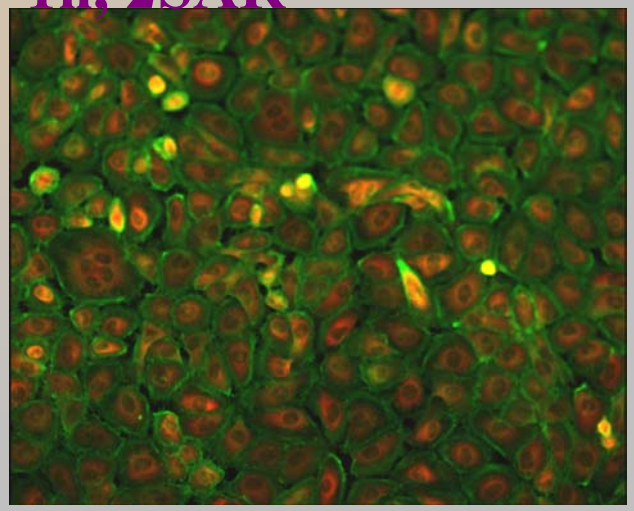
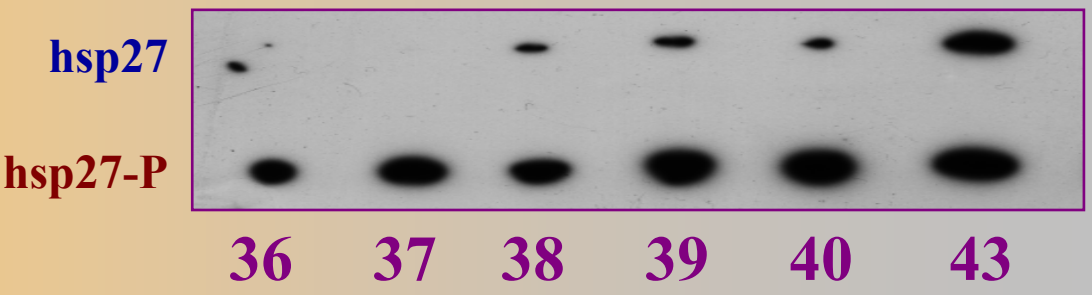
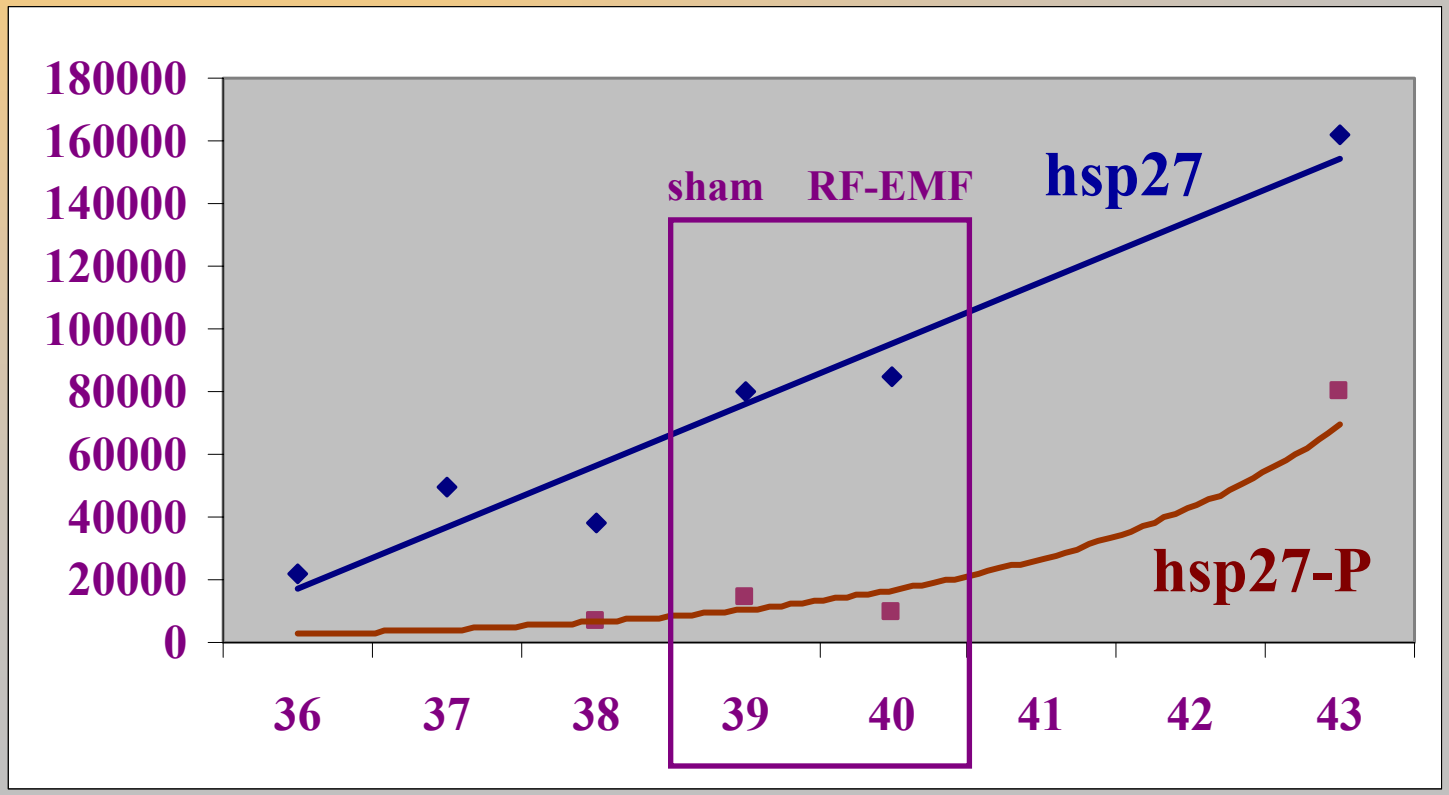


1h, 2SAR



Thermal induction of hsp27 & hsp27-P





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Thermal effects

- term used in safety standards
- average SAR vs. “real” distribution
- assumption that 4 SAR is cut-off point
- “thermal effects are taken care of in safety guidelines”

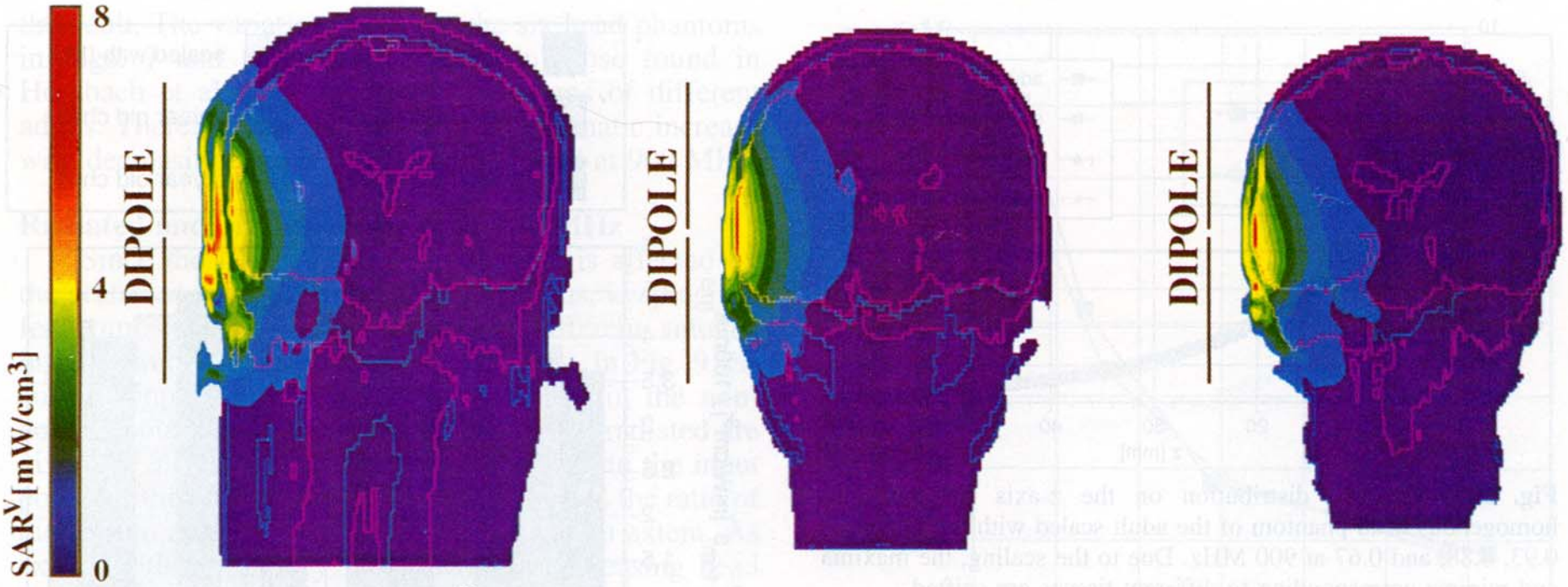
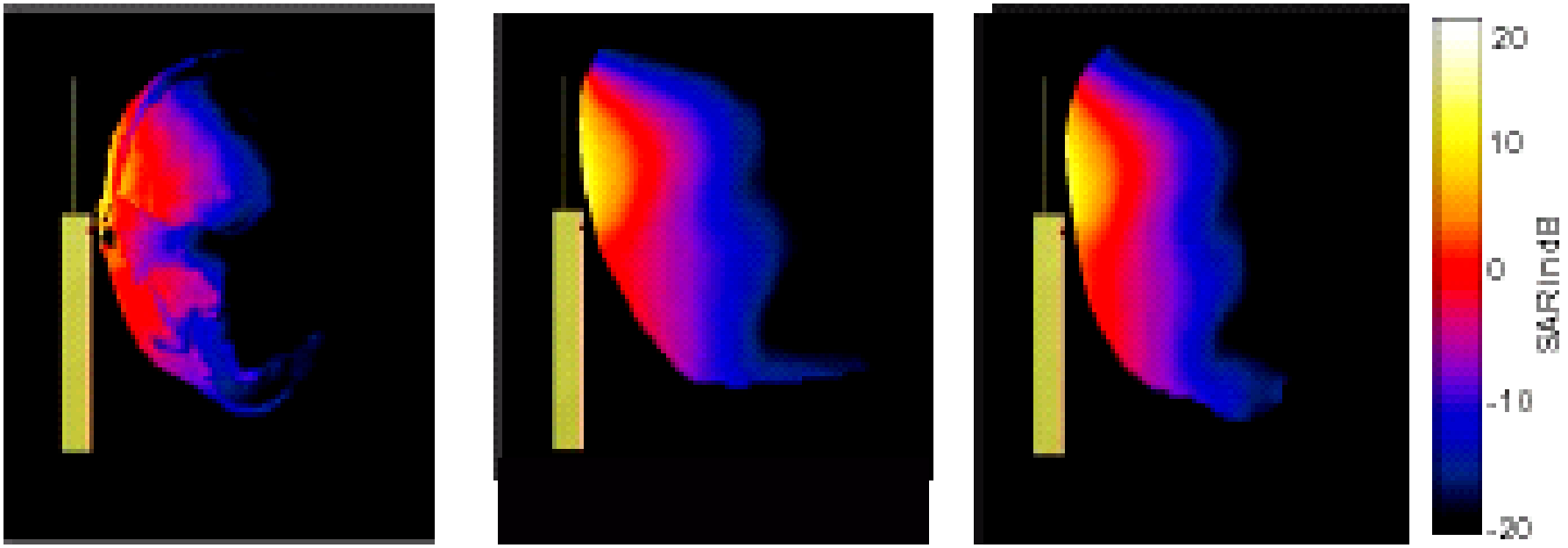


Fig. 2. Comparison of the SAR^V distribution in the plane y = 0 between the nonhomogenous head phantom of the adult (left) and those of the two children of the ages 7 y (center) and 3 y (right) at 900 MHz.

Health Physics 74, 1998, 160-168

SAR Distribution: "Tilted"-Position at 900 MHz



Anatomical Generic SAM

Niels Kuster's presentation at COST 281 meeting in Rome 2002 on Children and Mobile Phones

Thermal effects - questions

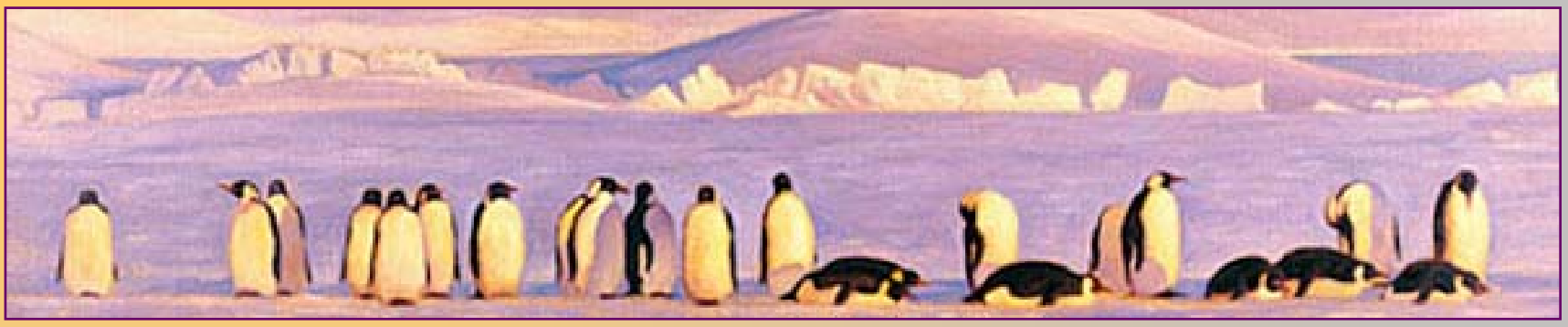
- what temperature activates stress kinases ?
  - how rapid temperature increase ?
  - how big increase ?
  - timing of the increase ?
  - other concomitant insults ?
- is it followed by cell physiological response ?
- can it affect physiology of organ/body ?

Do we know what we are talking when referring to: thermal vs. non-thermal effects?

We do not have precise definition of what is the thermal effect…

Should we rather talk about effects at SAR levels allowed by safety standards because we do not know what temperature elevation causes activation of cellular stress kinases or other cellular responses?

STUK: Bio-NIR Research Group



Bio-effects

Reetta Kuokka
Sakari Joenväärä
Jukka Reivinen
Hanna Tammio
Pia Kontturi
Teemu Kallonen

Dosimetry

Kari Jokela
Tim Toivo
Ari Pekka Sihvonen
Niels Kuster
Juergen Schuderer

Cells

Cora-Jean Edgell
Jacques Landry

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- *5th Framework Programme of the European Union (REFLEX project)*
- *The Academy of Finland*
- *STUK-Radiation and Nuclear Safety Authority*