Presentation at the University of Melbourne, Australia; Dec. 11, 2015

MOBILE PHONE RADIATION & BLOOD-BRAIN BARRIER

EFFECTS OF MOBILE PHONE RADIATION ON HUMAN ENDOTHELIUM

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Adjunct Professor

Department of Biosciences, Division of Biochemistry & Biotechnology
University of Helsinki, Finland

WHO I AM… EDUCATION AND WORK

- Two doctorates and docentship in biochemistry
- Independent expert; actively advising and lecturing
  - 2014 – e.g. Norway, South Africa, USA, India, Australia
  - 2015 – e.g. Switzerland, USA, Serbia, Turkey, *Australia*
- 22 years (1992-2013) at STUK – Radiation and Nuclear Safety Authority
  - 2003-2007 as Head of Radiation Biology Laboratory
  - 2000-2013 as Research Professor
- Assistant Professor at Harvard Medical School, USA; 1997-1999
- Guangbiao Prof. at Zhejiang Univ., Hangzhou, China; 2006-2009
- Visiting Prof. at Swinburne Univ. Technology, Melbourne, Australia; 2012-2013

WHO I AM… EXPERT EXPERIENCE

- 18 years of experimental work on EMF and health
- Testified
  - In the Canadian Parliament's House of Commons' hearing on cell phones and health in 2015
  - before Minister of Health and Family Welfare of India in 2014
  - In the US Senate Appropriations Committee hearing on cell phones and health, in 2009
- Member of 2011 IARC Working Group for classification of the carcinogenicity of cell phone radiation
- Advised e.g.: Parliament of Finland; National Academies, USA; World Health Organization; Bundesamt für Strahlenschutz, Germany; International Commission on Non-Ionizing Radiation Protection (ICNIRP); Swiss National Foundation; The Netherlands Organization for Health Research and Development;

WHY STUDY HEALTH EFFECTS OF CELL PHONE RADIATION?

NO PRE-MARKET TESTING OF HEALTH EFFECTS OF CELL PHONE RADIATION

- Commercialization of cell phone technology, developed for the US Department of Defense
- US Food and Drug Administration
- Permitted sales of cell phones without pre-market safety testing
- Rationale: "low power exclusion" when compared with microwave ovens
- Only thermal effects known at that time and considered

RESEARCHING HEALTH IMPACT OF CELL PHONE RADIATION

- Acute effects
  - Immediate health effect – not known
  - Safety standards based on lack of acute effects
- Delayed effects
  - Change in physiology that may later affect health
    - Health effect (brain cancer?; individual sensitivity?)
    - Physiology adapts and develops resilience
  - Safety standards do not take into account possible delayed effects

RESEARCH OF LESZCZYNSKI'S BioNIR/FunProt GROUP IN FINLAND (selected examples)

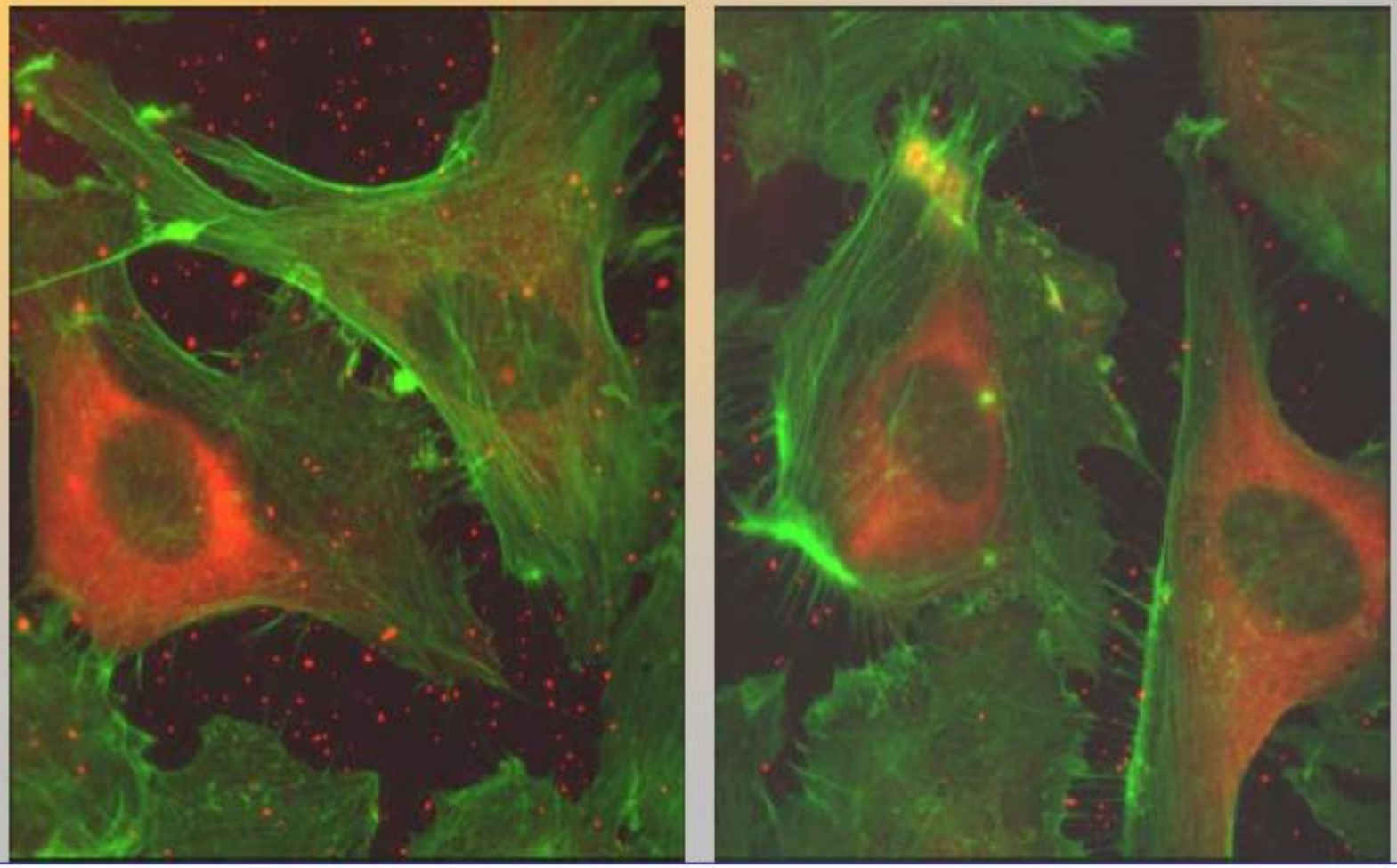
Stress response, proteome & transcriptome

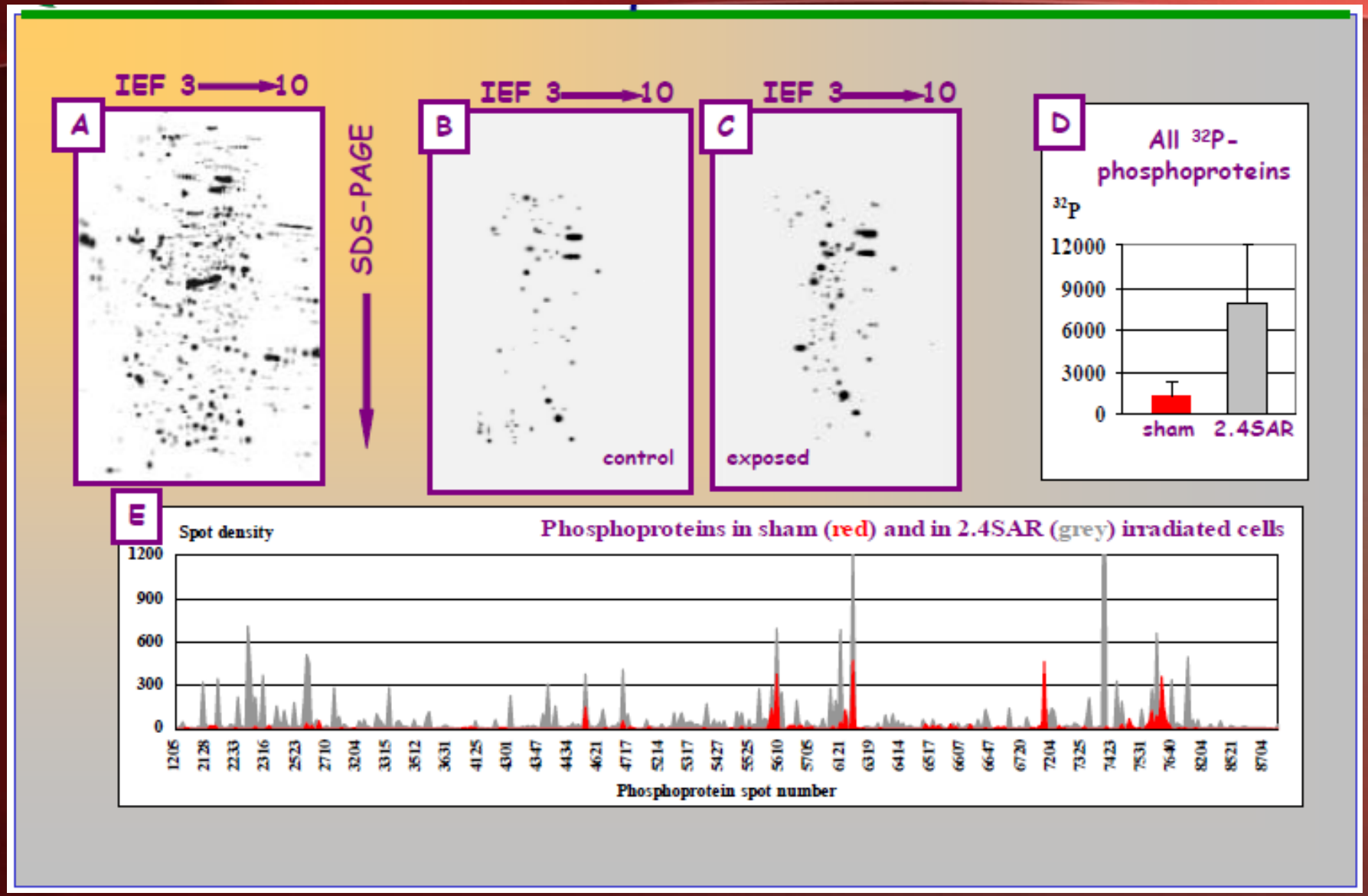
- Nylund et al. Proteome Sci 2010, 8:52
- Nylund et al. J. Proteomics & Bioinformatics 2, 2009, 455-462
- Karinen et al. BMC Genomics 9, 2008, 77-
- Nylund & Leszczynski Proteomics 6, 2006, 4769-4780
- Nylund & Leszczynski Proteomics, 4, 2004, 1359-1365
- Leszczynski et al. Proteomics 4, 2004, 426-431
- Leszczynski et al. Differentiation 70, 2002, 120-129

FINDINGS OF LESZCZYNSKI'S BioNIR/FunProt RESEARCH GROUP IN FINLAND

- Is cell phone radiation inducing physiological effects in human endothelial cell line in vitro?
- Yes – stress response – activated Hsp27/p38MAP kinase pathway (2002)
- Is activation of Hsp27/p38MAPK causing cellular responses?
- Yes – stabilization of F-actin stress fibers, shrinkage of cells, changes in gene expression, changes in protein expression (2002-2008)
- Are cell phone radiation effects occurring in humans?
- Yes – changes in expression of proteins in human skin in vivo (2008)

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 of the cells...

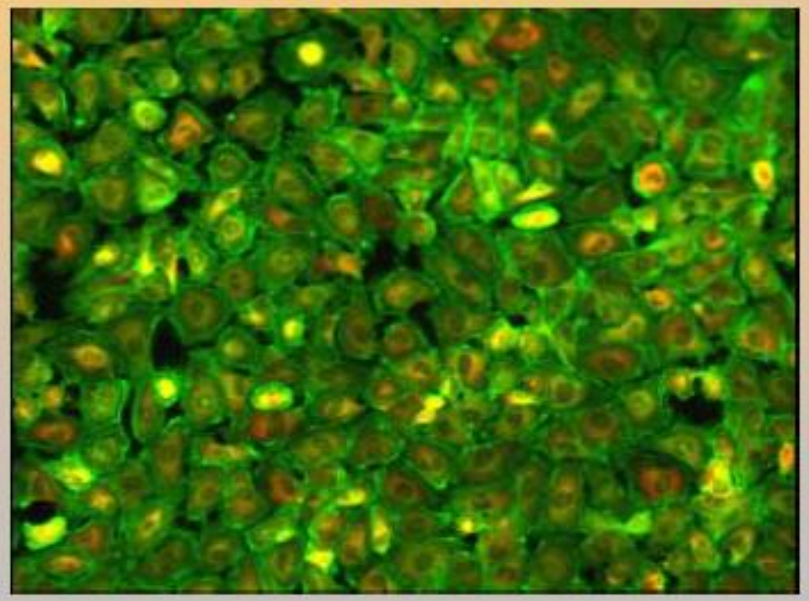



IEF 3→10
A
SDS-PAGE
IEF 3→10
B
control
IEF 3→10
C
exposed
D
All 32P-phosphoproteins
32P
12000
9000
6000
3000
0
sham
2.4SAR
E
Spot density
Phosphoproteins in sham (red) and in 2.4SAR (grey) irradiated cells
1200
900
600
300
0
1205
2128
2233
2316
2523
2710
3204
3315
3512
3631
4125
4301
4347
4434
4621
4717
5214
5317
5427
5525
5610
5705
6121
6319
6414
6517
6607
6647
6720
7204
7325
7423
7531
7640
8204
8521
8704
Phosphoprotein spot number

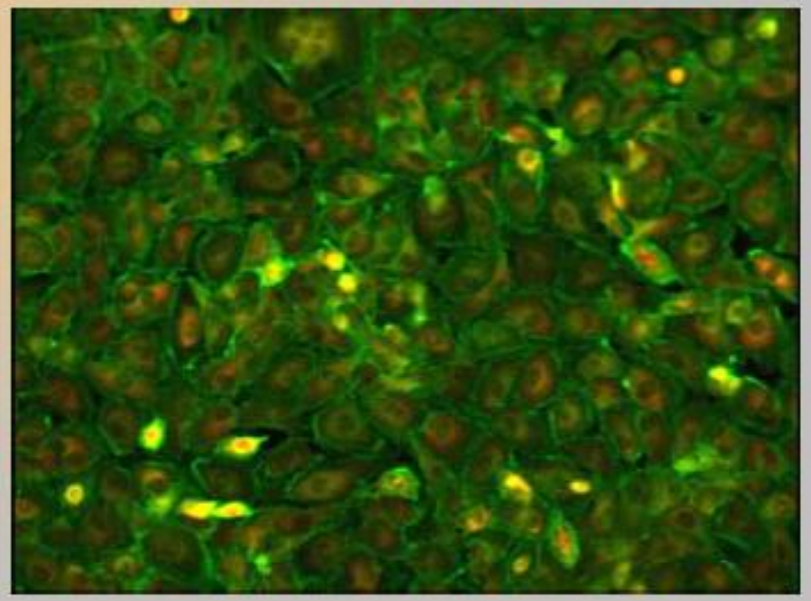
Active hsp27 regulates stability of stress fibers in EA.hy926

SB203580 – inhibitor of p38MAP kinase

1h 2.4SAR without SB203580

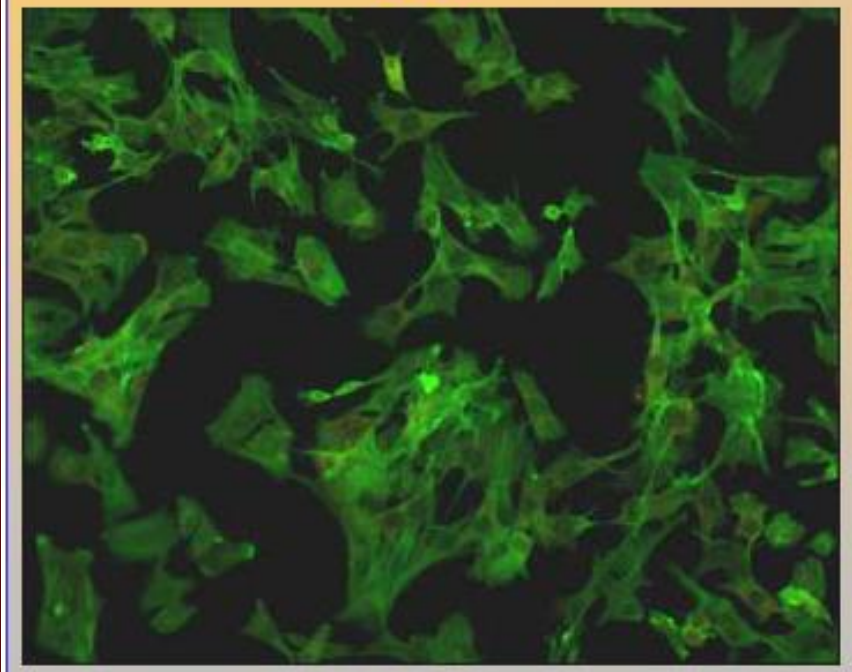


1h 2.4SAR with SB203580

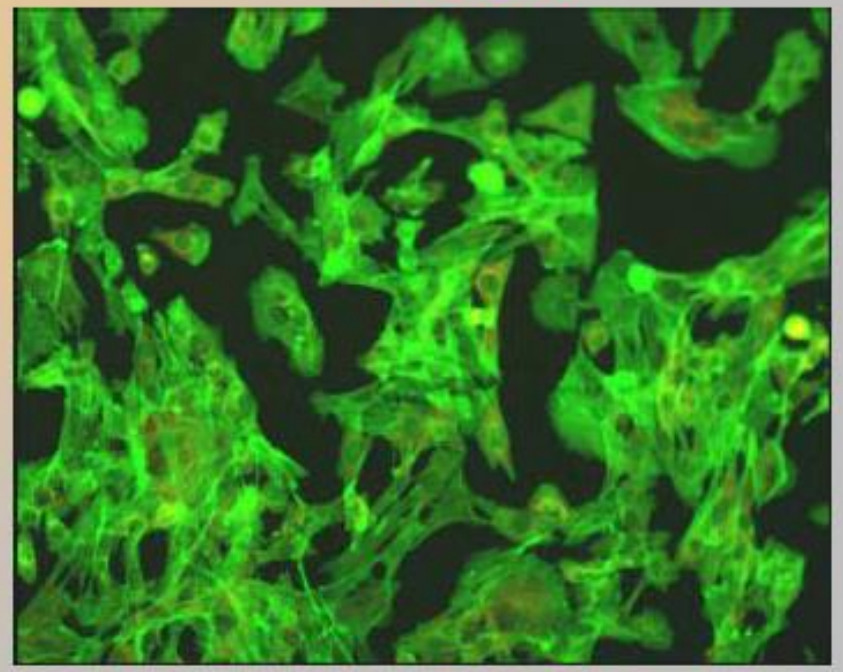


hamster cell line CCL39 over-expressing human wild-hsp27

sham

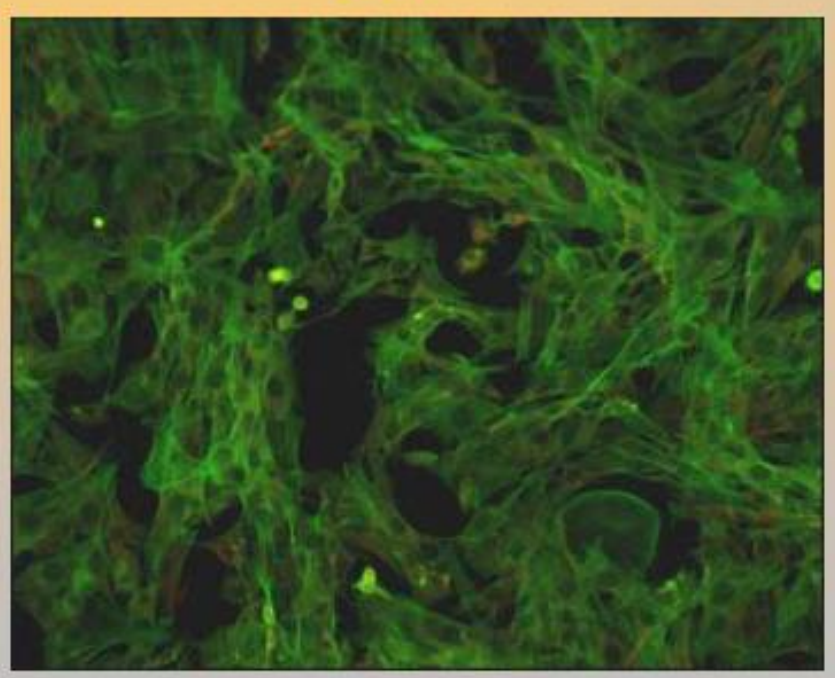


1h 2.4SAR

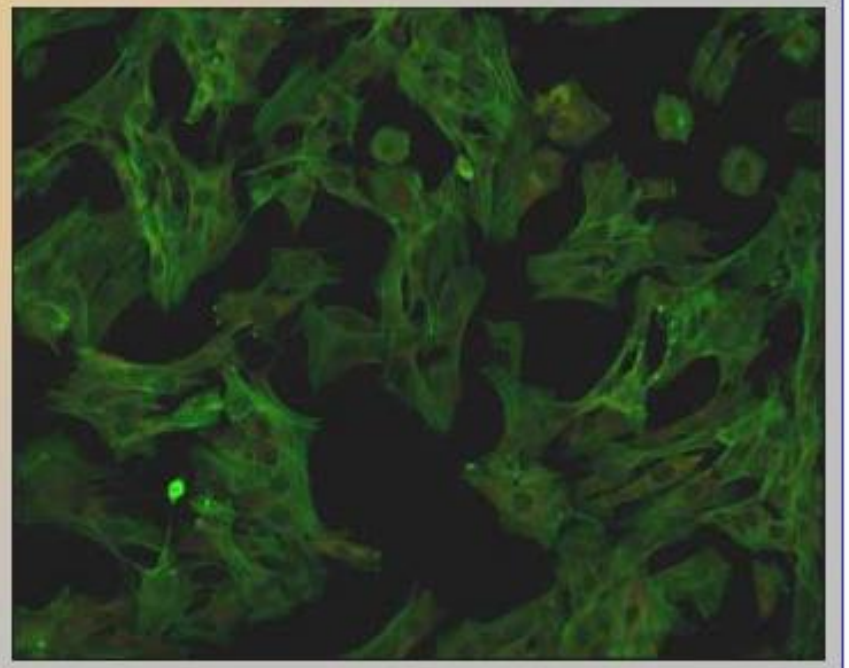


hamster cell line CCL39
over-expressing human mutant-hsp27

sham



1h 2.4SAR



CELLULAR STRESS RESPONSE IS ACTIVATED BY THE MOBILE PHONE RADIATION

Leszczynski et al. 2002

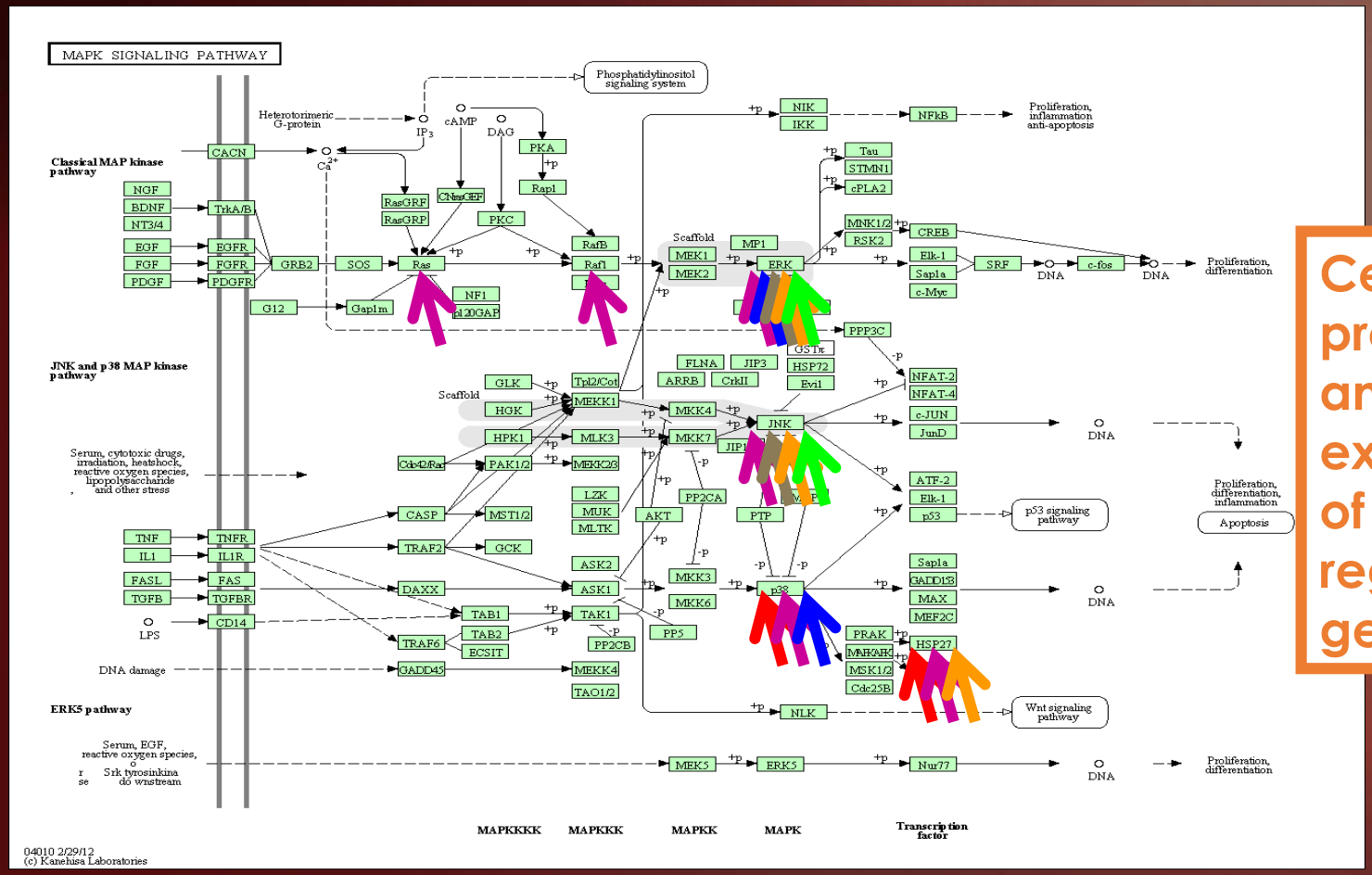
Caraglia et al. 2005

Friedman et al. 2007

Buttiglione et al. 2007

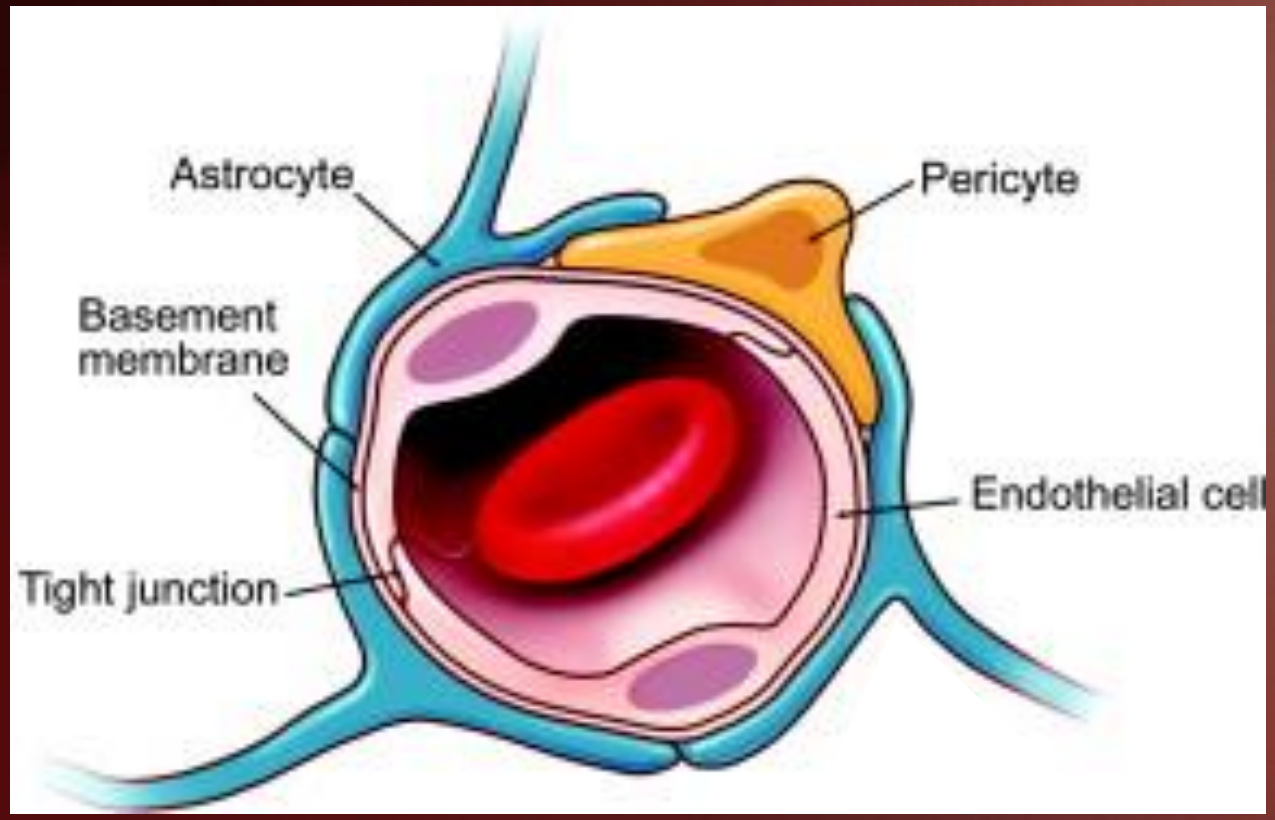
Yu et al. 2008

Lee et al. 2008



Cell proliferation and expression of cancer regularory genes

BLOOD-BRAIN BARRIER

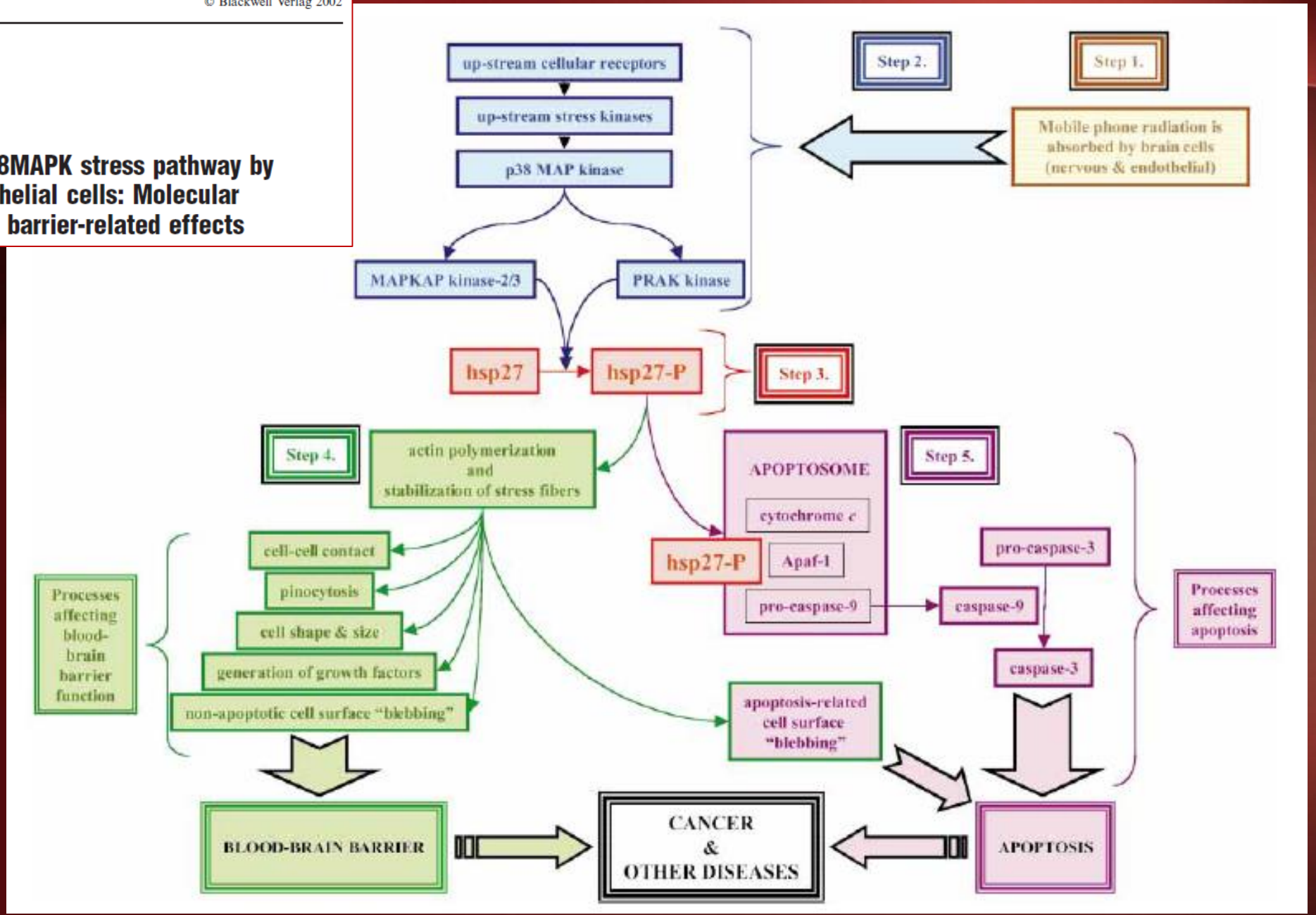


Differentiation (2002) 70:120–129

ORIGINAL ARTICLE

Dariusz Leszczynski · Sakari Joenväärä
Jukka Reivinen · Reetta Kuokka

Non-thermal activation of the hsp27/p38MAPK stress pathway by mobile phone radiation in human endothelial cells: Molecular mechanism for cancer- and blood-brain barrier-related effects



LEIF SALFORD'S GROUP ON BBB

Increased blood-brain barrier permeability in mammalian brain 7 days after exposure to the radiation from a GSM-900 mobile phone. Nittby H, Brun A, Eberhardt J, Malmgren L, Persson BR, Salford LG. Pathophysiology. 2009 Aug;16(2-3):103-12.

Cognitive impairment in rats after long-term exposure to GSM-900 mobile phone radiation. Nittby H, Grafström G, Tian DP, Malmgren L, Brun A, Persson BR, Salford LG, Eberhardt J. Bioelectromagnetics. 2008 Apr;29(3):219-32.

Exposure of rat brain to 915 MHz GSM microwaves induces changes in gene expression but not double stranded DNA breaks or effects on chromatin conformation. Belyaev IY, Koch CB, Terenius O, Roxström-Lindquist K, Malmgren LO, H Sommer W, Salford LG, Persson BR. Bioelectromagnetics. 2006 May;27(4):295-306.

Permeability of the blood-brain barrier induced by 915 MHz electromagnetic radiation, continuous wave and modulated at 8, 16, 50, and 200 Hz. Salford LG, Brun A, Sturesson K, Eberhardt JL, Persson BR. Microsc Res Tech. 1994 Apr 15;27(6):535-42.

Research | Article

Nerve Cell Damage in Mammalian Brain after Exposure to Microwaves from GSM Mobile Phones

Leif G. Salford,[1] Arne E. Brun,[2] Jacob L. Eberhardt,[3] Lars Malmgren,[4] and Bertil R. R. Persson[3]

[1]Department of Neurosurgery, [2]Department of Neuropathology, [3]Department of Medical Radiation Physics, and [4]Department of Applied Electronics, Lund University, The Rausing Laboratory and Lund University Hospital, Lund, Sweden

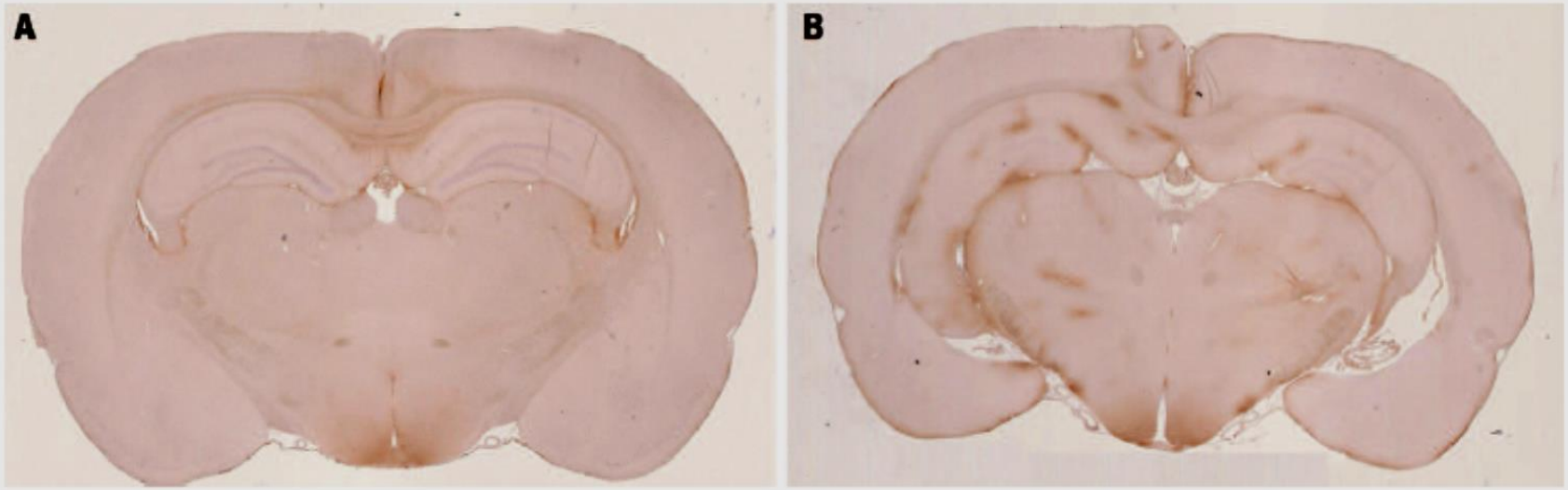


Figure 1. Cross-section of central parts of the brain of (*A*) an unexposed control rat and (*B*) an RF EMF-exposed rat, both stained for albumin, which appears brown. In (*A*), albumin is visible in the central inferior parts of the brain (the hypothalamus), which is a normal feature. In (*B*), albumin is visible in multiple small foci representing leakage from many vessels. Magnification, about ×3.

REPLICATION: ONE FAILURE… ONE SUCCESS…

In a study published in 2009, Patrick Mason and his co-workers from the Air Force Research Laboratory at the Brooks City-Base, TX, USA, have failed to replicate observations from Salford's group.

Radiofrequency-radiation exposure does not induce detectable leakage of albumin across the blood-brain barrier. McQuade JM, Merritt JH, Miller SA, Scholin T, Cook MC, Salazar A, Rahimi OB, Murphy MR, Mason PA. Radiat Res. 2009 May;171(5):615-21.

This year, well recognized and established journal - Brain Research - published in March 2015 issue an article from the scientists at the Department of Neurosurgery, Southwest Hospital, Third Military Medical University, Chongqing, 400038, China:

Exposure to 900 MHz electromagnetic fields activates the mkp-1/ERK pathway and causes blood-brain barrier damage and cognitive impairment in rats.Tang J, Zhang Y, Yang L, Chen Q, Tan L, Zuo S, Feng H, Chen Z, Zhu G. Brain Res. 2015 Mar 19;1601:92-101.

STRESS RESPONSE ACTIVATION… AGAIN

Gang Zhu et al. have shown that activation of stress response pathway is involved in the effect on blood-brain barrier. Quote from the abstract:

"Taken together, these results demonstrated that exposure to 900 MHz EMF radiation for 28 days can significantly impair spatial memory and damage BBB permeability in rat by activating the mkp-1/ERK pathway."

POTENTIAL MECHANISM: CELLULAR STRESS RESPONSE

Leszczynski et al. 2002

Caraglia et al. 2005

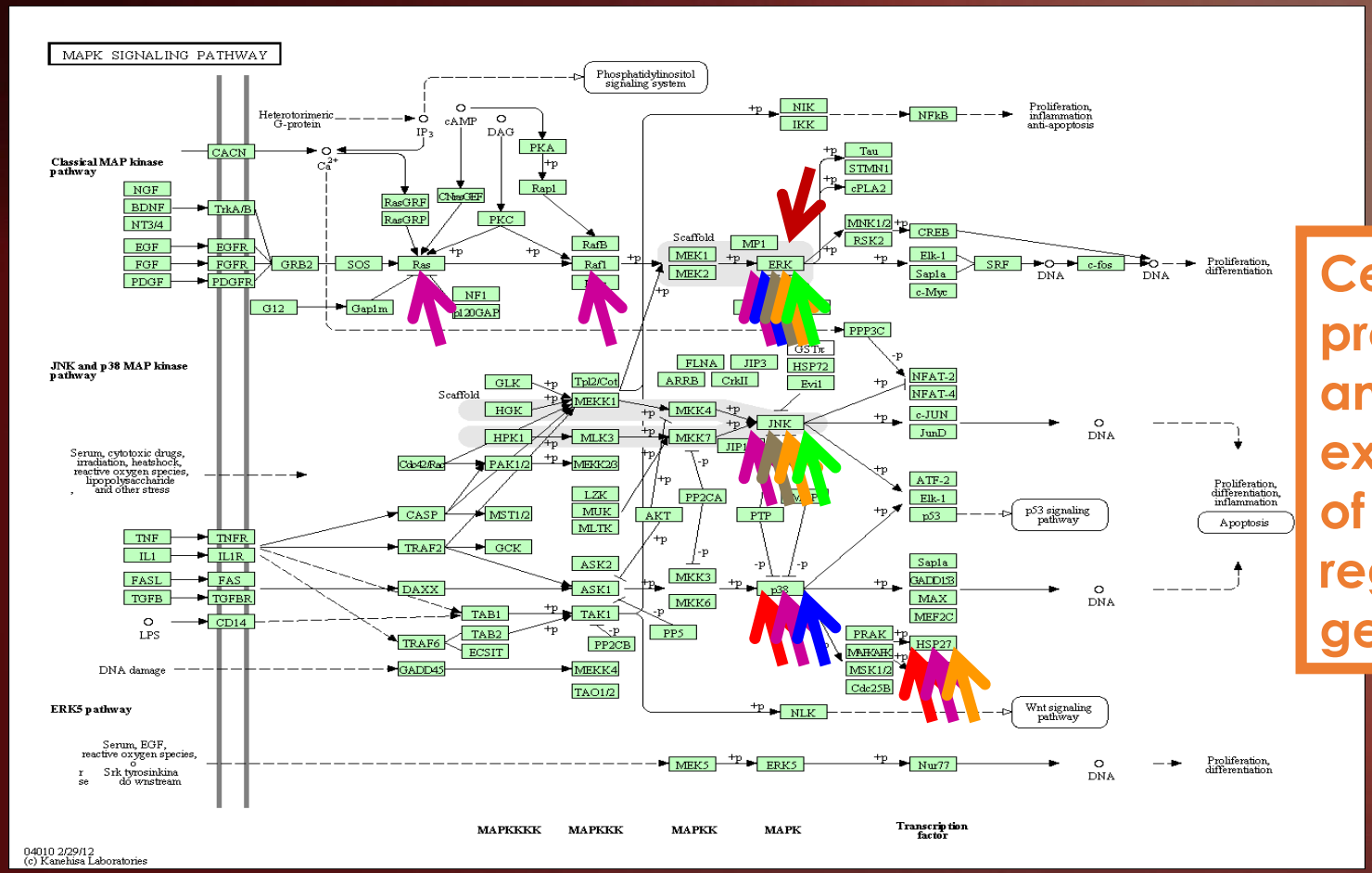
Friedman et al. 2007

Buttiglione et al. 2007

Yu et al. 2008

Lee et al. 2008

Zhu et al. 2015



Cell proliferation and expression of cancer regularory genes

FUTURE RESEARCH NEEDS

Unlike the genome, the transcriptome and the proteome are highly dynamic and change rapidly and dramatically in response to perturbations or even during normal cellular events

strong stimulus
↓
robust response

weak stimulus
↓
response will very much depend on the transcriptome and proteome expressed by the cells at the time of exposure

Nylund R. & Leszczynski D.
Mobile phone radiation causes broad changes in gene and protein expression in human endothelial cell lines and the response appears to be genome- and proteome-dependent.
Proteomics 6, 2006

THE FUTURE
HEALTH RESEARCH THROUGH PROTEOMICS

L.Hood et al. PROTEOMICS,12, 2012, 2773–2783

- **The Proteome** is the operating system for nearly all biological functions. It is the link between the genome and phenotypes
- It undergoes dynamic changes in different cells and organs, during development, in response to environmental stimuli, and in disease processes
- Understanding the dynamics of protein interactions with other proteins, nucleic acids, and metabolites is the key to delineating biological mechanisms and understanding disease

GAME CHANGER

G. Schmid & N. Kuster. The Discrepancy Between Maximum In Vitro Exposure Levels and Realistic Conservative Exposure Levels of Mobile Phones Operating at 900/1800 MHz; Bioelectromagnetics 2015

- Exposure of skin, blood, and muscle tissues may well exceed 40 W/kg at the cell level.
- In vitro studies reporting minimal or no effects in response to maximum exposure of 2 W/kg or less averaged over the cell media, which includes the cells, may be of only limited value for analyzing risk from realistic mobile phone exposure.
- Future in vitro experiments use specific absorption rate levels that reflect maximum exposures and that additional temperature control groups be included to account for sample heating.

CONCLUSIONS

- Mobile phone radiation activates cellular stress response in vitro and in vivo
- Stress response pathways, activated by mobile phone radiation, appear to be cell-type specific
- Activation of stress response indicates that cells recognize mobile phone radiation as a potentially damaging agent and launch protective response
- Activation of stress response in endothelial cells forming blood-brain barrier may potentially impair functioning of the barrier
- Further research, including this with omics techniques, should continue to determine potential effects of mobile phone radiation on human blood-brain barrier
- New exposure protocols need to be considered in the context of the "game changer" observation by Schmid & Kuster