Influence of RF Fields on the Expression of Stress Proteins

Workshop Consensus Statement

The workshop attendees agreed at the beginning of the summary session to focus on the issue of induction of stress proteins (HSPs) by radio frequency radiation exposures. Other information presented at the workshop can be found in the meeting abstracts and presentations. Based largely on the evidence presented at the workshop, there is no substantiation of the hypothesis that RF exposures result in the induction of stress proteins. Evidence was presented that an increase in heat shock proteins (HSPs) was observed in *in vitro* systems at levels of RF exposure which do not induce a temperature increase. Other studies described during the Workshop, however, including some replication experiments with the same types of exposure, found an absence of influence of RF exposure on HSP expression. The results presented by Dr de Pomerai, considered significant by many, indicated that he was not able to replicate his earlier results using a modified exposure system. He stated that an extremely small measurable increase in temperature may have played a significant role in his earlier observation of increased HSP expression in *C. elegans*. This effect may be particularly relevant in thermally challenged organisms and underlines the requirement of extremely exact methods of field application and dosimetry.

Only one possibility of an initiation point for HSP regulation was described at the meeting. A report was presented by Dr Goodman of an electromagnetic (EM) response element with a specific DNA sequence different from the Heat Shock Element (HSE). The methodology used in the exposure experiments described at the workshop was challenged.

A genomics study presented by Dr Maercker showed no alteration of HSP at the transcription level. It was pointed out that this was from a single time point (1hr) at a single exposure level.

Small HSP phosphorylation either was not influenced by RF exposure, or was only marginally influenced by RF exposure. Several papers were presented showing increased mono-phosphorylation after exposure to 900 or 1800 MHz (GSM RF, the European standard). Other studies at 835 (TDMA RF, the North American standard) and 1950 MHz were presented, with no change being observed.

A published paper was referred to during the meeting (Fritze et al. 1997) as being one of the only published reports investigating HSP response *in vivo*. Rats were exposed to 900 MHz GSM modulated RF at various intensities (up to a SAR of 7.5 W/kg). No evidence was found of a change in HSP70 in the brain on either a transcriptional (RNA synthesis) or translational (protein synthesis) level for the exposure times used. At a high SAR, evidence was seen of a slight increase in the transcription of hsp70.

- Recommendations were made at the Workshop in support of the need for accumulation of further scientific knowledge, which would allow an informed judgement of whether RF exposure results in the induction of heat shock proteins.

- The consensus was that a weight of evidence is required to show whether or not HSP induction or modulation is influenced by exposure to RF.

- When it was suggested that efforts should be made to replicate those study designs already reported, it was pointed out that two independent replication studies were

currently underway. These, along with the original studies presented at the meeting, should be used to draw conclusions.

- It was further recommended that experimentation at both the *in vitro* and *in vivo* level should continue, to gain further knowledge of the basic underlying processes of an interaction between RF and biological systems.

A general consensus of the meeting was that the newly available high-throughput techniques of genomics and proteomics should be used to investigate the possibility of non-hypothesized biological effects of RF exposure. Opposing opinions to this view were aired by some members of the Workshop, however. It was pointed out that interpretation of the results of high-throughput studies is not even close to being definitive, and that analysis of high-throughput experiments requires detailed knowledge about the biological and statistical significance of the results obtained.

Another general consensus was that methods should be established to further investigate microthermal effects, which may be an important confounding factor in *in vitro* and some *in vivo* experiments.

The issue was raised of how meaningful the SAR values reported for *in vitro* experiments are in relation to *in vivo* SARs, due in part to the small volumes and geometries often involved in *in vitro* studies.

Concern was expressed that insufficient correlation is seen between *in vivo* studies and *in vitro* results.

Comments were also made about the relatively low (less than 30%) increase in the expression or phosphorylation status of HSP that was reported at the Workshop. Concern about this, along with other reports where no effects were demonstrated, served to remind the participants that a physiologically relevant effect may require a many-fold increase in expression or phosphorylation. Even if a physiological change was demonstrated, it was pointed out that this could still lie within the range of normal human response, and not lead to a health effect. This matter was addressed in part by an accepted workshop consensus that if *in vitro* HSP studies reveal a biological effect, the possibility of health effects would require further investigations.

The Workshop was in accord that if HSPs were demonstrated to be altered in response to RF exposure, no conclusion could be drawn as to whether this would lead to adverse health effects, or could in fact be beneficial.

References:

Fritze K, Wiessner C, Kuster N, Sommer C, Gass P, Hermann DM, Kiessling M, Hossmann KA. Neuroscience. 1997 Dec;81(3):627-39. Effect of global system for mobile communication microwave exposure on the genomic response of the rat brain.