

Key

Supplementary Material – Karipidis et al. experimental study review

	Effect – statistically significant
	Uncertain Effect – may or may not be relevant to topic
	Trend – non significant changes seen
	No Significant Effect
	Protective or Therapeutic Effect
	Questionable Topic Relevance
	Antagonistic Effect

Note: Colours represent findings in relation to the specific endpoint being covered in the tables below and not representative of all end points that may have been tested in a study

[number] – Paper reference taken directly from Karipidis *et al.* review bibliography.¹ Refer to the bibliography in Karipidis review paper for specific reference information.

Table 1 Experimental studies investigating low-level RF fields above 6 GHz and genotoxicity.

Important Note: Columns from “Reference” through to “Quality Issue” reproduced from Karipidis¹ tables. “Issues with Karipidis Classification” and “Our Finding” columns are our addition.

Issues with Karipidis Classification/Interpretation/Data	Our Finding	Reference	Biological System	Frequency Range	Intensity	Exposure Duration	Results [Claimed]	Quality Issue [Claimed]
<p>Misclassified – Although oxidative stress (OS) can be implicated in genotoxicity, the assay was for lipid peroxidation and so would be more appropriately assigned to “Membrane” effects and/or to a new topic related to oxidative stress. Crouzier <i>et al.</i> has assumed no DNA damage has occurred because cell vitality was not impacted and claimed, “The vitality results do not show any effect of ROS on DNA.” This is not a sufficient measure for recording DNA damage. Only direct measurements with a Comet assay, Micronuclei assay, Chromosomal Aberration assay or an assay that measures DNA fragmentation or oxidative base damage (such as measuring 8-OHdG levels or 8-oxoG levels) can DNA damage be confirmed or dismissed. None of the aforementioned assays were used.</p> <p>Frequency Observation – Specific frequency of 9.71 GHz was used.</p> <p>Incorrect Biological System – No Bacteria were exposed. <i>Saccharomyces Cerevisiae</i> Cells i.e., Yeast which are fungi.</p> <p>Incomplete Results – Reduced membrane fluidity was also noted making this study a candidate for the membrane effects table.</p> <p>Misstatement – Karipidis has incorrectly claimed “No change in ROS production at low exposure levels.” A clear dose response for increased ROS production measured using 4-POBN spin trap was shown starting from an RF exposure level of 1 W/kg. Crouzier <i>et al.</i> stated that “overall results of this study show significant and dose dependant effects of EMF at 9.71 GHz on ROS promotion, even at low power density (non-thermal condition)”</p> <p>Funding – Délégation Générale de l’Armement (Military).</p>	Oxidative stress, lipid peroxidation (Not a genotoxicity paper) reduced membrane fluidity	[26] Crouzier <i>et al.</i>	Bacteria & Yeast	9 GHz	0.5 to 16 W/kg	20 min	No change in ROS production at low exposure levels. SAR above the limit	No Blinding

Issues with Karipidis Classification/Interpretation/Data	Our Finding	Reference	Biological System	Frequency Range	Intensity	Exposure Duration	Results [Claimed]	Quality Issue [Claimed]
<p>Incomplete Results - This study found evidence of an aneugenic effect in foetal fibroblasts as indicated by the immunofluorescent antikinetochore (CREST) micronuclei test. There was also evidence of non-disjunction which can result in aneuploidy (the presence of an abnormal number of chromosomes in a cell) and can lead to genetic disorders.²</p> <p>Comment Only - Of interest is the result for DNA damage. A weak trend was seen for both single strand (SS) and double strand (DS) breaks, but more importantly, the % of DNA in the tail was almost 50% for both control and exposed (neutral comet assay). Either there was a significant problem with the way the assay was conducted or the units are incorrectly specified as one does not normally expect to see such a large % of DNA in the tail in unexposed cells.</p> <p>Comment Only - Wide band frequency used.</p> <p>Incorrect Exposure Time - Exposure duration was 20 minutes not "up to 24 hours"</p> <p>Funding - Italian Ministry of Defence (Government/Military).</p>	<p>Genotoxic - Aneugenic effect/CREST-positive micronuclei induction, aneuploidy. A weak trend for increased DNA breaks (both alkaline and neutral comet assays) was also seen, cell cycle changes seen (S-Phase), slight mitochondrial damage, transitory ultrastructure changes, No HSP expression changes or apoptosis (No significant BAX expression)</p>	<p>[18] De Amicis <i>et al.</i></p>	<p>Cells in culture</p>	<p>100-150 GHz</p>	<p>4 W/m²</p>	<p>Up to 24 h</p>	<p>No DNA damage but an increased occurrence of micro-nucleation. SAR above limit</p>	<p>Inadequate dosimetry and no blinding</p>
<p>Incomplete Results - This study found evidence of an aneugenic effect as indicated by the CREST micronuclei test. There was also evidence of non-disjunction which can result in aneuploidy (the presence of an abnormal number of chromosomes in a cell) and can lead to genetic disorders.²</p> <p>Comment Only - Authors noted that the incidence of micronuclei was higher in foetal fibroblasts (related study performed by De Amicis <i>et al.</i> [18]) than adult fibroblast suggesting that cells that are dividing are at a higher risk due to possible spindle disturbances. It is also noteworthy that a comet assay was not performed to directly check for SS and DS DNA damage as was performed in the related study.</p> <p>Comment Only - The temperature increase was only 0.6°C over the 20 minute exposure period.</p> <p>Incorrect Exposure Time - Exposure duration was 20 minutes not "up to 24 hours"</p> <p>Funding - Italian Ministry of Defence, (Government/Military).</p>	<p>Genotoxic - Aneugenic effect/CREST-positive micronuclei induction, aneuploidy, No significant cell cycle changes</p>	<p>[19] Franchini <i>et al.</i></p>	<p>Cells in culture</p>	<p>25 GHz</p>	<p>8 W/m²</p>	<p>Up to 24 h</p>	<p>No DNA damage but an increased occurrence of micro-nucleation. SAR above limit</p>	<p>No blinding</p>
<p>Frequency Observation - Specific frequency of 42.2 GHz was used.</p> <p>Funding - Russian Foundation for Basic Research (Government).</p>	<p>Reduced DNA damage (radioprotective) effect against X-ray exposure</p>	<p>[32] Gapeyev <i>et al.</i></p>	<p>Cells in culture</p>	<p>42 GHz</p>	<p>1 W/m²</p>	<p>20 min</p>	<p>MMW pre-exposure reduced DNA damage after x-ray exposure to leucocytes</p>	<p>Poor temperature control</p>
<p>Comment Only - This study is related to [32] above.</p> <p>Frequency Observation - Specific frequency of 42.2 GHz was used.</p> <p>Funding - Not declared.</p>	<p>Reduced DNA damage (protective) effect against other genotoxic agents including X-ray exposure, Hydrogen Peroxide exposure and Methyl Methanesulfonate exposure</p>	<p>[33] Gapeyev and Lukyanova</p>	<p>Cells in culture</p>	<p>42 GHz</p>	<p>1 W/m²</p>	<p>20 min</p>	<p>MMW pre-exposure reduced DNA damage after x-ray exposure to leucocytes</p>	<p>Poor temperature control</p>

Issues with Karipidis Classification/Interpretation/Data	Our Finding	Reference	Biological System	Frequency Range	Intensity	Exposure Duration	Results [Claimed]	Quality Issue [Claimed]
<p>Misstatement - Karipidis has incorrectly stated this study as showing no statistically significant chromosome aberrations. Garaj-Vrhovac <i>et al.</i> state very clearly "In comparison with the control samples there was a significantly higher frequency of specific chromosome aberrations such as dicentric and ring chromosomes in irradiated cells. The presence of micronuclei in irradiated cells confirmed the changes that had occurred in chromosome structure." These results suggest that Radiofrequency (RF) fields can induce damage in the structure of chromosomal DNA (p <0.05).</p> <p>Findings Not Reported - Statistically significant micronuclei induction.</p> <p>Frequency Observation - Specific frequency of 7.7 GHz was used.</p> <p>Funding - Self-Managed Community of Interest for Science.</p>	Genotoxic - Statistically significant chromosome aberrations (presence of dicentric and ring chromosomes), micronuclei induction and reduced colony forming.	[12] Garaj-Vrhovac <i>et al.</i>	Cells in culture	7 GHz	5-300 W/m ²	10-60 min	No statistically significant increase in chromosome aberrations	Inadequate dosimetry and no blinding
<p>Misstatement - Karipidis has incorrectly stated this study as showing no statistically significant chromosome aberrations. Garaj-Vrhovac <i>et al.</i> state "In all experimental conditions, the frequency of all types of chromosomal aberrations was significantly higher than in the control samples." A dose response was also noted.</p> <p>Findings Not Reported - Statistically significant micronuclei induction.</p> <p>Frequency Observation - Specific frequency of 7.7 GHz was used.</p> <p>Funding - Not declared.</p>	Genotoxic - Statistically significant chromosome aberrations (presence of dicentric and ring chromosomes) and micronuclei induction in human blood lymphocytes	[13] Garaj-Vrhovac <i>et al.</i>	Cells in culture	7 GHz	5-300 W/m ²	10-60 min	No statistically significant increase in chromosome aberrations	Inadequate dosimetry and no blinding
<p>Incorrect Exposure Time - The exposure duration was 0.5 Hours not 5 Hours.</p> <p>Funding - Bavarian Elite Network (Government) and the Erich-Becker-Stiftung.</p>	Spindle disturbances only (non-linear response observed) but no significant structural chromosome effects	[30] Hintzsche <i>et al.</i>	Cells in culture	106 GHz	0.43 - 43 W/m ²	5 h	Increase in spindle disturbances, but no indication of structural chromosome aberrations	Well designed
<p>Comment Only - No concerns with Karipidis classification. Note: Sham exposure of HaCaT cell showed higher DNA damage (mean >10% DNA in tail) compared with both control (~2%) and exposed (~5% @ 20 W/m²) - one wonders if the samples had been mixed up or whether there was contamination of the sham sample.</p> <p>Funding - German Radiation Protection Authority, which also funds ICNIRP.</p>	No significant effect for DNA damage - DNA strand breaks. No effect for micronuclei induction	[15] Hintzsche <i>et al.</i>	Cells in culture	106 GHz	0.4 - 20 W/m ²	2-24 h	No DNA strand breaks or chromosome damage. SAR above limit	Inadequate temperature and sham control
<p>Incomplete Results - Water structure changes, DNA melting point changes, thermostability changes. These parameters may or may not be directly related to genotoxicity, and was not the intention of the study protocol to verify. We question its inclusion in this table.</p> <p>Frequency Observation - Specific frequency of 64.5 GHz was used.</p> <p>Funding - Not declared.</p>	Water structure changes, DNA melting point changes, thermostability changes	[29] Kalantaryan <i>et al.</i>	Miscellaneous	65 GHz	0.5 W/m ²	Up to 120 min	Changes in DNA strand separation during artificial synthesis	Poor dosimetry and temperature control

Issues with Karipidis Classification/Interpretation/Data	Our Finding	Reference	Biological System	Frequency Range	Intensity	Exposure Duration	Results [Claimed]	Quality Issue [Claimed]
<p>Incomplete Results - Karipidis made no mention of statistically significant changes in the activity of a number of antioxidant enzymes, which is an indicator of oxidative stress in the exposed animals (other studies mentioned in the genotoxic table explicitly mention ROS findings - i.e. [25], [26]) so Karipidis has been inconsistent. Karipidis does cover ROS very briefly in supporting review text outside the table but does not discuss the implications of increased ROS on biology or its health implications if sustained.</p> <p>Comment Only - Small animal (rat) numbers do suggest low statistical power but should not mean the outcomes are ignored. Also, the hippocampus region of the brain is responsible for control of learning and memory. There are studies showing >6 GHz exposures negatively impacting memory, such as Sharma et al.³, a very relevant study that was not included in Karipidis paper selection, and an epidemiological study reviewed by Karipidis i.e., Mortazavi et al. [150].</p> <p>Funding - Council for Scientific and Industrial Research (Government).</p>	Genotoxic - DNA damage (DS DNA breaks), altered anti-oxidant enzyme activity and reduced protein kinase C levels in Hippocampus (brain) neurons	[24] Kesari and Behari	In vivo	50 GHz	0.0086 W/m ²	2 h/day for 45 days	Increase in DNA double-strand breaks and a decrease in the levels of Protein kinase C	Low animal numbers (6 exposed)
<p>Findings Not Reported - Karipidis classification is obscuring the results. Authors found genomic instability and aneuploidy (chromosome number). "<i>Aneuploidy is the most common chromosome abnormality in humans, and is the leading genetic cause of miscarriage and congenital birth defects</i>" Hassold et al.⁴ This is an important finding and should have been explicitly mentioned. It is also important to note that congenital anomalies were indicated in a study by Mageroy et al. [146], along with increased perinatal mortality in a study by Baste et al. [147]. Both papers were included in Karipidis epidemiological study review.</p> <p>Comment Only - SAR is below ICNIRP Occupational Limits which is the focus of the Karipidis review. Power Density (PD) is within limits.</p> <p>Funding - Commission of the European Communities (Government).</p>	Genotoxic - Genomic instability and aneuploidy	[14] Korenstein-Ilan et al.	Cells in culture	100 GHz	0.31 W/m ²	1-24 h	Chromosomal changes and asynchronous centromeres replications. SAR above limit	No blinding
<p>Funding - Japanese Ministry of Internal Affairs and Communications.</p>	No DNA damage - i.e., no DNA strand breaks or micronuclei induction, and no significant heat shock protein (HSP) expression	[16] Koyama et al.	Cells in culture	60 GHz	10 W/m ²	24 h	No increase in DNA strand breaks or heat shock protein expression	Well designed
<p>Incorrect Frequency - Karipidis specified 45 GHz but actual frequency was 40 GHz.</p> <p>Funding - Japanese Ministry of Internal Affairs and Communications.</p>	No significant effects for DNA damage - no DNA strand breaks or micronuclei or HSP expression	[17] Koyama et al.	Cells in culture	45 GHz	10 W/m ²	24 h	No increase in micronucleation, DNA strand breaks or heat shock protein expression	No blinding

Issues with Karipidis Classification/Interpretation/Data	Our Finding	Reference	Biological System	Frequency Range	Intensity	Exposure Duration	Results [Claimed]	Quality Issue [Claimed]
<p>Findings Not Reported - Karipidis failed to mention important results by not disclosing statistically significant micronuclei induction that was found. The method for detecting micronuclei was via flow cytometric determination.</p> <p>Intensity Observation - There were 2 intensities used based on the frequency of exposure. 10GHz intensity was 2.14 W/m² and the 50GHz intensity was 8.9 mW/m² (both are below ICNIRP public limits)</p> <p>Funding - Indian Council of Medical Research and Council for Scientific and Industrial Research (Government).</p>	Genotoxic - Micronuclei induction in blood cells for both frequencies	[25] Kumar et al.	In vivo	10 and 50 GHz	2.1 W/m ²	2 h/day for 45 days	Increase in ROS and increases and decreases in enzymes that control the build-up of ROS	Low animal numbers (6 exposed) and no blinding
<p>Misclassified - Lukashovsky and Belyaev were investigating mechanisms of prophage "gene switching" which does not necessarily mean it is damaging the DNA. It is possible Karipidis was confused by the authors suggestion that DNA damaging agents such as ionizing radiation do the same thing. One cannot automatically assume that it is a marker for DNA damage. The gene expression table would have been more appropriate for this study.</p> <p>Nonsensical Quality Issue - Karipidis claimed a lack of temperature control as a quality deficiency. Author has clarified that temperature was controlled and did not change within the error of measurement, 0.1°C.</p> <p>Misstatement - Karipidis. claimed SAR was above the limit. This is not correct. SAR values were from 0.8 W/kg (which is below ICNIRP public limit) to 4 W/kg (which is below ICNIRP occupational limit). Temperature was controlled and did not change within 0.1°C.</p> <p>Funding - Not declared.</p>	Lamda DNA gene switching	[28] Lukashovsky and Belyaev	Bacteria & Yeast	69-71 GHz	Up to 5 W/m ²	30 min	Increase in indicators of DNA damage. SAR above limit	Inadequate dosimetry and temperature control
<p>Findings Not Reported - Karipidis failed to disclose the exact nature of the DNA damage, which was found in the form of single strand DNA breaks. The word "indicator" is passive and so diminishes the significance of what the authors found.</p> <p>Comment Only - The Power Density (PD) specified is within the public limits for frequencies >6 GHz. The exposure was performed in the far field ($R > 2d^2/\lambda$).</p> <p>Funding - Indian Council of Medical Research (Government).</p>	Genotoxic - Statistically significant DNA damage in the form of single strand DNA breaks	[23] Paulraj and Behari	In vivo	16.5 GHz	10 W/m ²	2 h/day for 35 days	Increase in indicators of DNA damage. SAR above limit	Low animal numbers (6 exposed) and no blinding
<p>Frequency Observation - Specific frequency of 42.2 GHz was used.</p> <p>Comment Only - The findings of chromatin condensation may or may not necessarily be related to genotoxicity. Although cells undergoing apoptosis do exhibit changes in nuclear morphology, including DNA fragmentation and chromatin condensation, additional tests would need to be performed to confirm this is occurring. Chromatin condensation also occurs as a natural process during the cell cycle prophase, which is the first phase of mitosis where the nucleus of a parent cell separates into two identical daughter cells and is not directly associated with DNA damage. Authors state "<i>Chromatin condensation maybe induced by changing of DNA protein interaction evoked by electromagnetic field</i>" and so may be a stress related response.</p> <p>Comment Only - This paper is also relevant for membrane (nuclear) effects.</p> <p>Informative Comment - a differential response was noted between various donors providing possible evidence of sensitive receivers</p>	Chromatin condensation and changes in nuclei electrical charge	[20] Shckorbatov et al.	Cells in culture	42 GHz	2 W/m ²	1-60 s	Decreased nuclei electrical charge and increased chromatin condensation in the nuclei	No blinding, sham control not described

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and non-responders, which ICNIRP does not account for in the latest published RF guidelines (ICNIRP 2020). Funding – Not declared.								
Comment Only – Refer to the statement above in regards to chromatin condensation as a marker for genotoxicity as it also applies to this study classification too. Comment Only – Authors stated in their paper “ <i>Irradiation time in all experiments was 10 sec.</i> ” However, a picture of a buccal epithelial cell in the same paper suggests there was a 60 second irradiation at 0.2 mW/m ² Funding – Not declared.	Chromatin condensation and increased heterochromatin granule quantity	[21] Shckorbatov et al.	Cells in culture	35 GHz	0.3 W/m ²	10 s	Increase in chromatin condensation as indicated by an increase in heterochromatin granule quantity	Inadequate dosimetry and temperature control
Frequency Observation – Specific frequency of 36.65 GHz was used. Comment Only – Refer to the statement above in regards to chromatin condensation as a marker for genotoxicity as it also applies to this study classification too. Incorrect Exposure Time Range – Irradiation time in all experiments was 10 seconds. Funding – Not declared.	Chromatin condensation, increased heterochromatin granule quantity and increased membrane permeability	[22] Shckorbatov et al.	Cells in culture	36 GHz	0.01-1 W/m ²	1-10 s	Increase in chromatin condensation as indicated by an increase in heterochromatin granule quantity. SAR above limit	Inadequate dosimetry and temperature control
Misclassified – The authors of the paper state “ <i>From this point of view, millimeter-band radiation can be regarded as a fundamentally new agent that disturbs the functional regulatory mechanism of genetic elements in the cell, and extrachromosomal elements in particular, without causing direct damage to the DNA molecule.</i> ”. This paper would have been better placed in the gene expression table. Incorrect Biological System – No Yeast were used in the experiment. Escherichia coli (E. coli) Bacteria were exposed. Incorrect Frequency Range – A number of discrete frequencies were used λ (mm) = 5.8, 6.5 and 7.1, which translates to 51.69 GHz, 46.12 GHz and 42.22 GHz respectively. Additionally, 45.63 GHz and 48.75 GHz were also used. Funding – Not declared.	Increased Colicin synthesis (Not a Genotoxicity study)	[27] Smolyanskaya and Vilenskaya	Bacteria & Yeast	45-46 GHz	0.1-10 W/m ²	0.5-2 h	Increase in indicator of DNA damage	Statistical methods and dosimetry were not described

Issues with Karipidis Classification/Interpretation/Data	Our Finding	Reference	Biological System	Frequency Range	Intensity	Exposure Duration	Results [Claimed]	Quality Issue [Claimed]																																									
<p>Misstatement - Karipidis suggests there was no indication of DNA damage when there is definitely a trend for some donors (in relation to comet assay results). The results demonstrate that donors should not be treated as a single homogenous group. Some donors (donor 3 and donor 4) appear to react to the signals and show increased DNA damage from 50 to 250% using the comet assay, while other donors do not. For example, exposure to 130 GHz 5Hz modulation at SAR 1.4 W/kg showed:</p> <table border="1"> <thead> <tr> <th>Donor</th> <th>Exposure</th> <th>%migrate DNA</th> <th>Tail Length</th> <th>Tail Movement</th> </tr> </thead> <tbody> <tr> <td rowspan="2">1</td> <td>Sham-exposed</td> <td>2.41</td> <td>2.44</td> <td>0.27</td> </tr> <tr> <td>Exposed</td> <td>2.10</td> <td>3.98</td> <td>0.44</td> </tr> <tr> <td rowspan="2">2</td> <td>Sham-exposed</td> <td>0.97</td> <td>2.36</td> <td>0.12</td> </tr> <tr> <td>Exposed</td> <td>1.13</td> <td>1.29</td> <td>0.08</td> </tr> <tr> <td rowspan="2">3</td> <td>Sham-exposed</td> <td>1.82</td> <td>2.67</td> <td>0.26</td> </tr> <tr> <td>Exposed</td> <td>2.84</td> <td>3.57</td> <td>0.47</td> </tr> <tr> <td rowspan="2">4</td> <td>Sham-exposed</td> <td>0.53</td> <td>0.94</td> <td>0.04</td> </tr> <tr> <td>Exposed</td> <td>1.53</td> <td>2.28</td> <td>0.24</td> </tr> </tbody> </table> <p>This suggests there may be sensitive receivers and non-responders. Pooling the results (providing a mean value) will mask these differences.</p> <p>Funding - Commission of the European Communities (Government).</p>	Donor	Exposure	%migrate DNA	Tail Length	Tail Movement	1	Sham-exposed	2.41	2.44	0.27	Exposed	2.10	3.98	0.44	2	Sham-exposed	0.97	2.36	0.12	Exposed	1.13	1.29	0.08	3	Sham-exposed	1.82	2.67	0.26	Exposed	2.84	3.57	0.47	4	Sham-exposed	0.53	0.94	0.04	Exposed	1.53	2.28	0.24	No significant DNA damage or cell cycle changes. A trend for DNA damage seen in some donors (comet assay).	[31] Zeni et al.	Cells in culture	120-130 GHz	0.5-2.3 W/m ²	20 min	No indication of DNA damage or changes in cell cycle kinetics. SAR above limit	Inadequate temperature control
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Summary of issues with Karipidis *et al.* Table 1 investigating genotoxicity effects

- Table missing potential genotoxicity papers from collection of 107 papers that was reviewed by Karipidis *et al.*
 - Volkova *et al.* [103] who indicated fragmented DNA in spermatozoa was found
 - DNA repair inhibition Belyaev [67]
 - A paper from Pakhomova *et al.* [37] found combinative DNA damage effects with UV (this is very important since the skin will be exposed to both types of non-ionizing radiation in the real environment)
 - Potentially all Belyaev *et al.* papers that were classified in the gene expression table, which found chromatin/genome conformational changes. Refer to table 3 discussion for more information
- Inconsistent handling of chromatin condensation papers - Beneduci *et al.* was missed [52], if it is assumed this endpoint is a valid marker for genotoxicity.
- No mention of Manikowska *et al.* [101] who found aberrant metaphases and chromosome translocations. Translocations generate novel chromosomes and are often linked to aneuploidy and disorders like infertility and cancer. ⁵
- Missed or excluded important relevant papers available from Pubmed, EMF-Portal and ORSAA database that meet the Karipidis *et al.* criteria of >6 GHz and at levels that are at/or below ICNIRP occupational exposure limits. (red = statistically significant, green = protective and black = no significant effect), SAR = Specific Absorption Rate (W/kg) and PD = Power Density (W/m²)

- a. Karaca *et al.* (2001) The genotoxic effect of radiofrequency waves on mouse brain <http://link.springer.com/article/10.1007%2Fs11060-011-0644-z> (Micronuclei Induction) – 10.71GHz, SAR=0.725 W/kg, PD=84 W/m²
 - b. Kuma *et al.* (2012) Influence of electromagnetic fields on reproductive system of male rats <http://www.tandfonline.com/doi/full/10.3109/09553002.2013.741282> (Micronuclei Induction, No Chromosome Aberrations, Single Strand DNA Breaks) – 10 GHz, SAR=0.0098 W/kg, PD=146 mW/m²
 - c. Gapeev *et al.* (2011) Changes in the chromatin structure of lymphoid cells under the influence of low-intensity extremely high-frequency electromagnetic radiation against the background of inflammatory process <http://www.springer.com/physics/biophysics+%26+biological+physics/journal/11439> (Reduced DNA Damage) - 42.2GHz SAR=1.5W/kg, PD=1 W/m²
 - d. Figueiredo *et al.* Cytogenetic analysis of the effects of 2.5 and 10.5 GHz microwaves on human lymphocytes (2004) <http://www.scielo.br/pdf/gmb/v27n3/a24v27n3.pdf> (No Chromosome Aberrations) - 10 GHz, SAR=0.25W/kg
 - e. Hansteen *et al.* (2008) Cytogenetic effects of 18.0 and 16.5 GHz microwave radiation on human lymphocytes in vitro <http://ar.iijournals.org/content/29/8/2885.full.pdf+html?sid=b49de261-f8b8-4b14-a472-f6700903b284> (Chromosome Aberrations) – 18GHz, PD=1W/m² and 16.5 GHz, PD=10 W/m²
 - f. Zotti-Martelli *et al.* (2000) Induction of micronuclei in human lymphocytes exposed in vitro to microwave radiation <http://www.sciencedirect.com/science/article/pii/S1383571800001121> (Micronuclei Induction @ higher power levels) – 7.7 GHz, PD=100 to 300 W/m²
 - g. Garaj-Vrhovac *et al.* (1990) The effect of microwave radiation on the cell genome <http://www.sciencedirect.com/science/article/pii/0165799290900281> (Chromosome Aberrations) - 7.7 GHz, PD=300 W/m²
 - h. Zowail *et al.* (2006) In vivo cytogenetic effect of 9.865 GHz microwave radiation and garlic radioprotection <https://www.researchgate.net/publication/237774152> In vivo cytogenetic effect of 9865 GHz microwave radiation and garlic radioprotection (Chromosome Aberrations) – 9.865 GHz, PD=“Low Dose”
 - i. Franchini *et al.* (2018) Study of the effects of 0.15 terahertz radiation on genome integrity of adult fibroblasts <https://pubmed.ncbi.nlm.nih.gov/29602275/> (Micronuclei Induction, No Double Strand DNA Breaks) -100 to 150 GHz, SAR=15-20 W/kg, PD=4 W/m²
 - j. Scarfi *et al.* (2003) <https://pubmed.ncbi.nlm.nih.gov/23345833/> THz exposure of whole blood for the study of biological effects on human lymphocytes (Micronuclei Induction) – 120 to 140 GHz, SAR= not provided, PD=not provided
5. Most studies listed by Karipidis are very short duration exposures (ranging from 1 second to typically 24 hours or less) so they give no insight into long term chronic exposure scenarios and associated genotoxic potential, or whether cell adaptive responses/repair mechanisms are masking damage caused by RF exposure in the short term.
 6. A number of research papers found associations between exposure and chromosome instability as well as loss (i.e., aneuploidy), they include: Korenstein-Ilan *et al.* [14], De Amicis *et al.* [18], Franchini *et al.* [19] and Manikowska *et al.* [101]. It is important that reviews of experimental studies are not performed in isolation. Epidemiological evidence also needs to be considered. Aneuploidy is associated with adverse pregnancy outcomes and congenital defects⁴. Congenital anomalies were indicated by Mageroy *et al.* [146], along with increased perinatal mortality in a study by Baste *et*

al. [147]. Both of these epidemiological studies were reviewed by Karipidis. However, this potential converging evidence was not elaborated by Karipidis in their review.

7. Karipidis claimed “Overall, there was no confirmed evidence of MMWs causing genotoxic damage in epithelial and skin cells.” This is a misleading statement because there is evidence for genotoxicity in skin cells with De Amicis *et al.* [18] and Franchini *et al.* [19] who found statistically significant CREST-positive micronuclei induction in fibroblast cells i.e., skin cells. Also, there was another relevant study available from Franchini *et al.* (ORSAA paper id 4037) that was not selected by Karipidis for inclusion in their review, showing DNA damage (micronuclei) in dermal fibroblasts. Bias is clearly present in Karipidis discussion of other types of cell genotoxicity, more specifically, genotoxicity in blood cells (lymphocytes), where Karipidis only mentioning a no effect paper from Zeni [31] and 2 Russian papers showing a radio protective effect against X-rays [32] and [33]. Blood will be exposed to MMW and the balance of evidence demonstrates a strong case for genotoxicity. Examples where statistically significant genotoxicity was found in blood lymphocytes include research conducted by Garaj-Vrhovac *et al.* [13] and [149], Kumar *et al.* [25] as well as relevant papers missed by Karipidis that include Kumar *et al.* (ORSAA paper id 682), Hansteen *et al.* (ORSAA paper id 2052) and Zotti-Martelli *et al.* (ORSAA paper id 2315). There was also no real consideration by Karipidis in their genotoxicity summary for discussing DNA damage being observed in other cell types including brain tissue – Paulraj *et al.* [23], Kesari *et al.* [24] and Karaca *et al.* (ORSAA paper id 500), with the Karaca paper missed in Karipidis list. The observation of brain DNA damage could potentially explain why some epidemiological studies reviewed by Karipidis found an increase in brain tumours in exposed personnel Degraeve *et al.* [124], Grayson *et al.* [131] and potentially in infantrymen Santana *et al.* [132]. Sperm DNA damage was also not discussed by Karipidis however there are very few studies directly investigating >6 GHz radiofrequency radiation and sperm genotoxicity. We only identified Volkova *et al.* [103] and Kumar *et al.* (ORSAA paper id 682) as investigating this important endpoint and both finding DNA damage.
8. The final statement made by Karipidis for this section was “Overall, these studies had no independent replication” in relation to a number of studies showing genotoxicity in animal models. The fact that some of the studies show DNA damage and have not been independently replicated, does not mean they should simply be ignored. They all contribute to the balance of evidence and their findings constitute a potential health risk. Furthermore, different research groups, exposing different species are finding similar DNA damage (chromosome aberrations and micronuclei) across similar cell types – this is an example of converging evidence and so needs to be taken far more seriously than the Karipidis’ overly dismissive and biased assessment. Our assessment suggests genotoxicity is a probable risk factor for > 6GHz RF exposures, with reactive oxygen (ROS) formation from RF exposures being a possible mechanism for causing such damage. Further research is required to confirm the link.

Table 2 Experimental studies investigating low-level RF fields above 6 GHz and proliferation.

Issues with Karipidis <i>et al.</i> Classification/Interpretation/Data	Our Finding	Reference	Biological System	Frequency Range	Intensity	Exposure Duration	Results [Claimed]	Quality Issue [Claimed]
<p>Frequency Range Observation - There were 2 types of RF transmitters used. One provided a frequency range of 40 to 90 GHz and another generator producing a specific 53.534 GHz frequency.</p> <p>Comment Only - There was a reduction in cell density that was borderline significant $p = 0.051$ at $100\text{W}/\text{m}^2$ which is set at ICNIRP occupational limits.</p> <p>Findings Not Reported - Morphological changes with cell vacuolation was not mentioned. The degree of cytoplasm vacuolization increased with a corresponding increase in the MMW dose. Vacuoles play a major role in autophagy, maintaining a</p>	<p>Reduced cell viability at $100\text{W}/\text{m}^2$ ($P=0.051$), No significant cell proliferation changes at lower intensity and at levels above the ICNIRP occupational limits.</p> <p>Increased cell cytoplasm vacuolization and morphological changes seen</p>	[56] Badzhinyan <i>et al.</i>	Cells in culture	40-90 GHz	0.5-1000 W/m^2	8 min	No change in cell survival at exposure levels below the limits	Inadequate dosimetry and temperature control

Issues with Karipidis <i>et al.</i> Classification/Interpretation/Data	Our Finding	Reference	Biological System	Frequency Range	Intensity	Exposure Duration	Results [Claimed]	Quality Issue [Claimed]
balance between biogenesis (production) and degradation (or turnover) of many substances and cell structures in certain organisms. Transient vacuoles can be associated with osmotic pressure equilibration when water diffusion occurs across the cell membrane as a result of disturbed ionic balance. This action therefore could be an indicator of membrane effects. In contrast to transient vacuolization, irreversible vacuolization marks cytopathological conditions leading to cell death i.e., apoptosis. Shubin <i>et al.</i> ⁶ Funding – Not declared.								
Frequency Range Observation – Karipidis frequency range designation does not provide insight into the fact that there were a number of different frequencies used. A wideband signal that spanned 53.57 to 78.33 GHz and then discreet frequencies of 51.05 GHz and 65.00 GHz. Funding – Lega Italiana per la Lotta Contro i Tumori-LILT-Sezione Cosenza (Public not for profit).	Reduced proliferation of tumour cells and cell morphological changes	[51] Beneduci <i>et al.</i>	Cells in culture	53-78 GHz	1 μ W, 44-46mW	1-3 h/day for 5-10 days	Reduced cancer cell proliferation and changes in cell morphology	Inadequate dosimetry and temperature Control
Incorrect Reference Number – The actual bibliography reference number should have been [52] as there is another reference to [53] in the same list of studies presented in this table. Findings Not Reported – There was no mention of chromatid condensation or cell membrane effects (significant surface microvilli reduction) by Karipidis. The papers authors also state “All these findings represent distinctive features of a damaged cell system.” Frequency Range Observation – A wideband signal that spanned 53.57 to 78.33 GHz was used. Funding – Lega Italiana per la Lotta Contro i Tumori-LILT-Sezione Cosenza (Public not for profit).	Reduced proliferation of tumour cells, morphological and ultra-structural changes, Increased number of vesicles, chromatin condensation and membrane surface microvilli reduction. No effect on mitochondria size or morphology.	[53] Beneduci <i>et al.</i>	Cells in culture	53-78 GHz	0.0007 W/m ²	1-3 h/day for 5-10 days	Reduced cancer cell proliferation and changes in cell morphology	Inadequate dosimetry and temperature control
Findings Not Reported and Misclassified – Authors stated “It should be noted that there was no significant difference in the number of dead cells between the two samples.” So, this means that cell viability is not impacted but rather the irradiated sample had reduced proliferation. Karipidis also did not mention significant metabolic changes (increased glucose consumption). Frequency Range Observation – A wideband signal that spanned 53.57 to 78.33 GHz was used. Funding – Lega Italiana per la Lotta Contro i Tumori-LILT-Sezione Cosenza (Public not for profit).	Reduced proliferation of tumour cells, morphological changes, increased number of vesicles and mitochondria, increased glucose consumption. No significant changes in lactate synthesis, No effect on cell viability	[54] Beneduci <i>et al.</i>	Cells in culture	53-78 GHz	0.01 W/m ²	1 h/day for 4 days	Reduction in viable cancer cells and changes in cell structural morphology	Inadequate dosimetry and temperature control
Frequency Range Observation – The frequencies used by Beneduci <i>et al.</i> are not a range but two discreet frequencies, i.e., 42.20 and 53.57 GHz. Incorrect Intensity Range – Karipidis has mixed up the intensity values. Firstly, they are not a range but two discreet values, one for each exposure frequency. Karipidis has specified for the lower value the transmitted power density (TDP), which was 1.1 W/m ² . Karipidis then used the Incident Power Density (IDP) for the second frequency, which was 3.7 W/m ² . The TDP for 42.20 GHz was 1.1 W/m ² and for 53.57 GHz it was 2.6 W/m ² . The IDP for 42.20 GHz was 1.4 W/m ² .	No significant cancer cell proliferation changes	[53] Beneduci	Cells in culture	42-54 GHz	1.1-3.7 W/m ²	1 h/day for 4 days	No evidence of anti-proliferation effects in exposed cancer cells	Inadequate dosimetry and poor temperature control

Issues with Karipidis <i>et al.</i> Classification/Interpretation/Data	Our Finding	Reference	Biological System	Frequency Range	Intensity	Exposure Duration	Results [Claimed]	Quality Issue [Claimed]
<p>Comment Only – There was evidence of increased and decreased proliferation depending on the exposure duration and specific frequency, but in all cases, did not reach statistical significance.</p> <p>Funding – Regione Calabria (Government) and Lega Italiana per la Lotta Contro i Tumori-LILT-Sezione Cosenza (Public not for profit).</p>								
<p>Frequency Range Observation – Actual range is 53.57 to 78.33 GHz. Sometimes Karipidis rounds up when the fraction is greater than 0.5 GHz, while other times rounding is not applied. Inconsistent rounding has been applied in this instance.</p> <p>Comment Only – We contacted the author and he confirmed that the symbols in the caption of Figure 3 had been incorrectly inverted. Thus, the squares are supposed to refer to the control samples while the circles represent the exposed samples, therefore the findings presented in the abstract and discussion are correct. Tumour cell proliferation is reduced but a non-significant increase is seen in normal cells. There were also profound morphological changes of the cell membrane in MCF-7 (breast cancer cell line) and K562 (a human erythroleukemic cell line) cells.</p> <p>Funding – Lega Italiana per la Lotta Contro i Tumori-LILT-Sezione Cosenza (Public not for profit).</p>	Reduced tumour cell proliferation, membrane morphological changes, tumour growth suppression. No significant cell proliferation changes seen in healthy cells	[50] Chidichimo et al.	Cells in culture	53-78 GHz	7×10^{-4} W/m ²	1 h/day for 12 days	Unclear results due to the in text results not matching supporting conclusions	Poor temperature control and no blinding
<p>Comment Only – In regards to Karipidis claim of SAR being above the limit, the temperature did not go up by more than 0.5 degrees. The PD is within the limits.</p> <p>Incorrect Biological System – No Yeast were used in the experiment. Escherichia coli (E. coli) Bacteria were exposed.</p> <p>Funding – Not declared.</p>	No significant changes in metabolic activity, cell proliferation or cell viability	[38] Cohen et al.	Bacteria & Yeast	99 GHz	2 W/m ²	1-19 h	No statistically significant changes in cell proliferation or survival. SAR above limit	No blinding
<p>Frequency Range Observation – Three separate frequency ranges were used, namely, 41.65 to 41.658 GHz, 41.694 to 41.702 GHz and 41.776 to 41.788 GHz.</p> <p>Misstatement – Furia <i>et al.</i> state “except for some experiments at some of the frequencies at which $0.01 < P < 0.05$. This, however, never occurred for more than half of the total number of experiments done at each frequency.” This suggests there were changes observed and so does not align with Karipidis claim of “no change”.</p> <p>Comment Only – Authors suggested “no effect” was seen in cell growth. However, it is not so clear-cut as the authors have suggested in their conclusion due to some interesting statistically significant findings. The growth rate varied between exposure frequencies. In some cases, there were weak proliferative effects, in other cases there were weak anti proliferative effects. No details of SAR or PD were provided.</p> <p>Incorrect Biological System – No Bacteria were exposed. Saccharomyces Cerevisiae Cells i.e., Yeast which are fungi.</p> <p>Funding – United States Air Force (Military).</p>	Cell proliferation changes were seen, both increases and decreases depending on frequency. However, the results showed inconsistency and need to be interpreted with care	[48] Furia et al.	Bacteria & Yeast	42 GHz	Up to 0.08W	Up to 4 h	No change in cell proliferation or viability	No blinding

Issues with Karipidis <i>et al.</i> Classification/Interpretation/Data	Our Finding	Reference	Biological System	Frequency Range	Intensity	Exposure Duration	Results [Claimed]	Quality Issue [Claimed]
<p>Frequency Range Observation - Although the frequency range 40 to 43 GHz was mentioned, it was not tested. There was also mention of 40 to 45 GHz which was the capability of the signal generator. The specific frequencies used were as follows: 41.682 to 41.710 GHz and 41.698 GHz.</p> <p>Incorrect Exposure Time - There was no 2-hour exposure specified, only a 5.5-hour exposure.</p> <p>Misstatement and Important Note - Karipidis claimed "no change in cell proliferation". Gos <i>et al.</i> used non-synchronised cells in G1 and S Phase. Similar to Furia <i>et al.</i> study [48], significant cell proliferation differences were found but were dismissed as being likely due to "random variation" suggesting possible confirmation biases. Different <i>S. cerevisiae</i> strains were used compared to studies by Grundler and Keilmann [46] and [47] who found growth effects. Given the differences in a number of parameters it cannot be considered as a replication study of Grundler and Keilmann (Refer to paper by Belyaev, Shcheglov <i>et al.</i>⁷ for further details).</p> <p>Incorrect Biological System - No Bacteria were exposed. Saccharomyces Cerevisiae Cells i.e., Yeast which are fungi.</p> <p>Funding - Deutsche Bundespost Telekom and Swiss PTT (Industry).</p>	Cell proliferation changes, both increases and decreases seen depending on frequency. Results showed inconsistency and need to be interpreted with care	[49] Gos <i>et al.</i>	Bacteria & yeast	40-43 GHz	0.005-0.5 W/m ²	2 and 5.5 h	No changes in cell proliferation	Inadequate sham control and no blinding
<p>Incorrect Biological System - No Bacteria were exposed. Saccharomyces Cerevisiae Cells i.e., Yeast which are fungi.</p> <p>Intensity Observation - Up to a maximum of 40 mW exposure was used. One experiment used different (lower) exposure intensities with a fixed frequency of 41.782 GHz.</p> <p>Funding - Deutsche Forschungsgemeinschaft (Government).</p>	Increased and decreased cell growth rate dependent on the frequency (frequency windows/resonance effect)	[47] Grundler and Keilmann	Bacteria & Yeast	42 GHz	40mW	NS	Enhanced and inhibited rates of cell proliferation	Inadequate dosimetry, statistical analysis not described
<p>Incorrect Biological System - No Bacteria were exposed. Saccharomyces Cerevisiae Cells i.e., Yeast which are fungi.</p> <p>Frequency Range Observation - 41.412 to 41.70 GHz was the frequency range used.</p> <p>Comment Only - Cells were synchronised. Growth rate was both positive and negative depending on the frequency. It was noted that there was a lag of 3-4 hours before cell division was recorded.</p> <p>Funding - Not declared.</p>	Increased and decreased cell growth rate dependent on the frequency (frequency windows/resonance effect)	[46] Grundler and Keilmann	Bacteria & Yeast	42 GHz	1-20 W/m ²	Up to 12 h	Enhanced and inhibited rates of cell proliferation	Inadequate sham control and no blinding
<p>Incorrect Biological System - No Yeast were used in the experiment. Enterococcus hirae bacteria were exposed.</p> <p>Frequency Range Observation - A set of discreet frequencies were used rather than a range that is being suggested by Karipidis, namely 51.8 and 53.0 GHz.</p> <p>Funding - State Committee of Science, Ministry of Education and Science of Armenia (Government).</p>	Inhibited cell growth, cell morphological changes, evidence for frequency windows and possible resonance effect, intracellular hydration (membrane effect)	[45] Hovnanyan <i>et al.</i>	Bacteria & Yeast	51-53 GHz	0.6 W/m ²	Up to 2 h	Increase in cell diameter and inhibition of cell growth	Inadequate dosimetry and temperature control

Issues with Karipidis <i>et al.</i> Classification/Interpretation/Data	Our Finding	Reference	Biological System	Frequency Range	Intensity	Exposure Duration	Results [Claimed]	Quality Issue [Claimed]
<p>Incorrect Biological System - No Bacteria were exposed. Saccharomyces Cerevisiae Cells i.e., Yeast which are fungi.</p> <p>Frequency Range Observation - There was no 62 GHz frequency used. The specific frequencies were 61.02 to 61.42 GHz.</p> <p>Misstatement - SAR was not specified in this study. Additionally, there was a combinative effect with UV exposure for chromosome alterations, gene conversions and an increase but not statistically significant gene crossovers. Karipidis should have also included this study in the genotoxicity table (table 1).</p> <p>Funding - United States Army Medical Research and Materiel Command (Military) and National Research Council (Government).</p>	Combinative/synergistic effect with UV that included chromosome alterations, gene conversions and non-significant increase in gene cross overs. No effect on cell viability	[37] Pakhomova et al.	Bacteria & Yeast	61-62 GHz	1.3 W/m ²	30 min	MMW pre-exposure did not change cell survival or alter the frequency of mutations. SAR above limit	Inadequate temperature control
<p>Incorrect Exposure Time - One experiment used a 90 minute exposure and the UV/mm wave experiments were 30 minute exposures.</p> <p>Incorrect Biological System - No Yeast were used in the experiment. Escherichia coli (E. coli) Bacteria were exposed.</p> <p>Comment Only - SAR was 83 W/kg however the PD, which is the recommended method for >6 GHz, is well within the limits. A temperature control (Sham exposure) was also used and demonstrated effects were non-thermal in nature.</p> <p>Comment Only - A 4 GHz wideband signal was used.</p> <p>Funding - Richard J. Fox Foundation (Public not for profit).</p>	No effect on growth from MMW exposure alone. Improved cell viability (protective effect) when UV exposure is followed by EMF exposure	[36] Rojavin and Ziskin	Bacteria & Yeast	61 GHz	10 W/m ²	Up to 1 h	Increase in cell survival if MMW exposure occurred after UVC exposure. No effect of MMW exposure alone. SAR above limit	No blinding
<p>Misstatement - Karipidis states "no change in neurite outgrowth". However, changes were observed. In one experiment they were significant but were attributed to a thermal effect. The results were inconsistent particularly with the thermal control @38°C (third experiment compared to other two). There were statistical differences seen between exposed and sham but they were attributed to thermal actions rather than non-thermal effects.</p> <p>Informative Comment - Left hand circular polarised and linear polarised signals were used (independent experiments). Belyaev <i>et al.</i>⁷ found that it depends on the specific frequency as to whether a L or R circular polarised signal has a biological effect.</p> <p>Funding - Ministry of Internal Affairs and Communications (Government Communications dept.).</p>	Increased neurite growth was seen but attributed by Shiina <i>et al.</i> to temperature increase of medium. Results were inconsistent and need to be interpreted with care	[57] Shiina et al.	Neural activity	60 GHz	10 W/m ²	24 h	No change in neurite outgrowth	No blinding
<p>Frequency Range Observation - Two distinct frequencies were used, namely 51.8 and 53 GHz, not a range as implied by Karipidis designation.</p> <p>Incorrect Biological System - No Yeast were used in the experiment. Lactobacillus acidophilus bacteria were exposed.</p> <p>Funding - Ministry of Education and Science of Armenia (Government).</p>	Cell proliferation inhibited, reduced cell viability, ion transport changes across cell membrane (membrane effect), anti-microbial effect and reduced colony forming effect. non-significant synergistic/combinative effect with ceftazidime (antibiotic)	[44] Soghomonyan and Trchounian	Bacteria & Yeast	51-53 GHz	0.6 W/m ²	1 h	Changes in ion transport across the membrane and an inhibitory effect on bacteria proliferation and survival	Inadequate dosimetry and no blinding

Issues with Karipidis <i>et al.</i> Classification/Interpretation/Data	Our Finding	Reference	Biological System	Frequency Range	Intensity	Exposure Duration	Results [Claimed]	Quality Issue [Claimed]
<p>Frequency Range Observation - Two distinct frequencies were used, namely 51.8 and 53 GHz, not a range as implied by Karipidis designation.</p> <p>Incomplete Results - Karipidis neglected to mention statistically significant effects such as metabolic effects (decrease in DDCCD-inhibited ATPase activity), resonance frequency effects, increased lag phase (cell cycle effects) and combinative effects with antibiotics (growth inhibition).</p> <p>Incorrect Biological System - No Yeast were used in the experiment. Escherichia coli (E. coli) bacteria were exposed.</p> <p>Funding - Ministry of Education and Science (Government).</p>	Cell proliferation inhibited, combinative effect with antibiotics, reduced cell viability, H ⁺ efflux (membrane effects), ion transportation changes, altered enzyme activity (ATPase activity reduced), increased lag phase duration (cell cycle effects). frequency window/resonance effect	[39] Tadevosyan et al.	Bacteria & Yeast	51-53 GHz	0.6 W/m ²	Up to 1 h	Changes in ion transport across the membrane and an inhibitory effect on bacteria proliferation	Inadequate dosimetry and temperature control
<p>Frequency Range Observation - Two distinct frequencies were used, namely 70.6 and 73 GHz, not a range as implied by Karipidis designation.</p> <p>Incorrect Biological System - No Yeast were used in the experiment. Escherichia coli (E. coli) bacteria were exposed.</p> <p>Incomplete Results - Karipidis neglected to mention statistically significant increased lag phase duration (cell cycle effects), resonance frequency effects and bactericidal effects.</p> <p>Funding - Ministry of Education and Science (Government).</p>	Cell proliferation inhibited, increased lag phase duration (cell cycle effects), bactericidal effect, changes in the number of accessible sulfhydryl (SH) groups of membrane vesicles (membrane effects), frequency window/resonance effect	[40] Torgomyan and Trchounian	Bacteria & Yeast	70-73 GHz	0.6 W/m ²	Up to 1 h	Inhibition of proliferation and changes in membrane proteins	Inadequate dosimetry and temperature control
<p>Frequency Range Observation - Two distinct frequencies were used, namely 70.6 and 73 GHz, not a range as implied by Karipidis designation.</p> <p>Incorrect Biological System - No Yeast were used in the experiment. Escherichia coli (E. coli) bacteria were exposed.</p> <p>Incomplete Results - Karipidis neglected to mention statistically significant reduced colony forming and bactericidal effects.</p> <p>Funding - Ministry of Education and Science (Government).</p>	Cell proliferation inhibited, bactericidal, colony forming reduced, altered optical density and absorption characteristics of water, increased conductivity of water, changes in pH level	[41] Torgomyan et al.	Bacteria & Yeast	70-73 GHz	0.6 W/m ²	Up to 2 h	Effect on bacterial growth and surrounding water medium	Inadequate dosimetry and temperature control
<p>Frequency Range Observation - four distinct frequencies were used, namely 51.8, 53.0, 70.6 and 73 GHz, not a range as implied by Karipidis designation.</p> <p>Incorrect Biological System - No Yeast were used in the experiment. Escherichia coli (E. coli) bacteria were exposed.</p> <p>Incomplete Results - Karipidis failed to mention statistically significant redox/biochemical changes were also observed along with cell structural changes, reduced colony forming and membrane permeability changes.</p> <p>Funding - Ministry of Education and Science (Government).</p>	Cell proliferation inhibited, increased lag phase duration (cell cycle effects), reduced colony forming, cell structural and size changes, pH Level changes, biochemical changes, redox potential changes, increased cytoplasm vacuolization, membrane permeability changes (membrane effects)	[42] Torgomyan et al.	Bacteria & Yeast	51-73 GHz	0.6 W/m ²	1 h	Enhanced inhibitory effect of antibiotics on bacterial proliferation. Changes in ion transport	Inadequate dosimetry and temperature control

Issues with Karipidis <i>et al.</i> Classification/Interpretation/Data	Our Finding	Reference	Biological System	Frequency Range	Intensity	Exposure Duration	Results [Claimed]	Quality Issue [Claimed]
<p>Frequency Range Observation - Two distinct frequencies were used, namely 51.8 and 53 GHz, not a range as implied by Karipidis designation.</p> <p>Incorrect Biological System - No Yeast were used in the experiment. Enterococcus hirae bacteria were exposed.</p> <p>Incomplete Results - Karipidis failed to mention statistically significant cell membrane effects, increased lag phase duration (cell cycle effects) and combinative effect with antibiotics.</p> <p>Funding - Ministry of Education and Science and Armenian National Science and Education Fund (Government).</p>	K and H ⁺ ion flux changes, membrane ion transport changes, reduced ATPase activity, inhibited cell proliferation, increased lag phase duration (cell cycle effects), combinative effect with antibiotics	[43] Torgomyan et al.	Bacteria & Yeast	51-53 GHz	0.6 W/m ²	1 h	Changes in the bacterial proliferation and survival. Changes in ion transport	Inadequate dosimetry and temperature control
<p>Incorrect Reference Number - The actual bibliography reference number should have been [35] to match the frequency tested.</p> <p>Incorrect Biological System - No Yeast were used in the experiment. Escherichia coli (E. coli) bacteria were exposed.</p> <p>Incomplete Results - Karipidis neglected to mention metabolic effects, protein synthesis effects and amino acid uptake. They also failed to mention that viability was not impacted.</p> <p>Funding - Not declared.</p>	Growth changes (inhibition and stimulation), metabolic effects, changes in protein synthesis and amino acid uptake, No effect on viability	[34] Webb and Booth	Bacteria & Yeast	65-75 GHz	NS	NS	Inhibition and stimulation of bacterial growth at specific frequencies	No details on dosimetry and no blinding
<p>Incorrect Reference Number - The actual bibliography reference number should have been [34] to match the frequency tested.</p> <p>Incorrect Biological System - No Yeast were used in the experiment. Escherichia coli (E. coli) bacteria were exposed.</p> <p>Misstatement - Stimulation of growth is being overstated by Karipidis in the result column. There was one time period in the lag phase where growth was slightly (non-significant) higher but all other times exposures saw reduced growth.</p> <p>Incomplete Results - Karipidis neglected to mention cell viability was not impacted.</p> <p>Funding - Not declared.</p>	Reduced cell growth. No effect on viability	[35] Webb and Dodds	Bacteria & Yeast	136 GHz	7×10 ⁻⁶ W/m ²	Up to 4 h	Inhibition and stimulation of bacterial growth at specific frequencies	No details on dosimetry and no blinding
<p>Funding - Japanese Ministry of Internal Affairs and Communications (Government communications dept.).</p>	No significant changes in cell proliferation, cell viability or cell activity	[55] Yaekashiwa et al.	Cells in culture	70-300 GHz	Up to 0.0127 W/m ²	3-94 h	No change in proliferation, cell activity or cytotoxicity	No blinding

Summary of issues with Karipidis Table 2 investigating cell proliferation effects

- Given that some of the end points discussed by Karipidis in this table relate to cell viability, it would have been more appropriate to label the table "cell proliferation and viability effects".
- Table was missing potential cell proliferation/viability papers from the collection of 107 papers reviewed by Karipidis and include:
 - Bellossi [117] – RF exposure was shown to enhance tumour growth (synchronised Lewis cells)
 - Belyaev [70] – Observed growth changes depending on the frequency and RF signal polarisation type
 - Crouzier [26] – Measured yeast vitality at different RF power levels. Given the vitality was higher in some exposure scenarios compared with non-exposed, this provides evidence of increased proliferation and/or improved viability
 - Gapeyev [111] – Investigated exposure of tumour bearing mice and found inhibited cell proliferation

- e. Garaj-Vrhovac [12] – Investigated colony forming ability of Hamster fibroblast (skin) cells which saw reduced cell viability
 - f. Hintzsche [15] – Investigated effects of THz radiation on skin cell proliferation
 - g. Volkova [103] – Investigated RF exposures and sperm viability and thus could have been a candidate for inclusion for consistency with other papers investigating viability that were presented in the table
 - h. Zhadobov [61] – Exposed different types of cancer cells investigating the effect of RF on viability and so could have been a candidate for inclusion
3. Important findings were not always stated in the results column for a number of papers and have been identified with the label “Findings Not Reported”. Some of these effects provide evidence of the damaging effects of RF exposures and can be possibly used to clarify why cell proliferation and/or viability are impacted.
4. Missed or excluded important relevant proliferation papers available from PubMed, EMF-Portal and ORSAA database that meet the Karipidis *et al.* criteria of >6 GHz and at or below ICNIRP occupational exposure limits. (red = statistically significant, green = protective and black = no significant effect), SAR = Specific Absorption Rate (W/kg) and PD = Power Density (W/m²)
- a. Paulraj *et al.* (2012) Enzymatic alterations in developing rat brain cells exposed to a low-intensity 16.5 GHz microwave radiation <http://www.tandfonline.com/doi/full/10.3109/15368378.2012.700295> (Glial Cell Proliferation) - 16.5 GHz, SAR=2.01 W/kg, PD=10 W/m²
 - b. Mezhevikina *et al.* (2000) The simulation of the cooperative effect of development in a culture of early mouse embryos after irradiation with electromagnetic waves in the millimeter range <https://link.springer.com/article/10.1007/BF02758751> (Growth Stimulation – 30 minute exposure, Growth Inhibition – 24 hour exposure) - 54 to 78 GHz, PD=0.6 W/m²
 - c. Perez-Castejon *et al.* Exposure to ELF-pulse modulated X band microwaves increases in vitro human astrocytoma cell proliferation (2009) <http://europepmc.org/abstract/MED/19795354> (Increased Proliferation, No change to Viability) - 9.6 GHz, SAR=0.0004 W/kg
 - d. Wu *et al.* (2009) Experimental study of millimeter wave-induced differentiation of bone marrow mesenchymal stem cells into chondrocytes <https://www.spandidos-publications.com/10.3892/ijmm.00000152> (Cell Proliferation) - 30 to 40 GHz, PD=40 W/m²
 - e. Perera *et al.* (2018) Exposure to 18 GHz EMF triggers uptake of large nanosphere clusters by pheochromocytoma cells <https://www.dovepress.com/exposure-to-high-frequency-electromagnetic-field-triggers-rapid-uptake-peer-reviewed-article-IJN> (Cell Proliferation) - 18 GHz, SAR=1.17W/kg
 - f. Fesenko *et al.* (1999) Microwaves and cellular immunity. I. Effect of whole-body microwave irradiation on tumor necrosis factor production in mouse cells <https://www.sciencedirect.com/science/article/abs/pii/S0302459899000586> (Cell Proliferation) - 10 GHz, PD=0.01 W/m²
 - g. Novoselova *et al.* (1999) Microwaves and cellular immunity: II. Immunostimulating effects of microwaves and naturally occurring antioxidant nutrients <https://www.sciencedirect.com/science/article/abs/pii/S0302459899000598> (Reduced Cell Proliferation) - 8.15 to 18 GHz, PD=0.01 W/m²
 - h. Grundler *et al.* (1977) Resonant Growth-Rate Response of Yeast-Cells Irradiated by Weak Microwaves <https://www.sciencedirect.com/science/article/abs/pii/037596017790696X> (Cell Proliferation) – 41.412 to 41.898 GHz, PD=27 W/m²
 - i. Grundler *et al.* (1982) Resonant-Like Dependence of Yeast Growth-Rate on Microwave-Frequencies <https://pubmed.ncbi.nlm.nih.gov/7039651/> (Cell Proliferation) – 41.640 to 41.835 GHz, 6 – 34 mW

- j. Grundler et al. (1989) Resonant Microwave Effect on Locally Fixed Yeast Microcolonies <https://pubmed.ncbi.nlm.nih.gov/2686673/> (Cell Proliferation) – 41.776 to 41.788 GHz, PD=10 W/m²
 - k. Grundler et al. (1992) Mechanisms of electromagnetic interaction with cellular systems <https://link.springer.com/article/10.1007/BF01131411> (Cell Proliferation) – 41.7 GHz, SAR=0.04 W/kg, PD=10 W/m²
 - l. Grundler (1992) Intensity-Dependent and Frequency-Dependent Effects of Microwaves on Cell-Growth Rates <https://www.sciencedirect.com/science/article/pii/030245989287010R> (Cell Proliferation) – 41.685 to 41.705 GHz, SAR=0.04 W/kg, PD=10 W/m²
 - m. Webb (1975) Genetic Continuity and Metabolic-Regulation as Seen by Effects of Various Microwave and Black Light Frequencies on These Phenomena <https://pubmed.ncbi.nlm.nih.gov/1090232/> (Cell Proliferation) – 59.0 to 143 GHz, PD=100 to 500 W/m²
5. Missed or excluded important relevant cell viability papers available from PubMed, EMF-Portal and ORSAA database:
- a. Karaca *et al.* (2011) The genotoxic effect of radiofrequency waves on mouse brain <http://link.springer.com/article/10.1007%2Fs11060-011-0644-z> (Cell Loss via Apoptosis and Necrosis) - 10.175 GHz, SAR=0.725 W/kg, PD=84 W/m²
 - b. Figueiredo *et al.* (2004) Cytogenetic analysis of the effects of 2.5 and 10.5 GHz microwaves on human lymphocytes <http://www.scielo.br/pdf/gmb/v27n3/a24v27n3.pdf> (High Cell Mortality, High Rate of Cell Lysis) - 10.5 GHz, SAR=0.25 W/kg
 - c. Wu *et al.* (2011) Millimeter wave treatment inhibits the mitochondrion-dependent apoptosis pathway in chondrocytes (Reduced Apoptosis) - 30 to 40 GHz, PD=40 W/m²
 - d. Sharma *et al.* (2017) Ten gigahertz microwave radiation impairs spatial memory, enzymes activity, and histopathology of developing mice brain <https://link.springer.com/article/10.1007%2Fs11010-017-3051-8> (Purkinje Cell Loss, Pyramidal Cell Loss i.e., Reduced Viability) - 10 GHz, SAR=0.179 W/kg, PD=2.5 W/m²
6. A summary statement provided by Karipidis for this section “Overall, the results from studies on cell proliferation of bacterial cells have been inconsistent with different research groups reporting conflicting results.” Karipidis has taken an overly simplistic view by simply summarizing the studies and finding that the results are inconsistent. No attempt was made to understand the reasons behind the differing results. Many of the differences are explainable and relate to the following:
- a. Different frequencies used (no accounting by Karipidis for frequency windows or resonant frequencies) – the data provided by Karipidis suggests a frequency range or wideband is used in experimental studies when in reality many experiments use separate discreet frequencies. MHz differences can result in subtly different outcomes i.e., stimulating vs inhibiting effects
 - b. Different bacteria types and strains – DNA/genetic differences result in varying molecular weights and so will respond to different, but very specific resonant frequencies
 - c. Comparing yeast with bacteria – same as point b. above
 - d. Different exposure durations
 - e. Different methods for measuring changes
 - f. Different antenna models that produce different signals including left or right circular polarisation or linear polarisation etc.
7. When reviewing the relevant proliferation studies we note differing frequencies, intensities, cell types and exposure durations, and so it is not unexpected that results will differ. However, when considering all related studies from a research group, i.e., Beneduci *et al.* papers that use the same study protocol including frequency range and human cancer cells the outcome is consistent - reduced proliferation. To apply the same set

of frequencies to a bacterial cell and expect the same outcome is not reasonable. It is also important to recognise that the functional state of the organism/cell needs to be taken into consideration and can influence the outcome. Grundler *et al.* used synchronised cells while attempted replications by other scientists used different frequencies, different yeast strains and non-synchronised cells. Coupled together with these differences are exposure durations and intensity differences which can produce different results or no change.

Table 3 Experimental studies investigating low-level RF fields above 6 GHz and gene expression.

Issues with Karipidis <i>et al.</i> Classification/Interpretation/Data	Our Finding	Reference	Biological System	Frequency Range	Intensity	Exposure Duration	Results [Claimed]	Quality Issue [Claimed]
<p>Frequency Range Observation - The complete range between the specified frequencies was not tested. Instead, much narrower bands were tested and they were 41.25 to 41.50 and 51.62 to 51.84 GHz.</p> <p>Incorrect Biological System - No Yeast were used in the experiment. Escherichia coli (E. coli) bacteria were exposed.</p> <p>Incorrect Intensity Range - The maximum exposure should have been 30 W/m² (PD = 3 mW/cm² - refer to page 624).</p> <p>Incorrect Time Range - There was also an exposure for 30 minutes.</p> <p>Questionable Classification - The results are specified correctly but this cannot be confirmed to be an example of a gene expression study and so its inclusion in this table is questionable. Alternatively, if paper relevance is based on assumptions rather than direct tests, this paper could have also been potentially included as a genotoxicity paper given the AVTD method has been suggested by Belyaev <i>et al.</i> to have the sensitivity to detect single strand breaks (which cause genome conformational changes).</p> <p>Comment Only - AVTD depends strongly on the conformational state of the genome, which, in turn, is dependent on DNA parameters such as molecular weight and the number of proteins bound to the DNA. Belyaev <i>et al.</i> state "AVTD method is sensitive not only to damages of the sugar-phosphate bonds of the DNA secondary structure. The AVTD sensitivity to other changes of the genome conformation, particularly those caused by DNA-protein bonds". They are also state "Changes in the AVTD can be detected even with an X-ray dose of 10 cGy when less than one single-strand DNA break is induced per E. coli genome." Further discussion in relation to the relevance of this study, and related studies, for gene expression is provided in the summary table below.</p> <p>Nonsensical Quality Issue - Karipidis claimed a lack of temperature control and inadequate dosimetry as a quality deficiency. In all Belyaev <i>et al.</i> studies temperature was controlled with precision of 0.1°C. Incident and reflected PD along with its distribution over the exposed samples and SAR, where appropriate, was adequately measured and assessed.</p> <p>Funding - Not declared.</p>	<p>Frequency window effects, genome (DNA) conformational state changes, variations in repair of X-ray induced genome (DNA) conformational state changes, resonance effects</p>	<p>[64] Belyaev <i>et al.</i></p>	<p>Bacteria & Yeast</p>	<p>41-52 GHz</p>	<p>0.01-1 W/m²</p>	<p>5-10 min</p>	<p>Frequency dependant changes in DNA conformation based on AVTD method and changes in DNA repair</p>	<p>Inadequate dosimetry and temperature control</p>

Issues with Karipidis <i>et al.</i> Classification/Interpretation/Data	Our Finding	Reference	Biological System	Frequency Range	Intensity	Exposure Duration	Results [Claimed]	Quality Issue [Claimed]
<p>Frequency Range Observation - The complete range between the specified frequencies was not tested, much narrower bands were tested and they were 41.25 to 41.5 and 51.62 to 51.84 GHz.</p> <p>Incorrect Biological System - No Yeast were used in the experiment. Escherichia coli (E. coli) bacteria were exposed.</p> <p>Incorrect Intensity Range - The PD range specified is not accurate and should be 0.1 to 3.0 W/m².</p> <p>Incorrect Time Range - There was also an exposure for 30 minutes.</p> <p>Questionable Classification - The results are specified correctly but this cannot be confirmed to be an example of a gene expression study and so its inclusion in this table is questionable. (See above comment).</p> <p>Nonsensical Quality Issue - Karipidis claimed a lack of temperature control and inadequate dosimetry as a quality deficiency. In all Belyaev <i>et al.</i> studies temperature was controlled with precision of 0.1°C. Incident and reflected PD along with its distribution over the exposed samples and SAR, where appropriate, was adequately measured and assessed.</p> <p>Funding - Not declared.</p>	<p>Frequency window effects, genome (DNA) conformational state changes, variations in repair of X-ray induced genome (DNA) conformational state changes, resonance effects</p>	<p>[65] Belyaev <i>et al.</i></p>	<p>Bacteria & Yeast</p>	<p>52 GHz</p>	<p>1 W/m²</p>	<p>5-10 min</p>	<p>Frequency dependant changes in DNA conformation based on AVTD method and changes in DNA repair</p>	<p>Inadequate dosimetry and temperature control</p>
<p>Frequency Range Observation - The complete range between the specified frequencies was not tested, much narrower bands were tested and they were 41.25 to 41.5 and 51.62 to 51.84 GHz.</p> <p>Incorrect Biological System - No Yeast were used in the experiment. Escherichia coli (E. coli) bacteria were exposed.</p> <p>Questionable Classification - The results are specified correctly but this cannot be confirmed to be an example of a gene expression study and so its inclusion in this table is questionable. (See above comment - Row 1 of this table).</p> <p>Nonsensical Quality Issue - Karipidis claimed a lack of temperature control and inadequate dosimetry as a quality deficiency. In all Belyaev <i>et al.</i> studies temperature was controlled with precision of 0.1°C. Incident and reflected PD along with its distribution over the exposed samples and SAR, where appropriate, was adequately measured and assessed.</p> <p>Funding - Not declared.</p>	<p>Frequency window effects, genome (DNA) conformational state changes, variations in repair of X-ray induced genome (DNA) conformational state changes, resonance effects</p>	<p>[66] Belyaev <i>et al.</i></p>	<p>Bacteria & Yeast</p>	<p>41-52 GHz</p>	<p>0.01-3 W/m²</p>	<p>30 min</p>	<p>Frequency dependant changes in DNA conformation based on AVTD method and changes in DNA repair</p>	<p>Inadequate dosimetry and temperature control</p>
<p>Incorrect Frequency Range - The study did not conduct any exposures in the 42 GHz range. The actual range used was between 51.62 to 51.84 GHz.</p> <p>Incorrect Biological System - No Yeast were used in the experiment. Escherichia coli (E. coli) bacteria were exposed.</p> <p>Incorrect Intensity - A range of exposures was not used in this set of experiments. The intensity specified for all the exposures was 1 W/m². A reference intensity of 0.01 W/m² was provided for SAR estimation.</p> <p>Questionable Classification - The results are specified correctly but this cannot be confirmed to be an example of a gene expression study and so its inclusion in this table is questionable. (See above comment - Row 1 of this table).</p> <p>Nonsensical Quality Issue - Karipidis claimed a lack of temperature control and inadequate dosimetry as a quality deficiency. In all</p>	<p>Frequency window effects, genome (DNA) conformational state changes, variations in repair of X-ray induced genome (DNA) conformational state changes, resonance effects</p>	<p>[67] Belyaev <i>et al.</i></p>	<p>Bacteria & Yeast</p>	<p>41-52 GHz</p>	<p>0.1-1 W/m²</p>	<p>5-10 min</p>	<p>Frequency dependant changes in DNA conformation based on AVTD method and changes in DNA repair</p>	<p>Inadequate dosimetry and temperature control</p>

Issues with Karipidis <i>et al.</i> Classification/Interpretation/Data	Our Finding	Reference	Biological System	Frequency Range	Intensity	Exposure Duration	Results [Claimed]	Quality Issue [Claimed]
<p>Belyaev <i>et al.</i> studies temperature was controlled with precision of 0.1°C. Incident and reflected PD along with its distribution over the exposed samples and SAR, where appropriate, was adequately measured and assessed.</p> <p>Funding – Not declared.</p>								
<p>Frequency Range Observation – The complete range between the specified frequencies was not tested, much narrower bands were tested and they were 41.28 to 41.37 and 51.73 to 51.79 GHz.</p> <p>Incorrect Biological System – No Yeast were used in the experiment. Escherichia coli (E. coli) bacteria were exposed.</p> <p>Incorrect Intensity – There is a “-” missing in front of the exponent i.e., 10⁻¹⁶ not 10¹⁶.</p> <p>Misstatement – Karipidis stated in the result column “change in DNA repair”, however, there was no X-Ray exposure so changes in DNA repair were not tested.</p> <p>Questionable Classification – Most of the results are specified correctly but this cannot be confirmed to be an example of a gene expression study and so its inclusion in this table is questionable. (See above comment – Row 1 of this table).</p> <p>Nonsensical Quality Issue – Karipidis claim a lack of a thermal control as a quality deficiency. However, we question the relevance of a thermal control when the PD is so low, temperature changes would unlikely be measurable. Temperature was controlled with precision of 0.1°C and no measurable temperature changes were detected.</p> <p>Funding – Not declared.</p>	<p>Frequency window effects, genome (DNA) conformational state changes, resonance effects based on genome length</p>	<p>[68] Belyaev et al.</p>	<p>Bacteria & Yeast</p>	<p>41-52 GHz</p>	<p>10¹⁶ - 10⁻⁶ W/m²</p>	<p>10 min</p>	<p>Frequency dependant changes in DNA conformation based on AVTD method and changes in DNA repair</p>	<p>Inadequate dosimetry and temperature control</p>
<p>Frequency Range Observation – The complete range between the specified frequencies was not tested. two discrete frequencies were tested, namely 42.32 and 51.76 GHz.</p> <p>Incorrect Biological System – No Yeast were used in the experiment. Escherichia coli (E. coli) bacteria were exposed.</p> <p>Incorrect Intensity – A range of intensities was not used in the set of experiments. The intensity specified for all the exposures was 1 W/m².</p> <p>Informative Comment – This is the only study in the list of Belyaev <i>et al.</i> papers that specifically measures DNA-bound polypeptides before and after EMF exposure.</p> <p>Nonsensical Quality Issue – Karipidis claimed a lack of temperature control and inadequate dosimetry as a quality deficiency. In all Belyaev et al. studies temperature was controlled with precision of 0.1°C. Incident and reflected PD along with its distribution over the exposed samples and SAR, where appropriate, was adequately measured and assessed.</p> <p>Funding – Not declared.</p>	<p>Frequency window effects, genome (DNA) conformational state changes, variations in repair of X-ray induced genome (DNA) conformational state changes, changes in polypeptide density and resonance effects</p>	<p>[69] Belyaev et al.</p>	<p>Bacteria & Yeast</p>	<p>41-52 GHz</p>	<p>0.1-1 W W/m²</p>	<p>5 min</p>	<p>Frequency dependant changes in DNA conformation based on AVTD method and suppression of DNA repair</p>	<p>Inadequate dosimetry and temperature control</p>
<p>Frequency Range Observation – The frequency range was 41.56 to 41.67 GHz to be more precise.</p> <p>Questionable Classification – The results are specified correctly but this cannot be confirmed to be an example of a gene expression study and should probably not have been included in this table. Further discussion in relation to the relevance of this study, and</p>	<p>Frequency window effects, genome (DNA) conformational state changes, resonance effects</p>	<p>[71] Belyaev and Kravchenko</p>	<p>Cells in culture</p>	<p>41 GHz</p>	<p>10⁻⁷ - 1 W/m²</p>	<p>10 min</p>	<p>Frequency dependant changes in DNA conformation based on AVTD method. SAR above limit</p>	<p>Inadequate dosimetry and temperature control</p>

Issues with Karipidis <i>et al.</i> Classification/Interpretation/Data	Our Finding	Reference	Biological System	Frequency Range	Intensity	Exposure Duration	Results [Claimed]	Quality Issue [Claimed]
<p>related studies, for gene expression is provided in the summary table below.</p> <p>Misstatement - Karipidis. claimed SAR was above the limit. This is not correct. There was mention of a reference 5W/kg SAR in relation to 10 W/m² PD but the PD's used in this set of experiments were in the order of 10 to 10,000,000 times lower.</p> <p>Nonsensical Quality Issue - Karipidis claimed a lack of temperature control and inadequate dosimetry as a quality deficiency. In all Belyaev <i>et al.</i> studies temperature was controlled with precision of 0.1°C. Incident and reflected PD along with its distribution over the exposed samples and SAR, where appropriate, was adequately measured and assessed.</p> <p>Funding - Not declared.</p>								
<p>Incorrect Reference Number - The actual bibliography reference number should have been [70] as there is another reference to [72] in the same list of studies presented in the table. Reference [70] also matches the data provided by Karipidis. <i>et al.</i> for this entry.</p> <p>Incorrect Biological System - No Yeast were used in the experiment. Escherichia coli (E. coli) bacteria were exposed.</p> <p>Frequency Range Observation - The complete range between the specified frequencies was not tested. Instead, two specific discrete frequencies were used, namely 41.32 and 51.76 GHz.</p> <p>Questionable Classification - The results are specified correctly but this cannot be confirmed to be an example of a gene expression study and probably should not have been included in this table. Further discussion in relation to the relevance of this study, and related studies, for gene expression is provided in the summary table below.</p> <p>Nonsensical Quality Issue - Karipidis claimed a lack of temperature control and inadequate dosimetry as a quality deficiency. In all Belyaev <i>et al.</i> studies temperature was controlled with precision of 0.1°C. Incident and reflected PD along with its distribution over the exposed samples and SAR, where appropriate, was adequately measured and assessed.</p> <p>Funding - Not declared</p>	<p>Frequency window effects, genome (DNA) conformational state changes, resonance effects growth (proliferation) changes, cooperative reaction</p>	<p>[72] Belyaev et al.</p>	<p>Bacteria & Yeast</p>	<p>41-52 GHz</p>	<p>10⁻¹⁶ - 1 W/m²</p>	<p>10-50 min</p>	<p>Frequency dependant changes in DNA conformation based on AVTD method and changes in cell developmental dynamics</p>	<p>Inadequate dosimetry and temperature control</p>

Issues with Karipidis <i>et al.</i> Classification/Interpretation/Data	Our Finding	Reference	Biological System	Frequency Range	Intensity	Exposure Duration	Results [Claimed]	Quality Issue [Claimed]
<p>Frequency Range Observation - The frequency range was 51.64 to 51.85 GHz to be more precise.</p> <p>Incorrect Intensity - Units have not been converted correctly. The values provided by Belyaev <i>et al.</i> were in W/cm² and so need to be converted to W/m².</p> <p>Incorrect Biological System - No Yeast were used in the experiment. Escherichia coli (E. coli) bacteria were exposed.</p> <p>Questionable Classification - The results are specified correctly but this cannot be confirmed to be an example of a gene expression study and probably should not have been included in this table. Further discussion in relation to the relevance of this study, and related studies, for gene expression is provided in the summary table below.</p> <p>Nonsensical Quality Issue - Karipidis claimed a lack of temperature control and inadequate dosimetry as a quality deficiency. In all Belyaev <i>et al.</i> studies temperature was controlled with precision of 0.1°C. Incident and reflected PD along with its distribution over the exposed samples and SAR, where appropriate, was adequately measured and assessed.</p> <p>Funding - International Science Foundation and Russian Foundation for Fundamental Research (Government).</p>	<p>Genome (DNA) conformational state changes, resonance effects, window effects with power density, frequency and cell concentration dependency</p>	<p>[72] Belyaev <i>et al.</i></p>	<p>Bacteria & Yeast</p>	<p>52 GHz</p>	<p>10⁻¹⁹ - 0.003 W/m²</p>	<p>10 min</p>	<p>Frequency dependant changes in DNA conformation based on AVTD method</p>	<p>Inadequate dosimetry and temperature control</p>
<p>Frequency Range Observation - The complete range between the specified frequencies was not tested. The actual range tested was 38.0 to 48.0 GHz and 65.0 to 75.0 GHz.</p> <p>Misstatement - Karipidis claim of "No change in protein synthesis" cannot be readily confirmed. The way the data is presented makes it very difficult to do any kind of statistical analysis. There are clearly small changes given the plotted data is not a straight line, which can be best described as wavy lines so it is not correct to say there were no changes. There were subtle changes across the frequency range as demonstrated by the Optical Density differences but they did not appear to reach significance. A more accurate classification would have said no statistically significant changes were observed.</p> <p>Comment Only - Very high exposure levels with maximum average power densities for frequencies in each range (292 and 177 mW/cm², respectively.) This equates to 2,920 W/m² and 1,770 W/m². Environment was temperature controlled. Given these high exposure levels one does question why it was included? Perhaps because the edges of the exposed samples were at lower levels approaching zero?</p> <p>Comment Only - This is not a high-quality study and not very useful to be making judgements about gene expression/protein synthesis. It does not try to differentiate between different types of proteins that might be expressed. Experimental evidence in other more recent studies using real time PCR or Western Blot methods show gene expression can be increased for some proteins and decreased for other different proteins. This means looking at all (total) proteins pooled together may not show any significant differences.</p> <p>Funding - National Cancer Institute (Government) and Department of the Navy (Military).</p>	<p>No obvious frequency windows, power windows, no obvious athermal effects, no significant changes in protein synthesis/gene expression</p>	<p>[76] Bush <i>et al.</i></p>	<p>Cells in culture</p>	<p>38-75 GHz</p>	<p>Up to 5840 W/m²</p>	<p>15 min</p>	<p>No changes in protein synthesis and no resonance effects detected even at high exposure levels</p>	<p>Temperature control and dosimetry methods were not described</p>

Issues with Karipidis <i>et al.</i> Classification/Interpretation/Data	Our Finding	Reference	Biological System	Frequency Range	Intensity	Exposure Duration	Results [Claimed]	Quality Issue [Claimed]
<p>Comment Only – One needs to ask the question of whether exposure time is a parameter that enhances resonance effects? We believe it does as was demonstrated by Belyaev <i>et al.</i> [69] where a 10-minute exposure produced a greater effect than a 5-minute exposure. In the Gandhi <i>et al.</i> experiment the exposure duration (dwell time) for each frequency ranged from 5 milli-seconds to 5 seconds compared to Belyaev <i>et al.</i> who set their exposure times anywhere from 5 minutes to 50 minutes [69] and [70]. This is an apples and oranges comparison. It is also unlikely that significant optical density (O.D.) changes would be observed for such short exposures. O.D. is not only a measure for gene expression but also cell growth. It would be surprising to see a significant change in either growth or protein expression in such a short space of time. When it comes to gene expression, one needs to consider the timeframe varies between each activity relating to gene expression, starting with the signalling pathway activation, for the transcription factor to bind to the DNA and for transcription to initiate. Then there is process of exporting the mRNA to the cytosol where it will be processed by the endoplasmic reticulum and translated (on a Ribosome) to synthesize requisite proteins. Each of these steps requires many seconds to minutes to complete. In a similar vein to the study performed by Bush <i>et al.</i> [76], this is not a high-quality study and not useful to understand MMW effects on gene expression/protein synthesis.</p> <p>Funding – National Institute of Health (Government).</p>	<p>No significant absorbance spectra changes or frequency windows seen. Water absorbance</p>	<p>[75] Gandhi <i>et al.</i></p>	<p>Bacteria & Yeast</p>	<p>26.5-90.0 GHz</p>	<p>Up to 3000 W/m²</p>	<p>Up to 5 s</p>	<p>No resonance effects detected even at exposure levels above the limits</p>	<p>Statistical methods not described</p>
<p>Frequency Observation – Specific frequency of 60.4 GHz was used.</p> <p>Comment Only – No concerns with Karipidis classification or the experiment attributes. This is one of the few studies that are actually relevant to gene expression. The genes that were reported to have transient expression are:</p> <ol style="list-style-type: none"> 1. cysteine-rich protein 2 (CRIP2, t-test, P < 0.001 for a 6 h exposure), a zinc-binding protein involved in signalling, haematopoiesis, and cell proliferation; 2. Plexin D1 (PLXND1, t-test, P < 0.031 for a 6 h exposure), a transmembrane receptor involved in development; 3. Pentraxin-related gene (PTX3, t-test, P < 0.009 for a 6 h exposure), a protein involved in innate immunity and inflammatory response; 4. Serpin peptidase inhibitor (SERPINF1, t-test, P < 0.038 for a 6 h exposure), a secreted endopeptidase inhibitor that has anti-angiogenic and anti-proliferation functions; and 5. transient receptor potential cation channel (TRPV2, t-test, P < 0.001 for a 6 h exposure and P < 0.003 for a 24 h exposure), a calcium channel involved in sensory perception. <p>Funding – National Research Agency, Health and Radiofrequency Foundation, Centre National de la Recherche Scientifique and French Ministry of Higher Education and Research (Government).</p>	<p>Gene Expression changes 130 transcripts were potentially modulated by MMW. RT-PCR validation showed that only 5 genes out of the 24 tested were confirmed to be differentially expressed after a 6 h exposure. Namely CRIP2, PLXND1, PTX3, SERPINF1, TRPV2</p>	<p>[58] Le Quement <i>et al.</i></p>	<p>Cells in culture</p>	<p>60 GHz</p>	<p>18 W/m²</p>	<p>1-24 h</p>	<p>Five genes were reported to have transient expression changes after exposure. SAR above limit</p>	<p>No blinding, poor temperature control</p>
<p>Incorrect Reference Number – The actual bibliography reference number should have been [63]. When reviewing the experimental data and the reference numbers for [62] and [63], Karipidis has</p>	<p>For reference [63] – No significant secretion of alkaline phosphatase and</p>	<p>[62] Nicolaz <i>et al.</i></p>	<p>Cells in culture</p>	<p>60 GHz</p>	<p>1.4 W/m²</p>	<p>24-72 h</p>	<p>No change in ER homeostasis, protein folding,</p>	<p>No blinding</p>

Issues with Karipidis <i>et al.</i> Classification/Interpretation/Data	Our Finding	Reference	Biological System	Frequency Range	Intensity	Exposure Duration	Results [Claimed]	Quality Issue [Claimed]
<p>inadvertently reversed them so the experimental data no longer match the stated reference.</p> <p>Frequency Observation - Specific frequency of 60.4 GHz was used.</p> <p>Funding - Fondation Santé et Radiofréquences, which was set up as a partnership between French Government and Telecommunications Operators (Government and Industry).</p>	<p>luciferase secretions.</p> <p>There was no significant indication of endoplasmic reticulum stress. No significant changes in gene expression of BiP or HSP70</p>						secretions or transcription factors	
<p>Incorrect Reference Number - The actual bibliography reference number should have been [62]. When reviewing the experimental data and the reference numbers for [62] and [63], Karipidis has mixed them up so that the referenced papers do not match the experimental details.</p> <p>Frequency Range Observation - Specific discrete frequencies for [62] were used, namely 59.16, 59.87, 60.43, 60.83 and 61.15 GHz.</p> <p>Funding - French Agence Nationale de la Recherche (Government) and Fondation Santé et Radiofréquences, which was set up as a partnership between French Government and Telecommunications Operators (Government and Industry).</p>	<p>For reference [62] - No significant changes in gene expression of BiP, 150kDa oxygen-regulated protein (ORP150), HSP-70 or BiP/GRP78</p>	[63] Nicolaz et al.	Cells in culture	59-61 GHz	0.9-1.4 W/m ²	24 h.	No changes in mRNA expression of chaperone proteins. SAR above limit	No blinding
<p>Incorrect Biological System - No Yeast were used in the experiment. Escherichia coli (E. coli) bacteria were exposed.</p> <p>Frequency Range Observation - Specific discrete frequencies were used, namely 51.665 to 51.688 GHz and 51.755 GHz.</p> <p>Incorrect Intensity Range - Intensity range was 10⁻¹⁴ to 30 W/m²</p> <p>Questionable Classification - The results are specified correctly but this cannot be confirmed to be an example of a gene expression study and should probably not have been included in this table. Further discussion in relation to the relevance of this study, and related studies, for gene expression is provided in the summary table below.</p> <p>Comment Only - This study could have also been included in the Cell Signalling Table.</p> <p>Nonsensical Quality Issue - Temperature Control is not relevant particularly when authors state no temperature changes are detectable at PD <1/ W/m² and GCS effects were seen at much lower levels.</p> <p>Funding - Russian Foundation for Fundamental Research and International Science Foundation (Government).</p>	<p>Genome (DNA) conformational changes, resonance effect, left and right circular polarisation biological effect differences, window effects for power density, frequency and cell concentrations. cell-to-cell interaction implied by authors</p>	[73] Shcheglov et al.	Bacteria & Yeast	51 GHz	Up to 10 ⁻⁷ W/m ²	10 min	Frequency dependant changes in DNA conformation. Cell to cell communication reported to enhance this effect	Inadequate dosimetry and temperature control
<p>Frequency Observation - Specific frequency of 51.755 GHz was used.</p> <p>Questionable Classification - The results are specified correctly but this cannot be confirmed to be an example of a gene expression study and should probably not have been included in this table. Further discussion in relation to the relevance of this study, and related studies, for gene expression is provided in the summary table below.</p> <p>Comment Only - The study implied that cell-to-cell communication may have a role to play in the results but it was not formally tested and verified.</p> <p>Nonsensical Quality Issue - Karipidis claimed a lack of temperature control and inadequate dosimetry as a quality deficiency. In all Belyaev <i>et al.</i> studies temperature was controlled with precision of</p>	<p>Genome conformational changes and suggested intercellular communication</p>	[74] Shcheglov et al.	Bacteria & Yeast	52 GHz	10 ⁻¹⁴ - 10 W/m ²	Up to 10 min	Frequency dependant changes in DNA conformation. Cell to cell communication reported to enhance this effect	Inadequate dosimetry and temperature control

Issues with Karipidis <i>et al.</i> Classification/Interpretation/Data	Our Finding	Reference	Biological System	Frequency Range	Intensity	Exposure Duration	Results [Claimed]	Quality Issue [Claimed]
0.1°C. Incident and reflected PD along with its distribution over the exposed samples and SAR, where appropriate, was adequately measured and assessed. Funding – Russian Foundation for Fundamental Research and International Science Foundation (Government).								
Exposure Duration Clarification – Irradiation time was 1, 3, 6, 16 or 33 hours. Comment Only – It would have been more relevant and appropriate to use a skin cell rather than a brain cancer cell line. Cancer cell lines tend to be more resilient to potential environmental threats. Reporter genes were added by transfection using a plasmid to modify the cancer cell. Funding – Not declared.	No significant changes in reporter gene expression	[59] Zhadobov et al.	Cells in culture	60 GHz	2.7 W/m ²	1-33 h	No change in the expression of stress sensitive genes	Inadequate temperature control and no blinding
Intensity Observation – A range of intensities was not used in the set of experiments as suggested by Karipidis nomenclature. Two discreet intensities were used, namely 0.054 W/m ² and 5.4 W/m ² . Comment Only – It would have been more relevant and appropriate to use a skin cell rather than a brain cancer cell line. Cancer cell lines tend to be more resilient to potential environmental threats. Funding – Cancéropole Grand Ouest (Government).	No significant changes in mRNA accumulation and transcriptional activity for Heat Shock Protein 70 (HSP 70) or Clusterin (GLU)	[60] Zhadobov et al.	Cells in culture	60 GHz	0.054-5.4 W/m ²	1-33 h	No change in expression of chaperone proteins, heat shock proteins or reporting genes	No blinding
Frequency Observation – Specific frequency of 60.42 GHz was used. Funding – Agence Nationale de la Recherche (Government), National Institute of Health (US Government) and Fondation Santé et Radiofréquences, which was set up as a partnership between French Government and Telecommunications Operators (Government and Industry).	No significant changes in cell viability, gene expression or luciferase activity, No HSP70 expression changes for U251 cells, No significant changes in HSP70 expression for HaCaT cells, No significant changes in Immunoglobulin heavy-chain binding protein (BiP) in HaCaT cells	[61] Zhadobov et al.	Cells in culture	60 GHz	10 W/m ²	24 h	No change in protein conformation, gene expression, cell viability or cell growth. SAR above limit	Temperature control not described and no blinding

Summary of Issues with Karipidis *et al.* Table 3 gene expression

1. This section is potentially flawed and also incomplete. Karipidis has missed a number of relevant papers from the collection of 107 papers reviewed, with many showing statistically significant effects for gene expression.
 - a. De Amicis [18] – Found MMW exposure was not associated with gene expression changes for HSP stress proteins or apoptosis
 - b. Franchini [19] – Statistically significant increase in BCL2 gene expression in exposed skin cells
 - c. Koyama [16] – Investigated HSP27, HSP70 and HSP90 protein expression
 - d. Koyama [17] – Investigated HSP27, HSP70 and HSP90 protein expression
 - e. Lukashevsky [28] – MMW exposure was significantly associated with switching of prophage genes from the lysogenic to a lytic state

- f. Smolyanskaya [27] – Noted statistically significant increased colicin synthesis as a result of MMW exposure
 - g. Webb [35] – Demonstrated RF exposure frequency effects that resulted in growth, protein synthesis and amino acid uptake changes
2. Many papers are potentially misclassified and therefore probably should not have been included in this table i.e., most of Belyaev *et al.* papers are primarily focused on genome conformational state (GCS) changes and in a number of cases, X-ray induced GCS change and MMW induced GCS repair suppression. Some of Belyaev *et al.* papers do cover lysates which includes proteins that are bound to the DNA being evaluated but this is not necessarily directly related to gene expression changes. Some of these proteins are likely to be structural proteins that provide the scaffolding for “*maintaining the structural and functional integrity of chromosome DNA*” [64]. Of course, one cannot rule out the possibility that some of the proteins are also associated with gene transcription activities, DNA replication or even DNA repair. With the exception of one paper [69], there were no direct measurements taken to verify whether there were changes in protein levels and whether it was due to gene expression changes as a result of MMW exposure. Therefore, one cannot confidently assume they are all directly related to gene expression resulting exclusively from EMF exposure. Instead, they might only represent the functional state and phase of growth that the cells being investigated were currently in at the time of exposure.
3. In regards to Belyaev *et al.* papers, gene conformation can be altered by single and double strand DNA breaks suggesting a possible case for inclusion in the Genotoxicity table. A Belyaev *et al.* paper⁸ that was not included in the Karipidis *et al.* list of papers states “*It was found, that non-thermal levels of microwave exposure resulted with high efficiency in a transition of the plasmid from its supercoiled form into open circular and linear forms. This means that microwave radiation can produce breaks in single- and double-stranded DNA.*” This was in reference to a finding made by Sagripanti *et al.*⁹ many years before using 2.55 GHz microwave exposures on plasmid DNA.
4. There are more than 20 papers available (20 within the study review period) from PubMed and the ORSAA database that were not included in the Karipidis paper collection, with the majority showing gene expression changes, as such, potential cherry-picking by Karipidis cannot be excluded. The balance of evidence can be significantly skewed by having potentially biased paper selection criteria. SAR = Specific Absorption Rate (W/kg) and PD = Power Density (W/m²)
- a. Pyrpasopoulou *et al.* (2004) Bone morphogenetic protein expression in newborn rat kidneys after prenatal exposure to radiofrequency radiation <http://onlinelibrary.wiley.com/doi/10.1002/bem.10185/abstract> - 9.4 GHz, SAR=0005 W/kg, PD=0.010 W/m²
 - b. Mahamoud *et al.* (2016) Additive Effects of Millimeter Waves and 2-Deoxyglucose Co-Exposure on the Human Keratinocyte Transcriptome <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4986955/> - 60.4 GHz, PD=200W/m²
 - c. Paulraj *et al.* (2012) Biochemical Changes in Rat Brain Exposed to Low Intensity 9.9 GHz Microwave Radiation <http://link.springer.com/article/10.1007%2Fs12013-012-9344-3> - 9.9 GHz, SAR=1 W/kg, PD=1.25 W/m²
 - d. Wu *et al.* (2009) Experimental study of millimeter wave-induced differentiation of bone marrow mesenchymal stem cells into chondrocytes <https://www.spandidos-publications.com/10.3892/ijmm.00000152> - 30 to 40 GHz, PD=40 W/m²
 - e. Perez-Castejon *et al.* (2009) Exposure to ELF-pulse modulated X band microwaves increases in vitro human astrocytoma cell proliferation <http://europepmc.org/abstract/MED/19795354> - 9.6 GHz, SAR=0.0004 W/kg
 - f. Novoselova *et al.* (2017) Involvement of the p38 MAPK signaling cascade in stress response of RAW 264.7 macrophages <https://link.springer.com/article/10.1134%2FS0012496617050015> - 8.5 to 18 GHz, PD=0.010 W/m²
 - g. Tong *et al.* (2009) Millimeter-wave exposure promotes the differentiation of bone marrow stromal cells into cells with a neural phenotype <http://link.springer.com/article/10.1007%2Fs11596-009-0403-y> - 36.11 GHz, PD=100 W/m²
 - h. Gapeev *et al.* (2010) Responses of thymocytes and splenocytes to low-intensity extremely high-frequency electromagnetic radiation in normal mice and in mice with systemic inflammation <http://link.springer.com/article/10.1134%2FS000635091004010X> - 42.2 GHz, SAR=1.5 W/kg, PD=1 W/m²

- i. Novoselova *et al.* (2004) The Production of Tumor Necrosis Factor in Cells of Tumor-Bearing Mice after Total-Body Microwave Irradiation and Antioxidant Diet <http://www.tandfonline.com/doi/abs/10.1081/LEBM-200042320> - 8.15 to 18 GHz, PD=0.010 W/m²
- j. Fesenko *et al.* (1999) Microwaves and cellular immunity. I. Effect of whole body microwave irradiation on tumor necrosis factor production in mouse cells <https://www.sciencedirect.com/science/article/abs/pii/S0302459899000586> - 10 GHz, PD=0.010 W/m²
- k. Novoselova *et al.* (1999) Microwaves and cellular immunity: II. Immunostimulating effects of microwaves and naturally occurring antioxidant nutrients <https://www.sciencedirect.com/science/article/abs/pii/S0302459899000598> - 8.15 to 18 GHz, PD=0.010 W/m²
- l. Novoselova (2017) Extremely low-level microwaves attenuate immune imbalance induced by inhalation exposure to low-level toluene in mice <https://www.tandfonline.com/doi/abs/10.1080/09553002.2017.1270473> - 8.15 to 18 GHz, PD=0.010 W/m²
- m. Hass *et al.* (2017) Effect of acute millimeter wave exposure on dopamine metabolism of NGF-treated PC12 cells <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5569975/> - 60.4 GHz, PD=50 W/m²
- n. Kumar *et al.* (2012) Impact of microwave at X-band in the aetiology of male infertility <http://www.tandfonline.com/doi/full/10.3109/15368378.2012.700293> - 10 GHz, SAR=0.14 W/kg, PD=2.14 W/m²
- o. Franchini *et al.* (2018) Study of the effects of 0.15 terahertz radiation on genome integrity of adult fibroblasts <https://pubmed.ncbi.nlm.nih.gov/29602275/> - 100 to 150GHz, SAR- 15 to 20 W/kg, PD=4 W/m²
- p. Karaca *et al.* (2011) The genotoxic effect of radiofrequency waves on mouse brain <http://link.springer.com/article/10.1007%2Fs11060-011-0644-z> - 10.715 GHz, SAR=0.725 W/kg, PD=84 W/m²
- q. Veyret *et al.* (1991) Antibody responses of mice exposed to low-power microwaves under combined, pulse and amplitude modulation <https://onlinelibrary.wiley.com/doi/abs/10.1002/bem.2250120107> - 9.4 GHz, SAR=0.15 W/kg, PD=0.3 W/m²
- r. Sharma *et al.* (2014) Spatial memory and learning performance and its relationship to protein synthesis of Swiss albino mice exposed to 10 GHz microwaves <http://www.tandfonline.com/doi/full/10.3109/09553002.2013.835883> - 10 GHz, SAR=0.179 W/kg, PD=2.4 W/m²
- s. Perera *et al.* (2018) Exposure to 18 GHz EMF triggers uptake of large nanosphere clusters by pheochromocytoma cells <https://www.dovepress.com/exposure-to-high-frequency-electromagnetic-field-triggers-rapid-uptake-peer-reviewed-article-IJN> - 18 GHz, SAR=1.17 W/kg
- t. Webb (1975) Genetic Continuity and Metabolic-Regulation as Seen by Effects of Various Microwave and Black Light Frequencies on These Phenomena <https://pubmed.ncbi.nlm.nih.gov/1090232/> - 59 to 143 GHz, PD=100 to 500 W/m²

Table 4 Experimental studies investigating low-level RF fields above 6 GHz and cellular signalling and electrical activity.

Issues with Karipidis <i>et al.</i> Classification/Interpretation/Data	Our Finding	Reference	Biological System	Frequency Range	Intensity	Exposure Duration	Results [Claimed]	Quality Issue [Claimed]
<p>Incorrect Frequency Range - The frequency range specified by Karipidis was not used at all. What is quoted reflects the actual frequency range capability of the generator. Only 2 specific frequencies were used. Namely, 42.2 and 50.3 GHz.</p> <p>Incomplete Intensity Range - The specific intensities used were directly related to the frequency used. 1.9 W/m² for 42.2 GHz and 4.8 W/m² for 50.3 GHz.</p> <p>Incorrect Exposure Time Range - Karipidis may have mistaken the statement made by Minasyan <i>et al.</i> in their paper "<i>Considering</i></p>	Frequency specific effects on neurons, neuronal spike interval changes (regularity and dynamics)	[79] Minasyan <i>et al.</i>	Neural activity	38-54 GHz	4.8 W/m ²	20-60 min	Change in the duration of the inter-spike intervals	Inadequate dosimetry and temperature control

Issues with Karipidis <i>et al.</i> Classification/Interpretation/Data	Our Finding	Reference	Biological System	Frequency Range	Intensity	Exposure Duration	Results [Claimed]	Quality Issue [Claimed]
<p><i>that the biological effect appears some period of time after the start of irradiation and that the optimum duration of exposure is quite long (from 20 min to 1 h)"</i> as being the exposure duration. Actual exposure duration was 40 minutes.</p> <p>Comment Only - Results described are correct but to be more precise there were frequency specific effects on neurons, neuronal spike interval changes (regularity and dynamics).</p> <p>Funding - Not declared.</p>								
<p>Incorrect Frequency - The paper abstract suggests 10 GHz but the actual frequency used was 9.4 GHz.</p> <p>Incomplete Results - Result described is correct but Karipidis neglected to mention that the impulse train variance was significantly changed.</p> <p>Funding - Not declared.</p>	NS neuron spike amplitude and spike Interval changes, significant impulse train variance	[81] Munemori and Ikeda	Neural activity	10 GHz	2.5 W/m ²	4 min	Increase and decrease in the variance of interspike intervals.	No sham control and poor temperature control
<p>Incorrect Frequency - The paper abstract suggests 10 GHz, however, 2 discreet frequencies were used, namely 9.4 and 9.6 GHz</p> <p>Incorrect Intensity Range - Karipidis has specified incorrect intensity numbers. What was specified in the paper was ranges from 0.01 μW/cm² to 100m W/cm² which converts to 0.0001 W/m² to 1000 W/m².</p> <p>Incomplete Results - Result described is correct but Karipidis neglected to mention that the impulse train variance was significantly changed.</p> <p>Comment Only - We agree with Karipidis suggestion regarding poor temperature control. Study authors, Munemori and Ikeda, have assumed that impulse frequency changes are the result of heat because the same was seen with IR exposure. However, to confirm this is in fact heating related it should have been performed using a different thermal source. IR, like MMW, may cause thermal heating but there may also be non-thermal electromagnetic frequency (EMF) interactions occurring.</p> <p>Funding - Ministry of Education, Science & Culture (Government).</p>	NS neuron spike amplitude and spike Interval changes, significant impulse train variance, change in nerve impulse frequency	[82] Munemori and Ikeda	Neural activity	10 GHz	0.007-700 W/m ²	1 min	Decrease in the distribution of the interspike intervals with increasing exposure levels	No sham control and poor temperature control
<p>Frequency Range Observation - The frequency range was more specific (3 bands) and not so broad as being suggested by Karipidis. The specific frequencies bands used were 41.14 to 41.54 GHz, 45.89 to 45.93 GHz and 50.8 to 51.0 GHz.</p> <p>Incorrect Intensity - The actual incident power density used was 25W/m² for 45.89 to 45.93 GHz exposure and 2.5 W/m² for the other 2 frequency bands.</p> <p>Incorrect Exposure Time Range - The paper clearly says that a 38 min MMW exposure was applied to each nerve.</p> <p>Funding - US Army Medical Research and Materiel Command (Military).</p>	Resonance effect, non-thermal effect, frequency windows, changes in nerve action potential (spike) amplitude and nerve conduction velocity	[83] Pakhomov et al,	Neural activity	40-52 GHz	2.4-30 W/m ²	10 or 60 min	Reduction in the latency period and an increase in amplitude of CAPs	No blinding
<p>Incorrect Reference Number - The actual bibliography reference number should have been [85]. When reviewing the experimental data and the reference numbers for [84] and [85], Karipidis has mixed them up so that the referenced papers do not match the experimental details.</p>	Non thermal, non-linear effect on nerve action potential. MMW had no effect on the conditioning compound action potentials (CAPS), but significantly attenuated the high-rate	[84] Pakhomov et al.,	Neural activity	40 GHz	0.2-26 W/m ²	23 min	Reduction in the effect of high rate stimulus causing a decrease in the test CAP	No blinding

Issues with Karipidis <i>et al.</i> Classification/Interpretation/Data	Our Finding	Reference	Biological System	Frequency Range	Intensity	Exposure Duration	Results [Claimed]	Quality Issue [Claimed]
<p>Incorrect Frequency - Assuming reference [85], the actual frequency used was 41.34 GHz. All other parameters are specified correctly.</p> <p>Funding - US Army Medical Research and Materiel Command (Military).</p>	electrical stimulation of the nerve causing a decrease of the test CAPS.							
<p>Incorrect Reference Number - The actual bibliography reference number should have been [84]. When reviewing the experimental data and the reference numbers for [84] and [85], Karipidis has mixed them up so that the referenced papers do not match the experimental details.</p> <p>Incorrect Frequency Range - Assuming reference [84], the actual frequency range was split into 8 discreet bands with some overlap and included 40.50 to 46.50, 41.15 to 41.30, 41.30 to 41.70, 41.70 to 42.10, 41.80 to 42.00, 49.50 to 53.50, 51.60 to 51.70 and 51.70 to 51.80 GHz. In summary, frequencies used were between range of 40.50 to 53.50 GHz.</p> <p>Incorrect Intensity Range - Assuming reference [84], the actual intensity ranged from 2.3 W/m² to 30 W/m² from table 1 on p 328.</p> <p>Incorrect Exposure Time - Assuming reference [84], the exposure duration ranged from 10 minutes to 1 hour.</p> <p>Funding - US Army Medical Research and Materiel Command (Military).</p>	Frequency window, nerve action potential (spike) amplitude changes with high-rate stimulus. low-rate stimulation did not alter the functional state of the nerve	[85] Pakhomov et al.	Neural activity	40-50 GHz	2.5-25 W/m ²	12-50 min	Reduction in the effect of high rate stimulus causing a decrease in the test CAP	No blinding
<p>Frequency Observation - Specific frequency used was 60.125 GHz</p> <p>Incorrect Intensity Range - The calculated incident power density was in the range of 100 to 600 μW/cm² which equates to 1 to 6 W/m².</p> <p>Incorrect Exposure Time - A 60 second exposure was mentioned on page 4. "An averaged Rn value was calculated for each 10-sec period during the 60-sec exposure to MMWs (Figure 2)".</p> <p>Incomplete Results - The results provided by Karipidis are incomplete and missing additional findings that include significant plasma membrane permeability and membrane resting potential changes, action potential latency changes, dose response relationship and possible therapeutic use to control neuronal excitability.</p> <p>Funding - Not Declared.</p>	No significant action potential amplitude changes, statistically significant changes observed for action potential latency, plasma membrane permeability and membrane resting potential, considerable suppression of neuronal firing during the exposure and strong facilitation of firing immediately after the exposure, membrane conductivity changes, possible therapeutic use to control neuronal excitability	[86] Pikov and Siegel	Neural activity	60 GHz	0.00071-6 W/m ²	Not Stated	Reduced neuron firing rate and a decrease in input resistance	No blinding
<p>Frequency Observation - Specific frequency used was 60.125 GHz.</p> <p>Incomplete Results - The results provided by Karipidis are incomplete and missing additional findings that include plasma membrane permeability and membrane resting potential changes.</p> <p>Funding - Huntington Medical Research Institutes (Institution) and the Chief Scientist's Office of the Jet Propulsion Laboratory.</p>	Transient dose-dependent increase in the plasma membrane permeability, changes in the membrane input resistance and reduced neuron firing rate	[80] Pikov et al.	Neural activity	60 GHz	Up to 0.008 W/m ²	1 min	Reduced neuron firing rate and a decrease in input resistance	No blinding

Issues with Karipidis <i>et al.</i> Classification/Interpretation/Data	Our Finding	Reference	Biological System	Frequency Range	Intensity	Exposure Duration	Results [Claimed]	Quality Issue [Claimed]
<p>Frequency Observation – The generator was “capable” of producing signals in the range of 17 to 23 GHz. A 4x signal multiplier was used to obtain a 60 GHz signal.</p> <p>Incorrect Intensity Range – The upper limit was 144 W/m². “Several power levels ranging from 4 to 64mW at the output waveguide port (translating to power densities at the top surface of the ganglion from 0.9 to 14.4 mW/cm²) were applied”.</p> <p>Funding – Not declared.</p>	Neuron firing Inhibition effect	[87] Romanenko et al.	Neural activity	17-60 GHz	9-140 W/m ²	60 s	Reduction in the action potential firing rate	No blinding
<p>No Concerns</p> <p>Funding – Caltech/Huntington Medical Research Institutes (Institution) and Burroughs Wellcome Fund (Private Fund).</p>	No significant membrane resting potential changes and action potential narrowing changes. Neuron firing inhibition effect	[88] Romanenko et al.	Neural activity	60 GHz	10-40 W/m ²	60 s	Reduction in the action potential firing rate	No blinding

Summary of Issues with Karipidis Table 4 cellular signalling and electrical activity

- This section was supposed to cover both cellular signalling and electrical activity. Neuron firing covers both aspects but what is missing from the table are studies covering cellular signalling that do not relate to nerve impulses i.e., inter and intracellular signalling should be considered. Suitable candidates for “cellular signalling” are the following papers:
 - Chen [93] - Found MMW exposure inhibits 12-O-tetradecanoylphorbol-13-acetate (TPA) suppression of Gap Junction Intercellular Communication
 - De Amicis [18] – Found extracellular signal-regulated kinase (ERK) levels unchanged. ERK belongs to the mitogen activated protein kinase (MAPK) family and has a role in cell signalling cascades
 - Shcheglov [74] – Suggests intercellular communication via radicals and secondary radiation as a result of MMW exposure occur within specific power density and cell density windows
- There are also 4 studies available from PubMed and the ORSAA database that were not included in the Karipidis paper collection, investigating cellular signalling effects: SAR = Specific Absorption Rate (W/kg) and PD = Power Density (W/m²)
 - Donato *et al.* (2004) Low power microwave interaction with phospholipase C and D signal transduction pathways in myogenic cells <http://onlinelibrary.wiley.com/doi/10.1016/j.cellbi.2004.06.005/abstract> - 10.75 GHz, SAR=0.064 W/kg, PD=0.045 W/m²
 - Paulraj *et al.* (2012) Biochemical Changes in Rat Brain Exposed to Low Intensity 9.9 GHz Microwave Radiation <http://link.springer.com/article/10.1007%2Fs12013-012-9344-3> - 9.9 GHz, SAR=1.0 W/kg, PD=1.25 W/m²
 - Novoselova *et al.* (2017) Involvement of the p38 MAPK signaling cascade in stress response of RAW 264.7 macrophages <https://link.springer.com/article/10.1134%2FS0012496617050015> - 8.15 to 18 GHz, PD=0.010 W/m²
 - Novoselova *et al.* (2017) Extremely low-level microwaves attenuate immune imbalance induced by inhalation exposure to low-level toluene in mice <https://www.tandfonline.com/doi/abs/10.1080/09553002.2017.1270473> - 8.15 to 18 GHz, PD= 0.010 W/m²

3. There are a further 6 papers related to electrophysiological changes that are potentially relevant to this section available from PubMed and the ORSAA database that were not included in the Karipidis paper collection:
- Perez-Bruzon *et al.* (2010) Demodulation effect is observed in neurones by exposure to low frequency modulated microwaves <http://iopscience.iop.org/article/10.1088/1742-6596/200/12/122008/pdf> (Neuron Spike Frequency Changes) - 13.6 GHz, SAR=0.0031 W/kg
 - Godlevsky *et al.* (2013) Antiepileptic effects of short-wave radiation in hypogeomagnetic conditions <https://www.degruyter.com/view/j/med.2013.8.issue-4/s11536-012-0147-0/s11536-012-0147-0.pdf> (Cortical Neuron Excitability Changes) - 42.2 GHz, PD=1.0 W/m²
 - Ayrapetyan *et al.* (2009) The non thermal effect of weak intensity millimeter waves on physicochemical properties of water and water solutions <http://www.tandfonline.com/doi/abs/10.3109/15368370903206531?journalCode=iebm20> (Electrical Conductivity Changes) - 160 GHz, SAR=0.8 W/kg, PD=58 W/m²
 - Sivachenko *et al.* (2016) Effects of Millimeter-Wave Electromagnetic Radiation on the Experimental Model of Migraine <https://link.springer.com/article/10.1007/s10517-016-3187-7> (Neuronal Excitability Changes) - 40 GHz
 - Feldman *et al.* (2008) Human skin as arrays of helical antennas in the millimeter and submillimeter wave range <http://journals.aps.org/prl/abstract/10.1103/PhysRevLett.100.128102> (Skin Conductivity Changes) - 75 to 100 GHz
 - Feldman *et al.* (2009) The electromagnetic response of human skin in the millimetre and submillimetre wave range <https://iopscience.iop.org/article/10.1088/0031-9155/54/11/005> (Skin Conductivity Changes) - 75 to 100 GHz

Table 5 Experimental studies investigating low-level RF fields above 6 GHz and membrane effects.

Issues with Karipidis <i>et al.</i> Classification/Interpretation/Data	Our Finding	Reference	Biological System	Frequency Range	Intensity	Exposure Duration	Results [Claimed]	Quality Issue [Claimed]
<p>Frequency Range Observation - The specific wideband frequency was 53.57 to 78.33 GHz.</p> <p>Intensity Observation - Although some samples showed the highest specific absorption rate (SAR) was 0.0027 W/kg, the authors had earlier stated samples were exposed to a 53 to 78 GHz frequency range at SAR <12 mW/kg.</p> <p>Incorrect Exposure Time - Actual total duration was not specifically mentioned but if one looks at figure 6.0, it would suggest 6.5 hours not 4.</p> <p>Comment Only - Frequency generator emitted a wideband signal.</p> <p>Funding - Regione Calabria (Government).</p>	Change of membrane phase transition and reduction of water ordering at membrane interface	[89] Beneduci et al.	Artificial cell suspensions	53-78 GHz	Up to 0.0027 W/kg	4 h	Delays in the transition from gel to liquid phase or vice versa	Statistical methods were not described and no blinding

Issues with Karipidis <i>et al.</i> Classification/Interpretation/Data	Our Finding	Reference	Biological System	Frequency Range	Intensity	Exposure Duration	Results [Claimed]	Quality Issue [Claimed]
<p>Frequency Range Observation - The specific wideband frequency was 53.57 to 78.33 GHz. In addition to the wideband signal, specific discreet frequencies were also tested, namely 53.37 GHz, 62.10 GHz and 65.00 GHz.</p> <p>Intensity Observation - Karipidis specification is correct, however, to be more specific, the intensity range was 0.03 to 0.1 W/m² with a corresponding SAR between 0.001 to 0.003 W/kg.</p> <p>Findings Not Reported - Karipidis neglected to mention in the results that membrane structural changes occurred that affected membrane permeability.</p> <p>Comment Only - The effect for reduced water quadrupole splitting was only observed after some hours of exposure. It is important to note that the decrease of the water quadrupole splitting is reversible and the membrane system relaxes back to its pre-exposure state after a few hours from the end of the exposure. Among the three single-mode frequencies, only the exposure at 62.10 GHz induced a change of the quadrupole splitting similar to the one observed under wide-band mode exposure conditions.</p> <p>Funding - Not declared.</p>	Reduced water quadrupole splitting, frequency window effect, membrane structural changes and reduced permeability	[90] Beneduci et al.	Artificial cell suspensions	53-78 GHz	Up to 0.1 W/m ²	4 h	Reduction in water quadrupole splitting on simulated membrane	Statistical methods were not described and no blinding
<p>Frequency Range Observation - The specific wideband frequency was 53.57 to 78.33 GHz.</p> <p>Incorrect Exposure Time - 40 hours was the duration of the experiment but the actual microwave exposure was terminated after 26 hours.</p> <p>Findings Not Reported - Karipidis neglected to mention in the results the suggestion of membrane structural changes.</p> <p>Funding - Not declared</p>	Change of membrane phase transition (fluid-to-gel phase transition), membrane structural change	[91] Beneduci et al.	Artificial cell suspensions	53-78 GHz	< 0.03 W/m ²	Up to 40 h	Delays in the transition from gel to liquid phase or vice versa	Statistical methods were not described and no blinding
<p>Frequency Observation - the specific frequency used was 30.16 GHz.</p> <p>Result Clarification - MMW exposure did not directly impact Gap Junction Intercellular Communication. Gap junctions consist of arrays of intercellular channels that enable adjacent cells to communicate both electrically and metabolically. Cells can rapidly alter the number of gap junction channels at the plasma membrane in response to extracellular or intracellular cues. Gap junctions are plasma membrane domains containing arrays of intercellular channels that allow for the direct transfer of ions and small molecules (<sup>~</sup>1.2 kDa) between cells Totland <i>et al.</i>¹⁰ Membrane permeability is directly impacted by TPA, however, MMW interfered with the process by suppressing the action of TPA. Therefore, MMW affected membrane permeability indirectly by an antagonistic action against TPA.</p> <p>Funding - National Natural Science Foundation of China (Government).</p>	No direct effect on gap junction Intercellular communication, Inhibits TPA suppression of Gap Junction Intercellular Communication	[93] Chen et al.	Miscellaneous	30 GHz	10-35 W/m ²	1 h	Exposure increased membrane permeability	No sham control
<p>Intensity Range Observation - The actual intensity range used was 35 to 100 mW/m².</p> <p>Misclassified - The results presented by Karipidis are incomplete and potentially misleading. The results actually suggested irradiation does not affect the vesicle size distribution of a stabilized Giant unilamellar vesicles (GUV) suspension. MMW protected the vesicle from osmotic stress as the structure of the membrane becomes more compact. When comparing the results between sham and exposed with glucose solution addition, MMW exposed vesicles only reduced in size by a small amount over time when compared to the non-glucose controls.</p>	Inhibition of Ostwald ripening for large unilamellar vesicles, membrane structural changes resulting in increased membrane rigidity and reduced membrane permeability. Osmotic vesicle	[100] Cosentino et al.	Artificial cell suspensions	52-72 GHz	Up to 0.1 W/m ²	Up to 4 h	Change in size due to osmotic stress and a decrease in water permeability	Inadequate dosimetry and poor temperature control

Issues with Karipidis <i>et al.</i> Classification/Interpretation/Data	Our Finding	Reference	Biological System	Frequency Range	Intensity	Exposure Duration	Results [Claimed]	Quality Issue [Claimed]
Remembering osmosis is the passive flow of water to balance a chemical gradient via a membrane with selective permeability. Funding - Regione Calabria (Government) and Universita della Calabria (Institution).	shrinkage inhibition in glucose solution							
Frequency Observation - The specific frequency used was 53.37 GHz. Result Clarification - It is important to mention that membrane permeability changes occurred. Funding - Not declared.	Increasing transmembrane potassium efflux, membrane permeability change, and non-thermal mechanism	[97] D' Agostino et al.	Artificial cell suspensions	53 GHz	1.1 W/kg	Up to 30 min	Enhanced efflux of potassium from vesicles with increased amplitude of the electrical signals	Statistical methods were not described and no blinding
Exposure Duration Clarification - Actual exposure duration was 1 minute, 5 minutes and 10 minutes. Results Clarification - As part of the results discussion Karipidis made no specific mention of membrane effects - dehydration can only occur if the membrane is allowing water to escape due to permeability changes and/or an osmotic imbalance. Funding - Applied Scientific Research Fund (ASRF - Not for profit) and International Science and Technology Center (ISTC - Government).	Brain tissue dehydration, skin tissue dehydration, biphasic response along with intensity window. Neuron cell volume decrease suggesting possible membrane permeability effect	[96] Deghoyan et al.	Miscellaneous	90-160 GHz	1.49 W/kg	Up to 10 min	Decrease in the cell volume of neurons and rat brain tissue	Inadequate dosimetry and temperature control
Frequency Observation - The actual frequency used was 53.37 GHz Comment Only - Karipidis result description includes an acronym without providing a full description of what it represents. CA in this case represents Carbonic Anhydrase. Funding - Consiglio Nazionale delle Ricerche (Government).	Increased carbonic anhydrase activity, increased membrane permeability. No effect on carbonic anhydrase conformation	[99] Di Donato et al.	Artificial cell suspensions	53 GHz	Up to 1 W W/m ²	Up to 2 min	Enhancement of the CA reaction rate resulting in membrane permeability changes	No blinding
Frequency Observation - The actual frequency used was 42.25 GHz. Exposure Duration Clarification - 20 minute exposure with channel activity monitored occurring 30 minutes after irradiation ceases. Funding - Russian Foundation of Fundamental Investigations (Government) and Richard J. Fox Foundation (Public - not for profit).	Membrane channel effects, decreased current pulse duration, increased current pulse interval, decreased calcium activated K ⁺ channel opening frequency, calcium activated K ⁺ channel binding characteristic changes	[92] Geletyuk et al.	Cells in culture	42 GHz	1 W/m ²	Up to 30 min	Changes in binding affinity of channels for calcium with associated lowering of channel opening probability	No sham, dosimetry description or temperature control
Incorrect Biological System - No Yeast were used in the experiment. <i>Enterococcus hirae</i> bacteria were exposed. Frequency Range Observation - A set of discreet frequencies were used rather than ranges, namely 51.8 and 53.0 GHz. Exposure Duration Clarification - Irradiation times were 30 minutes, 1 hour and 2 hours. Result clarification - Karipidis makes no mention of why this study was included under the topic of membrane effects, i.e., intracellular hydration was seen. Funding - State Committee of Science, Ministry of Education and Science of Armenia (Government).	Inhibited cell growth, cell morphological changes, evidence for frequency windows and possible resonance effect, intracellular hydration (membrane effect)	[45] Hovnanyan et al.	Bacteria & Yeast	51-53 GHz	0.6 W/m ²	Up to 2 h	Increase in cell diameter and inhibition of cell growth	Inadequate dosimetry and temperature control

Issues with Karipidis <i>et al.</i> Classification/Interpretation/Data	Our Finding	Reference	Biological System	Frequency Range	Intensity	Exposure Duration	Results [Claimed]	Quality Issue [Claimed]
<p>Frequency Observation - The specific frequency used was 53.37 GHz</p> <p>Result Clarification - Artificial lipid vesicles are not cells, although "vesicle" morphological changes were seen.</p> <p>Funding - Consiglio Nazionale delle Ricerche (Government).</p>	Changes in membrane permeability, vesicle movement, vesicle elongation and vesicle Attraction	[98] Ramundo-Orlando <i>et al.</i>	Artificial cell suspensions	53 GHz	1 W/m ²	Up to 10 min	Cell morphology changes i.e. elongation and diffusion of dye across the membrane	Statistical methods were not described and no blinding
<p>Missing Frequency - 2 discreet frequencies were used, namely 18.75 and 37.5 GHz.</p> <p>Exposure Duration Clarification - Irradiation time was 1, 5, 15, 30, and 60 seconds.</p> <p>Comment Only - Initial physiological state (age and health) affects the base electronegativity of cell nuclei (ENN). The ENN changes can increase or decrease based on initial state with initial high ENN state decreasing and low ENN going to a higher level. Both scenarios are heading towards a middle point.</p> <p>Funding - Not declared.</p>	Changes in cell membrane permeability and nuclei electrokinetic properties	[94] Shckorbatov <i>et al.</i>	Cells in culture	37 GHz	2 W/m ²	1-60 s	Increase in cell permeability and both increased and decrease cell electronegativity	No sham and temperature control
<p>Comment Only - Karipidis used passive language "indication" to downplay findings. Authors are more direct in their conclusion by stating "<i>Low-level microwave irradiation induces chromatin condensation in human cells and damages of cell membranes</i>".</p> <p>Funding - Not declared.</p>	Cell membrane damage, increased membrane permeability, chromatin condensation, left vs right hand circular polarisation biological effect differences	[21] Shckorbatov <i>et al.</i>	Cells in culture	35 GHz	0.3 W/m ²	10 s	Reported an indication of cell membrane damage	Inadequate dosimetry and temperature control
<p>Incorrect Biological System - No Yeast were used in the experiment. <i>Lactobacillus acidophilus</i> (bacteria) was used.</p> <p>Frequency Range Observation - Two discreet frequencies, namely 51.80 and 53.0 GHz rather than a range as suggested by Karipidis nomenclature.</p> <p>Funding - Ministry of Education and Science (Government).</p>	Reduced growth rate, reduced viability, NS combinative effect with ceftazidime (antibiotic), changes in ion transport across cell membrane, anti-microbial effects, reduced colony forming	[44] Soghomonyan and Trchounian	Bacteria & Yeast	51- 53 GHz	0.6 W/m ²	1 h	Changes in ion transport across the membrane and inhibitory effect on bacteria proliferation and survival	Inadequate dosimetry and no blinding
<p>Incorrect Reference Number - The actual bibliography reference number should have been [39] as [38] refers to a paper from Cohen <i>et al.</i></p> <p>Incorrect Biological System - No Yeast were used in the experiment. <i>Escherichia coli</i> strain K12 wild type (bacteria) was used.</p> <p>Frequency Range Observation - Two discreet frequencies, namely 51.80 and 53.0 GHz rather than a range as suggested by Karipidis nomenclature.</p> <p>Exposure Duration Clarification - Irradiation times were for 30 and 60 minutes.</p> <p>Findings Not Reported - quite a few biological effects were not covered in the results description. Compare "Our Finding" description with Karipidis "Results" description.</p> <p>Funding - Ministry of Education and Science (Government).</p>	Reduced growth rate, combinative effect with antibiotic, reduced cell viability, H+ efflux, ion transportation changes, reduced ATPase activity, membrane effects, altered enzyme activity (ATPase), resonance frequency and increased lag phase duration (cell cycle effects)	[38] Tadevosyan <i>et al.</i>	Bacteria & Yeast	51-53 GHz	0.6 W/m ²	Up to 1 h	Changes in ion transport across the membrane and inhibitory effect on bacteria proliferation	Inadequate dosimetry and poor temperature control
<p>Incorrect Biological System - No Yeast were used in the experiment. <i>Escherichia coli</i> strain K12 wild type (bacteria) was used.</p> <p>Frequency Range Observation - Two discreet frequencies, namely 70.60 and 73.0 GHz rather than a range as suggested by Karipidis nomenclature.</p>	Reduced growth rate (proliferation), increased lag phase duration (cell cycle effects), bactericidal,	[40] Torgomyan and Trchounian	Bacteria & Yeast	70-73 GHz	0.6 W/m ²	Up to 1 h	Inhibition of proliferation and changes in membrane proteins	Inadequate dosimetry and temperature control

Issues with Karipidis <i>et al.</i> Classification/Interpretation/Data	Our Finding	Reference	Biological System	Frequency Range	Intensity	Exposure Duration	Results [Claimed]	Quality Issue [Claimed]
<p>Exposure Duration Clarification - Irradiation was for 1 hour and not less.</p> <p>Findings Not Reported - A number of biological effects were not covered in the results description. Compare "Our Finding" description with Karipidis "Results" description.</p> <p>Funding - Ministry of Education and Science (Government).</p>	reduced cell viability, change in accessibility of sulfhydryl (SH) groups of membrane vesicles, and resonant frequency							
<p>Incorrect Biological System - No Yeast were used in the experiment. Escherichia coli (bacteria) was used.</p> <p>Frequency Range Observation - Two discreet frequencies, namely 70.60 and 73.0 GHz rather than a range as suggested by Karipidis nomenclature.</p> <p>Exposure Duration Clarification - Irradiation times were for 30 minutes, one hour and 2 hours.</p> <p>Findings Not Reported - A number of biological effects were not covered in the results description. Compare "Our Finding" description with Karipidis "Results" description.</p> <p>Funding - Ministry of Education and Science (Government).</p>	Reduced growth rate (proliferation), bactericidal, colony forming reduced, changed optical density and absorption characteristics of water, Increased conductivity of water, and altered pH levels	[41] Torgomyan et al.	Bacteria & Yeast	70-73 GHz	0.6 W/m ²	Up to 2 h	Effect on bacterial growth and changes in ion transport	Inadequate dosimetry and temperature control
<p>Incorrect Biological System - No Yeast were used in the experiment. Escherichia coli (bacteria) was used.</p> <p>Frequency Range Observation - Four discreet frequencies, namely 51.80, 53.0, 70.60 and 73.0 GHz rather than a range as suggested by Karipidis nomenclature.</p> <p>Findings Not Reported - A number of biological effects were not covered in the results description. Compare "Our Finding" description with Karipidis "Results" description.</p> <p>Misstatement - Karipidis mentions changes in ion transport in the result but this end point was not directly tested in this particular study. It was only mentioned in the discussion section based on previous work.</p> <p>Funding - Ministry of Education and Science (Government).</p>	Reduced growth rate, frequency windows, increased lag phase duration (cell cycle effects), reduced colony forming, morphological changes (cell structure and size), pH level changes, biochemical changes, redox potential changes, surface tension changes, increased cytoplasm vacuolization, membrane permeability changes	[42] Torgomyan et al.	Bacteria & Yeast	51-73 GHz	0.6 W/m ²	1 h	Enhanced the inhibitory effect of antibiotics on bacterial proliferation. Changes in ion transport	Inadequate dosimetry
<p>Incorrect Biological System - No Yeast were used in the experiment. Enterococcus hirae (bacteria) was used.</p> <p>Frequency Range Observation - two discreet frequencies, namely 51.80 and 53.0 GHz rather than a range as suggested by Karipidis nomenclature.</p> <p>Findings Not Reported - A number of biological effects were not covered in the results description. Compare "Our Finding" description with Karipidis "Results" description.</p> <p>Funding - Ministry of Education and Science and National Science and Education Fund (Government).</p>	K and H ⁺ ion flux changes, membrane ion transport effects, reduced ATPase activity, reduced growth (proliferation), increased lag phase duration (cell cycle effects), combinative effect with antibiotics	[43] Torgomyan et al.	Bacteria & Yeast	51-53 GHz	0.6 W/m ²	1 h	Changes in the bacterial proliferation and survival. Changes in ion transport	Inadequate dosimetry and temperature control
<p>No Concerns</p> <p>Funding - Not declared.</p>	Increase in lateral membrane pressure. No changes in cell membrane morphology	[95] Zhadobov et al.	Artificial cell suspensions	60 GHz	Up to 9 W/m ²	Up to 5 h	Increases in lateral membrane pressure but no changes to the microdomain organisation	Statistical analysis not described and no blinding

Issues with Karipidis <i>et al.</i> Classification/Interpretation/Data	Our Finding	Reference	Biological System	Frequency Range	Intensity	Exposure Duration	Results [Claimed]	Quality Issue [Claimed]
<p>Summary of Issues with Karipidis <i>et al.</i> Table 5 membrane effects</p> <ol style="list-style-type: none"> 1. This section missed a number of relevant papers from the collection of 107 papers reviewed that investigate membrane effects and includes: <ol style="list-style-type: none"> a. Beneduci [52] – found membrane surface microvilli reduction b. Crozier [26] – found membrane fluidity changes c. Pikov [80] – found plasma membrane effects d. Pikov [86] – found plasma membrane permeability changes and membrane resting potential changes e. Volkova [103] – found cell membrane permeability changes 2. Compared with other end points that Karipidis investigated, there was good coverage of membrane effects. We were only able to find an additional 4 papers that had been missed when searching PubMed and the ORSAA database: SAR = Specific Absorption Rate (W/kg) and PD = Power Density (W/m²) <ol style="list-style-type: none"> a. Szabo <i>et al.</i> (2006) Millimeter wave induced reversible externalization of phosphatidylserine molecules in cells exposed in vitro https://www.researchgate.net/publication/227726252 Reaction of keratinocytes to in vitro millimeter wave exposure (Membrane Effects) - 42.25 GHz, PD=5.5 to 345 W/m² b. Wu <i>et al.</i> (2011) Millimeter wave treatment inhibits the mitochondrion-dependent apoptosis pathway in chondrocytes https://www.spandidos-publications.com/10.3892/mmr.2011.522 (Mitochondrial Membrane Potential Changes) – 30 to 40 GHz, PD=40 W/m² c. Ramundo-Orlando <i>et al.</i> (2007) Permeability changes induced by 130 GHz pulsed radiation on cationic liposomes loaded with carbonic anhydrase http://onlinelibrary.wiley.com/doi/10.1002/bem.20343/abstract (Membrane Permeability Changes) - 130 GHz, PD=50 to 170 W/m² d. Perera <i>et al.</i> (2018) Exposure to 18 GHz EMF triggers uptake of large nanosphere clusters by pheochromocytoma cells https://www.dovepress.com/exposure-to-high-frequency-electromagnetic-field-triggers-rapid-uptake-peer-reviewed-article-IJN (Transient Cell Membrane Permeability Changes) – 18 GHz, SAR=1.17 W/kg 3. Overall, there is overwhelming evidence that cell membrane effects are occurring. The implications of some of these effects can impact cell morphology (including histopathological effects) and membrane permeability. This is likely to result in the activation of cellular adaptive responses to achieve homeostasis and comes at a cost of additional energy needs and potentially an oxidative stress state. Membrane permeability changes can lead to a cascade of cellular activity (cellular signalling, activation of active transport proteins to balance ion flux changes, gene expression and potential epigenetic changes, increased mitochondrial activity i.e., changes to cellular metabolism). 								

Table 6 Experimental studies investigating low-level RF fields above 6 GHz and other effects.

Issues with Karipidis <i>et al.</i> Classification/Interpretation/Data	Our Finding	Reference	Biological System	Frequency Range	Intensity	Exposure Duration	Results [Claimed]	Quality Issue [Claimed]
<p>Findings Not Reported - Karipidis has not listed all outcomes found in the study, particularly the tumour promotion effects for mice with Lewis cell grafts (10^6 cell grafts). Compare "Our Finding" description with Karipidis "Results" description.</p> <p>Funding - Not declared.</p>	<p>No change in growth or organ weight.</p> <p>Individual sensitivities seen, tumour promotion in synchronised Lewis cells (10^6 cell grafts), increased food intake, increased activity in tumour bearing mice, non-significant increased survival time - Leukaemia (L1210 cells), non-significant reduced survival for Lewis Tumours</p>	<p>[117] Bellossi et al.</p>	<p>In vivo</p>	<p>60 GHz</p>	<p>5.1 W/m²</p>	<p>30 min/day to death</p>	<p>Increased survival for the leukaemia inoculated mice</p>	<p>No temperature control and sham controls</p>
<p>Frequency Range Observation - The specific frequency range used was 41.75 to 42.15 GHz.</p> <p>Incorrect Exposure Time - The actual exposure duration was 40 minutes.</p> <p>Incorrect Intensity - The intensity varied from 0.001 W/m² (far field) to 0.5 W/m² (near field). Paper used different units with 0.1 μW/cm² for far field and up to 500 μW/cm² for near field.</p> <p>Result Clarification - The study investigated ROS production inhibition in activated neutrophils.</p> <p>Funding - Richard J. Fox Foundation (Public not for profit) and Russian Foundation for Basic Research (Government).</p>	<p>Resonance frequency, reactive oxygen species inhibition, frequency windows (near field only), non-linear interaction</p>	<p>[106] Gapeyev et al.</p>	<p>Cells in culture</p>	<p>41 to 42 GHz</p>	<p>0.24-0.5 W/m²</p>	<p>20 min</p>	<p>Frequency dependant change in ROS production</p>	<p>Inadequate dosimetry and temperature control methods not described</p>
<p>Frequency Range Observation - A number of frequencies bands were used in this study, namely 41.75 to 42.15, 41.8 to 41.9 and 41.95 to 42.05 GHz.</p> <p>Incorrect Intensity Range - The range shown in Table 1, page 269 was 0.07 mW/m² to 1.46 W/m² (0.007 μW/cm² to 146.0 μW/cm²).</p> <p>Findings Not Reported - Missing important result findings including modulation effects, synergistic effects with phorbol ester PMA and calcium ionophore A23187, inhibitory effect with continuous wave (CW).</p> <p>Nonsensical Quality Issue - Karipidis claim a lack of a thermal control as a quality deficiency. However, we question the relevance of a thermal control when the PD is so low for some of the exposures, temperature changes would unlikely be measurable.</p> <p>Funding - Richard J. Fox Foundation (Public not for profit) and Russian Foundation for Basic Research (Government).</p>	<p>Resonance effect, reactive oxygen species inhibition, modulation effects (1Hz), non-linear effect, Synergistic effect with phorbol ester PMA and calcium ionophore A23187 (AM modulated) but inhibition with continuous wave</p>	<p>[107] Gapeyev et al.</p>	<p>Cells in culture</p>	<p>41 to 42 GHz</p>	<p>0.24-2.4 W/m²</p>	<p>20 min</p>	<p>Frequency dependant change in ROS production</p>	<p>Inadequate dosimetry and poor temperature control</p>
<p>Frequency Observation - The specific frequency used was 42.2 GHz. It is important to specify the frequency used as resonance effects can have a very narrow band of effect (within a few MHz). Providing the specific frequency also allows discerning scientists to verify bio-active frequencies and check whether claimed replications studies are what they say they are.</p>	<p>Increased poly-unsaturated fatty acid, reduced mono-unsaturated fatty acids and changes in some saturated acids in Thymic cells. Less</p>	<p>[110] Gapeyev et al.</p>	<p>Cells in culture</p>	<p>42 GHz</p>	<p>1 W/m²</p>	<p>20 min</p>	<p>Changes in fatty acid concentrations in thymus cells and blood plasma</p>	<p>Poor temperature control and no blinding</p>

Issues with Karipidis <i>et al.</i> Classification/Interpretation/Data	Our Finding	Reference	Biological System	Frequency Range	Intensity	Exposure Duration	Results [Claimed]	Quality Issue [Claimed]
Funding - Russian Foundation for Basic Research (Government).	pronounced changes including increased saturated fatty acids seen in blood plasma							
Incorrect Frequency - The actual frequency was 42.2 GHz. Incorrect Exposure Time - The actual exposure duration was 20 minutes per day for 5 days for a total of 100 hours. Funding - Not declared.	Reduced tumour growth, muscle/ thymus hepatic effects - fatty acid profile change, mono-saturated fatty acid level changes, poly-unsaturated fatty acid level change, saturated fatty acid level change	[111] Gapeyev et al.	Cells in culture	40 GHz	1 W/m ²	20 min	Changes in fatty acid concentrations of tumour bearing mice and restoration of fatty acid levels in the thymus	Poor temperature control and no blinding
Incorrect Frequency - The actual frequency was 42.2 GHz. Findings Not Reported - A combinative biological effect (changes to fatty acid profiles and thymus weight reduction with X-ray exposure was seen when pre-exposure to MMW occurred followed by the x-ray exposure and then another subsequent exposure to MMW. Funding - Russian Foundation for Basic Research and the Government of Moscow Region grant (Government).	No mortality changes, no significant thymus weight change. No change in total fatty acid content, adaptive response, X-ray biological protection with MMW exposure (pre or post X-ray exposure) combinative effects when MMW exposures precedes an x-ray exposure and then followed up with an additional MMW exposure.	[112] Gapeyev et al.	Cells in culture	40 GHz	1 W/m ²	20 min	Accelerated recovery of fatty acid after X-ray exposure	Poor temperature control and no blinding
Incorrect Intensity - There was no mention of 0.31 W/m ² in the paper reviewed. Instead, the paper mentioned the power density of the radiation at the bottom of the microplate wells was measured at 0.08 W/m ² . Incorrect Exposure Time - There was no 24-hour exposure to radiofrequencies. The specific exposure durations were 1.0, 1.5 and 2 hours. Funding - Commission of the European Communities (Government) and Department of Chemical Engineering and Biotechnology (Institution).	Reduced enzyme activity, increased instability of antigen-antibody complexes	[109] Homenko et al.	Miscellaneous	100 GHz	0.31 W/m ²	1, 2 and 24 h	Reduction in enzyme activity and decreased stability of antigen antibody complexes	No blinding
Incorrect Frequency - There was no 10 GHz exposure Findings Not Reported - Karipidis failed to mention in the results that there was also increased apoptosis (cell death) in sperm cells, which has implications in fertility. The changes in the activity of enzymes (increases and decreases of different REDOX enzymes) is a marker of oxidative stress and is consistent with what other studies investigating radiofrequency exposures and these endpoints typically find. Funding - Council for Scientific and Industrial Research (CSIR) and Indian Council for Medical Research (ICMR) (Government).	Apoptosis, sperm cell cycle effects, oxidative stress (increase catalase activity, decreased glutathione peroxidase and superoxide dismutase enzyme activity, reduced histone kinase enzyme activity, spermatogenesis cell cycle effects	[104] Kesari and Behari	In vivo	10 and 50 GHz	0.0086 W/m ²	2 h/day for 45 days	Increase and decrease in enzymes that control the build-up of ROS. Changes in cell cycle kinetics	Low animal numbers (6 exposed)
Incorrect Exposure Time - The study was performed doing two cycles of 30-minute exposures (for a total of 60 minutes). As Karipidis has indicated a number of experiments were also performed up to 40 minutes, namely 30 to 40 minute exposures. Funding - Richard J. Fox Foundation (public not for profit).	Temperature Oscillations (via toroidal vortex created by exposure), "hysteresis-type" effect	[119] Khizhnyak and Ziskin	Miscellaneous	53-78 GHz	0.1 - 10000 W/m ²	Up to 40 min	Temperature oscillations in the liquid medium. SAR above limit	Inadequate dosimetry, no sham control and no blinding

Issues with Karipidis <i>et al.</i> Classification/Interpretation/Data	Our Finding	Reference	Biological System	Frequency Range	Intensity	Exposure Duration	Results [Claimed]	Quality Issue [Claimed]
<p>Findings Not Reported - there is no mention in the results that the exposures affected spermatozoa and that there are implications to fertility.</p> <p>Funding - Indian Council of Medical Research (ICMR) (Government).</p>	Increased apoptosis, spermatozoa cell cycle effects, reduced histone kinase activity, increased reactive oxygen species levels. These effects suggest metabolic and biochemical changes, oxidative stress and has implications on fertility	[105] Kumar et al.	In vivo	10 GHz	2.1 W/m ²	2 h/day for 45 days	Decrease in the activity of histone kinase and an increase in ROS and the rate of apoptosis. There was also changes in cell cycle kinetics	Low animal numbers (6 exposed), no blinding
<p>Incorrect Intensity Range - The range used was 1 - 100 W/m². The paper used different units so likely a conversion problem by Karipidis. What the paper declared was a range from 0.1 mW/cm² to 10.0 mW/cm²</p> <p>Misclassified - Aberrant metaphases (Meiotic), chromosomal translocations, metaphases with univalents. Translocations can generate novel chromosomes and are often linked to aneuploidy and disorders like infertility and cancer. This paper should have been included under genotoxicity because issues in meiosis can have implications for genotoxicity and carcinogenicity, particularly if the aberrant sperm were to fertilize an egg.</p> <p>Funding - Centre International des Etudiants et Stagiaires and Direction des Recherches et Etudes Techniques du Ministère de Defense (Military).</p>	Aberrant metaphases (Meiotic), chromosomal translocations, metaphases with univalents	[101] Manikowska et al.	In vivo	9.4 GHz	10-100 W/m ²	1 h/day for 2 weeks	Increase in occurrence of translocations and unpaired chromosomes during meiosis in sperm cells of mice	Inadequate dosimetry and temperature control
<p>Incomplete Results - Karipidis result summary is lacking in details.</p> <p>Funding - Not declared.</p>	No changes seen for autonomic nervous system, cardiovascular function (ECG), skin conductance, skin temperature, respiration rate or systolic effects, non-significant changes were observed in diastolic blood pressure	[114] Muller et al.	Human volunteers	77 GHz	0.03 W/m ²	15 min	No alterations of autonomic nerve activity or cardiovascular function	Inadequate dosimetry and temperature control
<p>Frequency Observation - Actual frequency used was 53.57 GHz, Karipidis has been inconsistent with their frequency rounding. In some cases, they round up if the decimal portion is 0.5 or higher, while in other cases they do not perform rounding as is the case with this study.</p> <p>Comment Only - Hydrocortisone is used to treat adrenocortical deficiency, swelling and inflammation, and to slow down a person's immune system. EMF blocks its effects (antagonistic) and so could have negative implications in a medical treatment scenario.</p> <p>Funding - Unknown.</p>	Hepatic effects, gamma-glutamyl transpeptidase (GGT) activity changes, anti- hydrocortisone effect (antagonistic effect with steroid)	118] Olchowik and Maj	In vivo	53 GHz	10-100 W/m ²	20 min/day for 30 days	No effects below limit, above the limit the effect of hydrocortisone on gamma-glutamyl transpeptidase was blocked	No description of dosimetry and poor temperature control
<p>Findings Not Reported - Karipidis has been very selective in what effects are described. There was no mention of an initial statistically significant increase in spleen mass or reduced leukocyte count and, decreased % of granulocytes, increased thymus mass and reduced adrenal gland mass. These changes all together</p>	Increased spleen mass, NS increased thymus mass, NS reduced adrenal gland mass, no significant effect on erythrocyte	[113] Rotkowska et al.	In vivo	34 GHz	0.2 W/m ²	17 h/day for 10 days	Increase in progenitors of granulocytes and macrophages in the bone marrow of exposed mice	Poor temperature control and

Issues with Karipidis <i>et al.</i> Classification/Interpretation/Data	Our Finding	Reference	Biological System	Frequency Range	Intensity	Exposure Duration	Results [Claimed]	Quality Issue [Claimed]
<p>suggest implications on the immune system with potential health consequences.</p> <p>Comment Only - The paper's authors have assumed that "practical" use of radar, which would be infrequent, is unlikely to cause any issues. One cannot then take this outcome to suggest MMW exposures are safe because in many instances, future MMW exposures as a consequence of the rollout of advanced forms of 5th Generation (5G) technology, may not be short term or acute exposures.</p> <p>Funding - Not declared.</p>	count or haemoglobin concentration, significant reduction in leukocyte count, decreased % of granulocytes, no significant body mass changes, Increased number of progenitors of granulocytes and macrophages (GM-CFC), No skin or cornea damage, no significant changes in DNA synthesis							statistical analysis not described
<p>Frequency Observation - Specific frequency used is 41.95 GHz</p> <p>Findings Not Reported - Enhanced ROS production when neutrophil is primed was not mentioned. Differential effects are noted depending on whether cell was primed or un-primed, this has implications on immune responses. When a neutrophil is primed, usually as a result of inflammatory mediators - changing its functional state makes it susceptible to MMW exposures which can lead to an increased production of ROS. This may have a therapeutic benefit when dealing with pathogens but also can have a negative side effect when it comes to situations dealing with chronic inflammation.</p> <p>Funding - Richard J. Fox Foundation (Public) and Russian Ministry of Sciences and Education (Government).</p>	No effect on reactive oxygen species (ROS) production (un-primed), increased ROS production (fMLP primed)	[108] Safronova et al.	Cells in culture	42 GHz	0.195 W/m ²	20 min	Enhanced response of primed neutrophils to a chemotactic peptide	No blinding and poor temperature control
<p>Incorrect Frequency Range - Two discreet frequencies were used not a wide and or a range of frequencies as implied by Karipidis. nomenclature. Frequencies were 1 GHz and 10 GHz.</p> <p>Comment Only - Evidence from this study suggest transgenerational effects.</p> <p>Funding - Federal Target Program Scientific and Scientific-Pedagogical Personnel of Innovative Russia (Government), EMF Biological Research Fund and Cancer Research UK (Not for profit).</p>	Transgenerational effects, reduced ciliate motility	[120] Sarapultseva et al.	Miscellaneous	1-10 GHz	0.05-0.5 W/m ²	Up to 10 h	Exposure decreased the motility of the protozoa <i>S. ambiguum</i> and their non-exposed offspring	Inadequate dosimetry and no blinding
<p>Incorrect Exposure Time - How can one have 32 hours of exposure for 63 days? What Karipidis should have said is there were 30-minute exposures daily for 63 days (group 1) and a range of days of exposure from 7 to 35 for group 2.</p> <p>Findings Not Reported- Karipidis failed to mention specific degenerative changes in spermatozoa, which included deformation of the sperm head, increase in DNA content, chromosomal imbalances (diploid sperm). These can have fertility and foetal developmental consequences. Author's conclusion "<i>indicates that nonthermal EHF EMR is a pathogenic factor for mammalian spermatogenesis</i>".</p> <p>Funding - Not declared.</p>	Spermatogenesis effects, abnormal sperm, sperm head defects, increased DNA content (diploid), chromosomal imbalances, increased litter size	[102] Subbotina et al.	In vivo	NS	3 W/m ²	3.5-32 h for 63 days	Increase in the occurrence of abnormal sperm and an increase in litter size of exposed male mice	No description of dosimetry or temperature control
<p>Frequency Observation - The specific frequency of 41.80 and 74.0 GHz were used and not a range as suggested by Karipidis nomenclature.</p> <p>Incorrect Intensity Range - Peak Power density was 20,000 W/m². i.e., cells in the centre of the wave guide that were exposed at</p>	Ultrastructural alterations included breakage of cell processes, progressive detachment of cells from	[116] Stensaas et al.	Cells in culture	41-74 GHz	Up to 10000 W/m ²	1 h	No effect on the ultracellular structure of the cells when temperature was controlled	Inadequate dosimetry, statistical analysis not described

Issues with Karipidis <i>et al.</i> Classification/Interpretation/Data	Our Finding	Reference	Biological System	Frequency Range	Intensity	Exposure Duration	Results [Claimed]	Quality Issue [Claimed]
<p>the maximum power density of 2,000 mW/cm². The average power density ranged between 3200 and 4500 W/cm².</p> <p>Comment Only - The morphological changes occurred as a result of thermal exposure levels (where temperature was not controlled). No significant effects seen in temperature-controlled experiments</p> <p>Funding - National Cancer Institute (Government) and Department of the Navy (Military).</p>	<p>the substrate, increased clumping of heterochromatin in the nuclei, and the appearance of large empty vesicles in the cytoplasm</p>							
<p>Frequency Observation - The specific frequency used was 42.25 GHz.</p> <p>Misclassified and Findings Not Reported - Karipidis description of the biological effects is not entirely accurate or complete. This discrepancy is likely to be due in some part to the way the authors of the paper framed their conclusions and information provided in the abstract. The results however paint a less optimistic picture. The study results show statically significant reduced motility for normozoospermia (i.e., normal sperm). Cell membrane effects were seen, including the level of spermatozoa with impaired membranes increased after 15-min exposure of samples by 8.6 ± 1.2%. Increased sperm motility was seen but only in asthenozoospermia, which is an infertility condition where sperm have low motility. This suggests MMW exposure maybe have therapeutic potential for men with asthenozoospermia. Apoptosis was also claimed to not have been detected by the authors (except a small non-significant indication of early apoptosis.) However, when looking at the results and instructions for the test kit that they used suggests there was indication of late apoptosis which was statistically significance when compared to the control for 15-minute exposure (i.e., Annexin V+/7AAD+ test for 15-minute exposure was 4.75 ± 0.11%* where * represents statistical significance p <0.05 compared to control). The test kit instructions indicates "7-AAD (7-amino-actinomycin D) has a high DNA binding constant and is efficiently excluded by intact cells. It is useful for DNA analysis and dead cell discrimination during flow cytometric analysis. Apoptosis is further defined as early apoptosis (Annexin V+/7-AAD-) and late apoptosis (Annexin V+/7-AAD+)".</p> <p>Findings Not Reported - There was no mention by Karipidis of DNA fragmentation findings that were associated by the author to "incomplete apoptosis". This paper should have been a potential inclusion for the genotoxicity table.</p> <p>Funding - Not declared</p>	<p>Significantly reduced sperm motility (Normozoospermia), cell membrane permeability, improved sperm motility (Asthenozoospermia), apoptosis, fragmented DNA. No significant changes in sperm viability</p>	<p>[103] Volkova et al.</p>	<p>Cells in culture</p>	<p>42 GHz</p>	<p>0.3 W/m²</p>	<p>5-15 min</p>	<p>No change to sperm membrane integrity or nuclear chromatin status. Increase in percentage of mobile sperm</p>	<p>Inadequate dosimetry and temperature control</p>
<p>No Concerns</p> <p>Funding - Not declared</p>	<p>MMW frequency absorption spectra change between normal cells and tumour cells. Changes in absorption characteristic likely due to macromolecular differences</p>	<p>[115] Webb and Booth</p>	<p>Cells in culture</p>	<p>66-76 GHz</p>	<p>2 × 10⁻⁵ - 0.000103W</p>	<p>NS</p>	<p>Frequency specific differences in the attenuation of MMW in healthy and tumour cells</p>	<p>Inadequate dosimetry, no sham or temperature control</p>

There were a number of problematic issues found with the overall experimental review, including:

1. Not all biological effects found in papers reviewed by Karipidis *et al.* are documented or discussed.
2. Many frequencies are misstated or have had inconsistent rounding applied. Wideband exposures are not discernible from multiple discrete frequencies. It is important to list all specific frequencies tested and only provide a range if a frequency range was tested. The rationale is to:
 - a) Validate whether claimed replicated studies are indeed true replications and that we are able to compare “apples with apples” where it is reasonably possible
 - b) To ensure the reader is able to discern when different discrete frequencies are used and where wide band or sweep like exposures are performed
 - c) The constrained frequency granularity (GHz rounding) used by Karipidis *et al.* reduces any chance of validating the existence of MHz specific frequency windows
3. Karipidis excluded therapeutic papers without providing any justification. Therapeutic papers are important because they confirm biological effects can also be beneficial. However, some therapeutic papers investigating tumour growth suppression with MMW exposures demonstrate how timing and duration of the dose is very important because opposite (promotion) effects can also occur Radziewsky *et al.* ¹¹
4. Karipidis has also missed a large number of relevant papers for inclusion in their review, particularly those studies investigating immune system effects, with many showing significant findings. Whether this oversight is due to the search criteria being insufficient or the specific inclusion/exclusion criteria applied being biased remains unclear and unresolved. We recommend that Karipidis consider using the ORSAA database for future literature searches, as another potential source of papers. We found an additional 70 experimental papers (refer to table below) and 16 epidemiological papers that were relevant and these would have provided a more accurate and balanced assessment of the state of the science.
5. Many experimental studies do not take into consideration delayed responses. An example includes the time required for a cell to react to signals, particularly when it comes to gene expression. Cells rarely respond instantaneously nor do they respond in a linear manner. It can take time from when a signal transduction pathway is invoked to when a protein is expressed, including all the intermediary steps of mRNA transcription from DNA and translation of the mRNA to protein. Some experiments reviewed by Karipidis do not take this into consideration when performing assays. Latent changes can appear many hours later, which protein assays won't pick up if they are performed during or immediately after exposure ceases.
6. A number of quality issues that have been identified by Karipidis are questionable and appear to be used to diminish findings. Examples include blinding, which only becomes a critical issue if the measurements being taken are subjective (i.e., manual counting of chromosomal aberrations using a microscope), while blinding is not so critical where objective measurements are taken (i.e., optical density, MTT assay etc.). The requirement for providing temperature control details is also not seen to be essential if precision measurements, i.e., within 0.1°C are taken and the applied MMW power density is clearly lower than where measurable heating would be present as was the case with many of Belyaev *et al.* papers.
7. When looking at funding source and comparing outcomes we note that all studies funded by industry found no significant effects. Additionally, all studies funded by the Japanese Ministry of Internal Affairs and Communications also found no significant effects. Reviewing all papers in the ORSAA database against funding sources and comparing published outcomes, we have determined that researchers who receive funding from Government agencies that derive income from spectrum sales are more likely to report “no effects”, similar to industry funded papers.

Conversely, government funding papers that are not related to military, radiation protection or government communications departments have a stronger tendency to report significant effects, Leach and Weller¹² and is similar to findings made by Huss *et al.*¹³

8. In relation to the 70 candidate experimental papers that were not included by Karipidis, 67 papers found statistically significant outcomes, while one paper has been classified by ORSAA as showing an uncertain effect with the remaining three papers finding no statistically significant effects. Eight additional experimental papers were found that were missing adequate dosimetry. However, a number of them indicated they were low power with seven showing statistically significant effects, and one paper showing no effects. Some of the effects noted in the large number of missing papers include:
 - a) Learning/behavioural effects (3 papers all showing an association with exposure)
 - b) Short term memory impairment (4 papers with 3 showing an association)
 - c) Brain/neuronal effects (6 papers – all showing an association with RF exposure)
 - d) Markers for oxidative stress – (5 papers with 4 showing increase and 1 showing inhibition)
 - e) Apoptosis/necrosis – cell death (4 papers – 2 showing an effect, 1 showing protective effect and 1 showing no RF exposure effect)
 - f) Fertility effects – particularly in relation to sperm and testicular effects (3 papers all showing an impairment effect)
 - g) Immune system effects (15 papers with 11 papers showing significant effects, 3 showing therapeutic effects and one paper finding no effect from RF exposure)
 - h) Synergistic/combinative effects with other agents (5 papers with 3 showing a significant interaction, 1 showing a trend and 1 paper showing therapeutic benefit)
 - i) Morphological and/or histopathological changes (11 papers with 9 showing changes and 2 showing no changes)
 - j) Developmental effects (2 papers showing developmental effects)
9. Additional categories (tables) could have been established covering immune system effects, oxidative stress, fertility and morphological/histopathological changes when adding the experimental papers that were missed by Karipidis. We also note that oxidative stress was not discussed in any detail much like previously by some of the same authors who wrote the ARPANSA TRS-164 report¹⁴. This is a very important topic that needs to be addressed as it was recently by well-respected Swiss expert (BERENIS) group in a newsletter (January 2021)¹⁵. The Swiss experts recognised that pre-existing health conditions may compromise body defence mechanisms and could lead to more severe health effects due to changes in oxidative balance caused by RF exposures.

Experimental Papers missed by Karipidis et al. (70 in total)

ORSAA ODEB Paper ID	Title	Biological Effect Category	Main Author	Year Published
500	The genotoxic effect of radiofrequency waves on mouse brain	Genotoxicity	Karaca	2011
568	Effects of fetal microwave radiation exposure on offspring behavior in mice	Learning/Memory Impairment	Zhang	2015
640	Spatial memory and learning performance and its relationship to protein synthesis of Swiss albino mice exposed to 10 GHz microwaves	Learning/Memory Impairment	Sharma	2014

682	Influence of electromagnetic fields on reproductive system of male rats	Genotoxicity	Kumar	2012
1144	Nonthermal effects of extremely high-frequency microwaves on chromatin conformation in cells in vitro—dependence on physical, physiological, and genetic Factors	Chromatin Conformation	Belyaev	2000
1239	The effects of microwave frequency electromagnetic fields on the development of <i>Drosophila melanogaster</i>	Developmental/ Offspring Numbers	Atli	2006
1332	Effects of microwaves and ELF magnetic field on the phagocytic activity of variously treated rat macrophages	Immune Response	Dasdag	2001
1408	Changes in the chromatin structure of lymphoid cells under the influence of low-intensity extremely high-frequency electromagnetic radiation against the background of inflammatory process	Therapeutic/ Immune System	Gapeev	2011
1409	Responses of thymocytes and splenocytes to low-intensity extremely high-frequency electromagnetic radiation in normal mice and in mice with systemic inflammation	Therapeutic/ Immune System	Gapeev	2010
1410	Anti-inflammatory effects of low-intensity extremely high-frequency electromagnetic radiation: frequency and power dependence	Therapeutic/ Immune System	Gapeev	2007
1502	Suppression of nonspecific resistance of the body under the effect of extremely high frequency electromagnetic radiation of low intensity	Immune Response	Kolomytseva	2002
1512	Impact of microwave at X-band in the aetiology of male infertility	Fertility	Kumar	2012
1518	Shielding effect of mineral schungite during electromagnetic irradiation of rats	Haematological	Kurotchenko	2003
1553	Effect of extremely high frequency electromagnetic radiation of low intensity on parameters of humoral immunity in healthy mice	Immune Response	Lushnikov	2001
1554	Effects of low-intensity ultrahigh frequency electromagnetic radiation on inflammatory processes	Therapeutic/ Immune System	Lushnikov	2004
1593	The production of tumor necrosis factor in cells of tumor-bearing mice after total-body microwave irradiation and antioxidant diet	Therapeutic/ Immune System	Novoselova	2004
1624	Biochemical changes in rat brain exposed to low intensity 9.9 GHz microwave radiation	Cell Signalling/ Enzyme Activity	Paulraj	2012
1625	Enzymatic alterations in developing rat brain cells exposed to a low-intensity 16.5 GHz microwave radiation	Enzyme Activity/Brain Cells	Paulraj	2012
1633	Bone morphogenetic protein expression in newborn rat kidneys after prenatal exposure to radiofrequency radiation	Gene Expression	Pyrpasopoulou	2004
1634	Single millimeter wave treatment does not impair gastrointestinal transit in mice	Colonic Propulsion	Radzievsky	2002
1636	Millimeter wave-induced suppression of B16 F10 melanoma growth in mice: involvement of endogenous opioids	Tumour Growth	Radzievsky	2004
1637	Hypoalgesic effect of millimeter waves in mice: dependence on the site of exposure	Nervous System/ Hypoalgesic	Radzievsky	2000
1638	Peripheral neural system involvement in hypoalgesic effect of electromagnetic millimeter waves	Nervous System/ Hypoalgesic	Radzievsky	2001
1684	Effect of delta-rhythm-modulated extremely high frequency	Sleep/ Behaviour Changes	Subbotina	2004

1960	The non thermal effect of weak intensity millimeter waves on physicochemical properties of water and water solutions	Biochemical Change	Ayrapetyan	2009
2023	Low power microwave interaction with phospholipase C and D signal transduction pathways in myogenic cells	Cellular Signalling	Donato	2004
2029	Denaturation of hen egg white lysozyme in electromagnetic fields: a molecular	Protein Folding	English	2007
2035	Cytogenetic analysis of the effects of 2.5 and 10.5 GHz microwaves on human lymphocytes	Genotoxicity	Figueiredo	2004
2052	Cytogenetic effects of 18.0 and 16.5 GHz microwave radiation on human lymphocytes in vitro	Genotoxicity	Hansteen	2008
2062	Effects of millimeter-wave electromagnetic radiation on the experimental model of migraine	Signalling/Neurons	Sivachenko	2016
2139	The simulation of the cooperative effect of development in a culture of early mouse embryos after irradiation with electromagnetic waves in the millimeter range	Developmental/ Metabolism	Mezhevikina	2000
2152	NF-kappaB DNA-binding activity after high peak power pulsed microwave (8.2 GHz) exposure of normal human monocytes	Cell Signalling/ Immune system	Natarajan	2002
2181	Demodulation effect is observed in neurones by exposure to low frequency modulated microwaves	Signalling/Neurons	Perez-Bruzon	2010
2182	Exposure to ELF-pulse modulated X band microwaves increases in vitro human astrocytoma cell proliferation	Cell Proliferation/ Gene Expression	Perez-Castejon	2009
2193	Permeability changes induced by 130 GHz pulsed radiation on cationic liposomes loaded with carbonic anhydrase	Membrane Effects	Ramundo-Orlando	2007
2242	Millimeter wave-induced modulation of calcium dynamics in an engineered skin co-culture model: Role of secreted ATP on calcium spiking	Cell Signalling/ Oxidative Stress	Sun	2012
2244	Millimeter wave induced reversible externalization of phosphatidylserine molecules in cells exposed in vitro	Membrane Effects	Szabo	2006
2255	Millimeter-wave exposure promotes the differentiation of bone marrow stromal cells into cells with a neural phenotype	Gene Expression/ Cell Differentiation	Tong	2009
2263	Cytogenetic studies in human blood lymphocytes exposed in vitro to 2.45 GHz or 8.2 GHz radiofrequency radiation	Genotoxicity	Vijayalaxmi	2006
2278	Non-thermal microwave effects on protein dynamics? An X-ray diffraction study on tetragonal lysozyme crystals	Protein Structure Changes	Weissenborn	2005
2284	Millimeter wave treatment inhibits the mitochondrion-dependent apoptosis pathway in chondrocytes	Apoptosis	Wu	2011
2285	Experimental study of millimeter wave-induced differentiation of bone marrow mesenchymal stem cells into chondrocytes	Cell Proliferation/ Gene Expression	Wu	2009
2316	Induction of micronuclei in human lymphocytes exposed in vitro to microwave radiation	Genotoxicity	Zotti-Martelli	2000
2320	The effect of microwave radiation on the cell genome	Genotoxicity	Garaj-Vrhovac	1990
2378	Ten gigahertz microwave radiation impairs spatial memory, enzymes activity, and histopathology of developing mice brain	Oxidative Stress/ Behaviour/ Memory Impairment/ Histopathological	Sharma	2017

2711	Involvement of the p38 MAPK signaling cascade in stress response of RAW 264.7 macrophages	Gene Expression/ Cell Signalling/ Immune System	Novoselova	2017
3004	Combined effects of circularly polarized microwaves and ethidium bromide on E. coli cells	DNA Conformational Change	Ushakov	1999
3017	Antiepileptic effects of short-wave radiation in hypogeomagnetic conditions	Epilepsy	Godlevsky	2013
3111	Extremely low-level microwaves attenuate immune imbalance induced by inhalation exposure to low-level toluene in mice	Gene Expression/ Cellular Signalling/ Immune System	Novoselova	2017
3118	Epitaxy of the bound water phase on hydrophilic surfaces of biopolymers as key mechanism of microwave radiation effects on living objects	Protein Conformation	Kuznetsov	2017
3187	Selective changes in locomotor activity in mice due to low-intensity microwaves amplitude modulated in the EEG spectral domain	Locomotor Activity	Van Eeghem	2017
3270	The effects of radar on avian behavior: Implications for wildlife management at airports	Behaviour	Sheridana	2015
3310	Exposure to 18 GHz EMF triggers uptake of large nanosphere clusters by pheochromocytoma cells	Membrane	Perera	2018
3372	Induced movements of giant vesicles by millimeter wave radiation	Membrane	Albini	2014
3378	Effect of acute millimeter wave exposure on dopamine metabolism of NGF-treated PC12 cells	Metabolism	Hass	2017
3646	Microwaves and cellular immunity. I. Effect of whole body microwave irradiation on tumor necrosis factor production in mouse cells	Immune System	Fesenko	1999
3651	Microwaves and cellular immunity: II. Immunostimulating effects of microwaves and naturally occurring antioxidant nutrients	Immune System	Novoselova	1999
3653	Antibody responses of mice exposed to low-power microwaves under combined, pulse and amplitude modulation	Immune System	Veyret	1991
4005	Additive effects of millimeter waves and 2-deoxyglucose co-exposure on the human keratinocyte transcriptome	Gene Expression/ Synergistic Action	Mahamoud	2016
4037	Study of the effects of 0.15 terahertz radiation on genome integrity of adult fibroblasts	Genotoxicity	Franchini	2018
4136	Features of anti-inflammatory effects of modulated extremely high-frequency electromagnetic radiation	Immune System	Gapeyev	2009
4141	Antipruritic effect of millimeter waves in mice: evidence for opioid involvement	Dermal	Rojavin	1998
4142	Pain relief caused by millimeter waves in mice: results of cold water tail flick tests	Behavioural/ Hypoalgesia	Rojavin	2000
4144	Intensity-Dependent and Frequency-Dependent Effects of Microwaves on Cell-Growth Rates	Cell Growth	Grundler	1992
4145	Electromagnetic millimeter waves increase the duration of anaesthesia caused by ketamine and chloral hydrate in mice	Therapeutic	Rojavin	1997
4149	Resonant microwave effect on locally fixed yeast microcolonies	Cell Growth	Grundler	1989
4150	Resonant growth-rate response of Yeast-cells irradiated by weak microwaves	Cell Growth	Grundler	1977
4151	Resonant-like dependence of Yeast growth-rate on microwave-frequencies	Cell Growth	Grundler	1982

4153	Genetic continuity and metabolic-regulation as seen by effects of various microwave and black light frequencies on these phenomena	Cell Growth/ Gene Expression	Webb	1975
4154	Factors affecting the induction of Lambda prophages by millimeter microwaves	Gene Expression	Webb	1979

References

1. Karipidis K, Mate R, Urban D, Tinker R, Wood A. 5G mobile networks and health-a state-of-the-science review of the research into low-level RF fields above 6 GHz. *J Expo Sci Environ Epidemiol.* 2021; 31:585-605.
2. Viotti M. (2020). Preimplantation Genetic Testing for Chromosomal Abnormalities: Aneuploidy, Mosaicism, and Structural Rearrangements. *Genes*, 11(6), 602. <https://doi.org/10.3390/genes11060602>
3. Sharma, A., Kesari, K.K., Saxena, V.K. et al. Ten gigahertz microwave radiation impairs spatial memory, enzymes activity, and histopathology of developing mice brain. *Mol Cell Biochem* 435, 1–13 (2017). <https://doi.org/10.1007/s11010-017-3051-8>
4. Hassold T, Hall H, Hunt P. The origin of human aneuploidy: where we have been, where we are going, *Human Molecular Genetics*, Volume 16, Issue R2, 15 October 2007, Pages R203–R208, <https://doi.org/10.1093/hmg/ddm243>
5. O'Connor, C. (2008) Human chromosome translocations and cancer. *Nature Education* 1(1):56
6. Shubin AV, Demidyuk IV, Komissarov AA, Rafieva LM, Kostrov SV. Cytoplasmic vacuolization in cell death and survival. *Oncotarget.* 2016;7(34):55863-55889. doi:10.18632/oncotarget.10150
7. Belyaev, I. Y., V. S. Shcheglov, et al. (2000). "Nonthermal effects of extremely high-frequency microwaves on chromatin conformation in cells in vitro - Dependence on physical, physiological, and genetic factors." *IEEE Transactions on Microwave Theory and Techniques* 48(11): 2172-2179
8. Belyaev IY. Some biophysical aspects of the genetic effect of low-intensity millimeter waves. *J Electroanal Chem (Lausanne)* 1992; 342 (1): 11-18
9. Sagripanti JL, Swicord ML, Davis CC. Microwave effects on plasmid DNA. *Radiat Res.* 1987 May;110(2):219-31.
10. Totland MZ, Rasmussen NL, Knudsen LM, et al. Regulation of gap junction intercellular communication by connexin ubiquitination: physiological and pathophysiological implications. *Cell. Mol. Life Sci.* 77, 573–591 (2020). <https://doi.org/10.1007/s00018-019-03285-0>
11. Radziewsky AA, Gordiienko OV, Szabo I, Alekseev SI, Ziskin MC. Millimeter wave-induced suppression of B16 F10 melanoma growth in mice: involvement of endogenous opioids. *Bioelectromagnetics.* 2004 Sep;25(6):466-73. doi: 10.1002/bem.20018.
12. Leach V and Weller S. Radio frequency exposure risk assessment and communication: Critique of ARPANSA TR-164 report. Do we have a problem? *Radiation Protection in Australasia*, 34(2), pp. 9-18 (2017).
13. Huss A, Egger M, Hug K, Huwiler-Muntener K, Roosli M. Source of funding and results of studies of health effects of mobile phone use: systematic review of experimental studies. *Environ Health Perspect.* 2007; 115(1): 1-4
14. Australian Radiation Protection and Nuclear Safety Agency (ARPANSA) Technical Series Report 164) <https://www.arpansa.gov.au/research-and-expertise/technical-reports> (last accessed 07 September 2021).
15. Newsletter of the Swiss expert group on electromagnetic fields and non-ionising radiation (BERENIS) - <https://www.bafu.admin.ch/dam/bafu/en/dokumente/elektrosmog/fachinfo->

[daten/newsletter_berenis_sonderausgabe_januar_2021.pdf/download.pdf/Newsletter%20BERENIS%20-%20Special%20Issue%20January%202021.pdf](https://www.berenis.de/daten/newsletter_berenis_sonderausgabe_januar_2021.pdf/download.pdf/Newsletter%20BERENIS%20-%20Special%20Issue%20January%202021.pdf)
(last accessed 07 September 2021).