Project:

The Mechanisms of Health Hazards of Electromagnetic Radiation and Basic Research in Medical Protection

Chief Scientist:

Yu Zhengping, Third Military Medical University, China

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项目名称： 电磁辐射危害健康的机理及医学防护的基础研究

首席科学家： 余争平 中国人民解放军第三军医大学

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一、研究内容

根据环境与职业电磁辐射暴露健康危害涉及的主要频谱特征,选择电磁污染的主要频段,即50-400 Hz 极低频电磁辐射(生活与工业用电)、900-2500MHz 射频电磁辐射(主要的通讯频段),作为主要研究对象,围绕拟解决的关键科学问题,拟开展以下研究:

1. 生物组织电磁能量转换与细胞电磁感受机制研究:① 依照电磁辐射源特

性和生物组织的介电常数、电导率等电磁特性参数,构建相应的辐射源模型以及人体、动物和细胞电磁仿真模型;采用理论计算与实体测量相结合的方法,揭示生物组织对电磁辐射能量吸收、耗散规律和电磁辐射剂量在生物组织中的分布特点,提出新的电磁辐射生物效应剂量指征与测量方法。② 从细胞微观结构与生物大分子的构象出发,研究电磁辐射对细胞间隙通讯(GJIC)、膜受体关键信号分子(EGFR 等)的微观构象和生物电信号传递过程的影响,明确细胞响应电磁辐射的生物物理基础。③ 应用Raman 光谱和红外光谱探测技术分析不同种类细胞对电磁辐射的响应特征,进一步用蛋白组学分析、基因操控等技术方法从细胞凋亡与周期调控、细胞信号转导、氧化与自由基损伤等方面,揭示细胞电磁辐射敏感性差异反应的分子基础。

2. 电磁辐射敏感器官与遗传损伤效应规律及机制研究:① 建立统一的实验

动物和细胞损伤模型,综合运用行为学、形态学、分子生物学和电生理学的研究技术手段,研究电磁辐射对中枢神经系统功能、形态、代谢的可逆和不可逆性损伤的时效、量效关系,确定损伤阈值;从神经系统结构和功能可塑性变化入手,研究阐明电磁辐射致认知功能、神经发育异常的细胞和分子生物学机制。② 从性激素代谢变化、生殖细胞发育及受精过程等方面研究电磁辐射生殖系统损伤特点与机理。③ 从染色体结构与数量改变、基因突变、基因组缺失与扩增、DNA 损伤特征、表观遗传修饰因子等不同层次上探讨电磁辐射致遗传损伤效应和机制。

3. 人群水平电磁辐射健康危害特征与危害监测研究:① 选择特定的环境与职业电磁辐射暴露人群,进行多中心大规模的人群流行病学研究,了解职业与环境电磁辐射暴露特征,在人群水平揭示电磁辐射健康危害特征,分析职业与环境电磁辐射暴露与相关疾病的关联性,明确职业与环境电磁暴露的危险度。② 以实验动物模型和职业暴露高危人群为对象,研究电磁辐射对神经认知、生殖功能损伤与遗传易感性的关联,明确电磁辐射暴露与遗传易感性相互作用的方式,分析独立和联合作用的贡献度。

1. Research Content

Taking into account the main spectrum of characteristics of the environmental and occupational health hazards related to EMF exposure, the main bands of electromagnetic pollution, which are 50-400 Hz or extremely low frequency (daily and industrial use of electricity), and 900-2500MHz or radio frequency (the main communication bands), were selected as the principal objects of study for this project. Focusing on the key scientific issues to be resolved, the following research is intended to be undertaken:

1. Study EM energy conversion in biological tissues and the mechanisms of cell sensitivity to EMF:

① According to the characteristics of EMF, and dielectric constants, conductivity and other electromagnetic parameters of biological tissue, build appropriate source models and simulation models for human, animal and cellular studies; use the combination of methods of electromagnetic theoretical calculations and measurements, reveal the characteristics of EMF absorption, dissipation rules, and distribution characteristics of EMF dose in biological tissue, and propose new dose indication and measurement methods for EMF biological effects.

② By starting from the microscopic structure of cells and conformation of biological macromolecules, study the EMF effects on gap junctional intercellular communication (GJIC), micro-conformation of key signaling molecules in membrane receptors (EGFR etc.) and biological electrical signal transfer processes, and clarify the biophysical basis of EMF cell responses.

③ Through using Raman and infrared spectroscopy detection techniques, analyze the characteristics of different types of cells responding to EMF, and moreover use proteomics, gene manipulation methods etc., and reveal the molecular basis of sensitivity differences in cells responding to EMF, from apoptosis and cell cycle regulation, cell signal transduction, to oxidative and free radical damage etc.

2. Study EMF sensitive organs and the laws and mechanisms of genetic damage effects:

① By building uniform models for experimental animal and cell injury studies, combining techniques such as behavior, morphology, molecular biology and electrophysiology, study time/dose-effects of reversible and irreversible damage on function, morphology, and metabolism of the central nervous system, determine the damage threshold; start from plasticity change of nervous system's structure and function, to research cell and molecular biological mechanisms of EMF-induced abnormalities in cognitive functions and neural development.

② From metabolic changes in hormones, germ cell development and fertilization processes, to analyzing the characteristics and mechanisms of EMF-induced injury in the reproductive system.

③ From different levels such as: the structure and numerical changes in chromosomes, gene mutation, deletion and amplification, characteristics of DNA damage, epigenetic factors etc., to the study of the effects and mechanisms of EMF-induced genetic damage.

3. Study characteristics of population level health hazards and EMF hazard monitoring:

① By selecting groups exposed to specific environmental and occupational EMF, study multi-center large-scale population epidemiology to understand the characteristics of occupational and environmental EM exposure, reveal the characteristics of EMF health hazards in the population level, analyze the relationship between occupational and environmental EMF exposure and related diseases, and clarify the risks by occupational and environmental EMF exposure.

② Based on experimental animal models and high-risk groups by occupational exposure, study

③ 以人群神经、生殖健康危害效应监测评估为重点，在明确损伤特点和机制的基础上，着重从外周血生化、细胞学指标等方面筛选电磁辐射健康危害监测的生物标志物，并在环境与职业电磁辐射暴露人群验证标志物的特异性与敏感性。

the relationship between EMF exposure and neurocognitive, reproductive impairment and genetic susceptibility, and understand the interaction between EMF exposure and genetic susceptibility, and analyze the contribution of independent and combined effects.

③ Focus on monitoring and evaluating nervous and reproductive health effects in the population, based on clarified injury characteristics and mechanisms; select biomarkers for monitoring the EMF health hazards mainly from biochemical, cytological markers etc., in the peripheral blood; and verify the markers' specificity and sensitivity in the population exposed to environmental and occupational EMF .

二、预期目标

（一）本项目的总体目标：

1. 坚持多学科交叉渗透的研究模式，围绕阐明电磁辐射健康危害机理这个基本点，以提出有针对性的医学防护措施为最终目标，从细胞、组织器官、人群三个不同层次，以生物组织感受并对电磁辐射产生响应的作用机制为突破口，研究阐明细胞与生物组织感受、吸收、转化、传递电磁辐射能量的规律，揭示神经系统、生殖系统对电磁辐射损伤敏感的生物学基础和分子机制，明确长期低剂量电磁辐射的遗传损伤效应，提出人群水平损伤效应的生物标志物与危害监测评估的指标，力争使我国电磁辐射生物效应研究与危害防治水平取得新的突破。

2. 推动我国电磁辐射生物学和相关学科的发展，培养一批高水平的中青年科学家，造就一支多学科交叉、具有国际竞争实力的研究队伍，保持我国在此领域已有的特色与领先优势。

（二）五年预期目标:

1. 建立定量检测生物组织电磁吸收剂量的方法与技术平台。建立生物组织电磁能量吸收的生物剂量表征，建立生物组织电磁辐射能量分布计算方法，建立高精度人体电磁仿真模型。这些模型和方法的建立将为电磁辐射生物效应研究实现统一的研究方法和手段奠定基础。

2. 阐明电磁辐射神经、生殖、遗传损伤机制。揭示敏感组织器官损伤过程中细胞信号传导系统的变化、重要功能基因与蛋白质谱表达变化的关键分子事件，明确电磁辐射的遗传损伤位点和效应机制，为电磁辐射危害的医学防治提供靶点。

3. 提出电磁辐射人群健康危害监测与评估体系的科学依据。明确我国电磁辐射健康危险度，发现电磁辐射危害监测的敏感生物标志物，建立通过人群验证的以损伤标志物为核心内容的评估指标体系。

4. 形成一批创新性研究成果。通过本项目研究在国际上本专业领域有影响的SCI 收录杂志上发表论文100-120 篇，获得8-10 项发明专利授权。

5. 促进研究基地建设和人才培养。通过本项目研究建设我国电磁生物学研究中心3-5个，预期培养教育部”长江学者奖励计划”特聘教授1-2名，国家杰出青年科学基金获得者1-2名。培养博士后10-20名，博士生60-80名，硕士生100-120名。

2. Targets

2.1 Main objectives of the project

1. Adhere to interdisciplinary studies, based on clarifying the mechanisms of the EMF health hazards, in order to provide pertinent medical protection strategies. From the three different levels of cells, organ tissues and population, take biological tissue receptors and mechanisms of action response to EMF as a breakthrough, study the laws of perception, absorption, transformation, and transmission of EMF energy in cells and tissues, reveal the biological basis and molecular mechanisms of EMF damage sensitivity in the nervous system, the reproductive system, identify clear genetic damage effects due to long-term low-dose EMF, and set biomarkers for population level damage effects and indicators for risk monitoring and evaluation. Aim to make new breakthroughs for our research in EMF biological effects and hazards control.
2. Promote the development of EMF biology and related disciplines in China; develop large quantities of high-level young scientists, and create a multi-disciplinary, internationally competitive research team to keep our individual features and leading advantages in this field.

2.2 Five-year targets

1. Establish the methods and technology platform for quantitative detection of absorbed dose in biological tissues. Make biological dose characterization for electromagnetic energy absorption in tissue, establish calculation methods for distribution of EMF energy in tissue, and build high-precision electromagnetic simulation models of the human body. The establishment of these models and methods are the basis for achieving a unified research method for the study of EMF biological effects.
2. Clarify the mechanisms of EMF introduced injury in nervous, reproduction, and hereditary systems. Reveal the key molecular events in cell signal transfer system change, important functional gene expression and protein spectrum change, during sensitive tissue organ damaging processes, and clarify the mechanisms of EMF induced genetic damage receptors and effects, in order to help to provide medical control of EMF hazards.
3. Propose scientific evidence for monitoring and evaluation systems of human health hazards due to EMF. Determine the EMF health risk level in China, find the sensitive biomarkers for EMF monitoring, and establish evaluation index systems with the core content as injury markers validated at the population level.
4. Generate a number of innovative research results. Through the project study, publish 100–120 papers in the SCI journals with international impact, obtain 8–10 invention patents.
5. Promote research bases and personnel training. Through this research project, construct 3-5 Electromagnetic Biology Research Centers, train 1–2 distinguished Professors for the “Changjiang Scholars Program”, get 1–2 winners of National Outstanding Youth Science Foundation, 10–20 Postdocs, 60–80 PhDs, and 100–120 Masters degrees.

三、研究方案

（一）总体思路：

1. 学术思路

本项目研究在总体设计上针对电磁辐射的损伤效应与危害防治需要解决的重大科学问题，综合应用多学科交叉的技术手段，围绕揭示生物组织与细胞感受电磁辐射物理信号—电磁辐射能量在生物组织转化、传递及剂量测量—引起敏感组织与细胞的损伤—人群健康危害特点与危险度—危害生物标志物与监测评估这一核心主线，将物理学、生物学、医学不同学科领域的共同关注的科学问题综合考虑、交叉融合，布置研究内容和设置研究课题，注重效应的观察与机理的探讨相结合，宏观层面整体效应与微观层面分子、细胞效应的观察相互印证，揭示电磁辐射对健康危害效应的规律和特点，为我国电磁辐射健康危害的综合防治奠定科学基础。基于上述指导思想，本项目总体设计的研究思路如图1 所示。

2. 技术途径：

① 严格设计与控制暴露参数与暴露条件。在本项目参与单位的不同实验室（中心），选择同样的生物学研究对象（包括动物和细胞），应用相同的电磁辐射

暴露物理参数，复制环境与职业暴露模型，通过物理指标与生物指标相结合、理论计算与实测验证相结合的方式，实现本项目研究中多实验室（中心）电磁辐射暴露物理剂量、生物吸收剂量、观察效应指标的定量化、规范化和统一性，以确保不同实验室（中心）研究结果的科学性、可靠性和可重复性。

② 应用不同频段的电磁辐射源，采用辐照法复制不同种属实验动物和体外培养细胞的实验模型，根据实验设计的要求分别模拟环境与职业暴露条件，在辐照暴露后的不同时相点取整体动物、生物组织与器官、细胞等生物样本，测试分析各种效应指标，比较不同频段电磁辐射效应的特点。

③ 综合应用蛋白质组、基因操纵和生物信息学等技术手段，大规模、高通量地在整体、细胞与分子层次解析电磁辐射暴露引起的重要分子事件，在不同层次寻找电磁辐射损伤敏感分子标志物，通过调控基因与蛋白的表达，探讨重要功能基因与蛋白的变化与生物学效应的关系，明确危害医学防治的靶点。

3. 可行性分析：

① 具备完成本项目研究的良好基础。在电磁辐射生物学效应和发生机理与危害防治研究领域，近二十年来我国已逐步形成了自己的优势和特色，某些研究方向的水平与贡献已在国际前沿占有一席之地，为进一步开展本项目的研究奠定

3. Research Program

3.1 General idea

3.1.1 Academic idea

The contents of this project are the major scientific issues related with the EMF damage effects and hazards control. Based on interdisciplinary techniques, the main research topics are set to reveal the following: biological tissue and cell response to the physical signals of EMF; conversion, transfer and dosimetry measurement of EMF energy in biological tissue; related damage in sensitive tissues and cells; characteristics and risks in population health hazards; risk biomarkers, and risk monitoring and evaluation; and consider these common scientific problems from various fields such as physics, biology, medicine. From various aspects, set research contents and tasks, focus on combination of effects observation and study of mechanisms, observe the general effects from the macro level, and molecular and cellular effects from micro level, reveal the rules and characteristics of the health hazards effects caused by EMF, and establish the scientific basis for EMF health hazards control. Based on the above guiding principles, the idea of the overall project study is shown in Figure 1.

3.1.2 Technical approach

① Strictly design and control exposure parameters and exposure conditions. In different laboratories/centers of the participants in this project, select the same biological object for research (including animals and cells), use the same physical parameters of EMF exposure, copy environmental and occupational exposure models, by combination of physical indicators and biological indicators, combination of theoretical calculations and measurements, achieve the quantification, standardization and uniformity of the physical dose, the biological absorbed dose, and the effects indicators for observation EMF exposure from multi-laboratory/centers study of the project, in order to ensure the scientific, reliability and repeatability of the research results from different laboratories/centers .

② Use EMF sources from different bands, use exposure methods replicating experimental models for different species of animals and cultured cells in vitro, simulate environmental and occupational exposure conditions according to the experiment requirements. At different time points after exposure, take the biological samples from whole animal, tissue and organs, cells etc., test and analyze different effect indicators, compare the characteristics of EMF effects from different frequencies.

③ Integrate different techniques such as proteomic/genetic manipulation, and bioinformatics techniques, analyze important molecular events caused by EMF exposure in the whole body, cell and molecular level, find molecular markers sensitive to EMF damage at different levels, through the regulation gene and protein expression, explore the relationship between changes of important functional genes/protein, and the biological effects, clarify targets of prevention and control of medical hazards.

3.1.3 Feasibility analysis

① Good foundation for completing the research project

In the past two decades, China has gradually formed its own advantages and characteristics in the

了良好的工作基础；本项目的主要研究内容的选择充分考虑了我国的特色与优势。本项目各课题的负责人各自依托的实验室已有相当的规模并取得了很好的科研成果，具备高质量完成本项目研究的科研条件。

② 业已形成物理学、生命科学领域多学科交叉的科技攻关队伍。特别需要强调的是，本项目集中了我国从事电磁辐射生物效应与危害防治研究领域的骨干优势单位，承担单位与主要学术骨干之间在此领域已形成良好的协作关系，近二十年来，在联合申请各类科研课题、共同主办国际学术会议、互相利用实验室工作条件、交流骨干科研人员等方面协作十分活跃；本项目的研究队伍是一个以优秀中青年科技骨干为主、站立于国际学科前沿、学风严谨求实的多学科协作攻关团队，多数是从海外留学归来的、并在本领域中取得了良好的研究业绩的中青年科学家。

③ 具备完成本项目研究的良好支撑条件。从事电磁辐射生物学研究与一般的生物医学研究不同，除应具备生物医学研究的支撑条件外，还需要具备不同物理参数的电磁辐射源及其相应的物理参数检测、屏蔽辐照条件，本项目研究将有四个国家重点实验室、十个省部级（军队）重点实验室共同参与，集中了国内本领域的骨干优势单位，具备完成本项目研究的支撑条件和技术平台，因此，完成本项目研究不需另行购置重大仪器设备。

④ 建立了通畅的国际合作与交流的渠道。本项目各课题的承担单位在不同的学科领域已经与美、日、欧洲发达国家的多个实验室建立了实质性长期合作关系，将确保本项目的研究工作与国际发展的前沿同步。

（二）创新点与特色：

① 学科交叉融合共同解决电磁辐射效应研究领域的重大科学问题。近十年来，生命科学的迅猛发展吸引了众多的物理学家进入生命科学的研究领域，在电磁辐射生物学方面物理学领域的研究工作较多地集中在微观层次观察电磁辐射对电子、带电离子、原子、分子的状态和运动的影响以及这些影响引起的生物大分子的结构、构象、构型的变化，并对这一物理过程进行数学建模，将研究无机物质的手段和方法简单引用到复杂的生命系统的研究中，所获得的结果往往缺乏机理和效应之间的有机联系，与生命科学融合不够；另一方面，生命科学领域尽管在生物体各个层次上对电磁辐射生物效应做了许多研究与观察，但是对这些生物效应的原初物理过程和规律缺乏深入检讨，例如对细胞感受电磁能量的生物物理学过程缺乏深入认识，生物学效应研究所获得的结果难以在统一的生物剂量量纲下对比分析。克服这些电磁辐射生物学研究领域的不足和技术难点，迫切需要物理学和生命科学在更深层次和更大范围的交叉融合。

research area of EMF biological effects and their mechanisms, and hazard control research. Some researchers' level and contributions have taken an important place in the international frontier, and this has laid a good working basis for further research in the project. The selection of the project's main research contents has taken full account of the characteristics and advantages that China has. The main responsible scientists and its laboratories have relative scales and have achieved excellent scientific research results, which have the high quality research conditions for this project.

② Multidisciplinary scientific research team in the area of physics, life sciences

An additional emphasis is that this project includes the key research groups of China in the area of EMF biological effects and hazard control, the main academic groups and researchers have already built good cooperative relations in this area. In the past two decades, they have active collaborations in application for various types of joint research projects, co-sponsoring international academic conferences, mutually using laboratories, researchers and other key aspects. The project research team stands in the international academic cutting-edge, based on rigorous and realistic multi-disciplinary study, contains mainly outstanding young researchers, most of whom have overseas study experience and have achieved good performance in these fields.

③ Good supporting conditions for completing the research project

There is a difference between EMF biological research and other biomedical research in general. Other than the support conditions for biomedical research, it also needs EMF exposure sources with different physical parameters, and corresponding conditions for physical parameters detection and EMF shielding. The project has four key national research laboratories and ten provincial (military) key laboratories as participators, including key research groups of China in this field, and the supporting conditions and technology platforms for the completion of this study. Therefore, major equipment purchase is not required for the completion of this research project.

④ A smooth channel for international cooperation and exchanges

The project's commitment uses established long-term partnerships in varioius disciplines with a number of laboratories in United States and Japan, which will ensure the synchronization of the research with the developments in the international frontier.

3.2 Innovation and features

① Interdisciplinary integration to solve major scientific issues in the research of EMF effects

Over the past decade, the rapid development of life sciences has attracted a large number of physicists entering the research of this field. In the field of physics for EMF biological research, the concentration was on the micro-level observation of the EMF influence on the status and movements of electrons, charged ions, atoms, molecules, and the changes in structure, conformation, configuration of biological macromolecules caused by these effects. In addition, mathematical models were built for these physical processes, which simply introduced the means and methods of inorganic substances research into and complex research of living systems. The obtained results often lacked an organic link between the mechanism and effect, and did not integrate enough with the life sciences.

On the other hand, in the field of life sciences, although a lot of research and observations have been done for the EMF biological effects at all levels of the organism, it lacked an in-depth review of primary physical processes and the laws of biological effects, such as biological, physical

本项目针对研究对象的复杂性和研究技术条件的特殊性，综合应用物理学、生物学和医学的技术策略，深入研究电磁辐射危害健康的效应，从研究思路、研究手段、研究内容都具有很强的创新性。

② 紧紧围绕生物损伤效应的量效关系，定量研究电磁辐射生物损伤效应。首先，用统一的物理量纲衡量暴露条件，将复杂的频段效应关系规律化而后简明化，使生物效应的数据可以相互比较，找到生物损伤效应的频段特征和与电磁辐射物理参数的关系；其次，生物效应研究设计中如能用统一的生物剂量单位来表征暴露强弱程度，将可能在细胞、器官与整体不同层次明确电磁辐射损伤效应的阈值，确定电磁辐射暴露的安全剂量范围，为进一步制订人员安全暴露标准奠定科学基础。

③ 结合我国已有的特色与优势，选择新的突破口。本项目拟解决的关键科学问题和研究内容都是电磁辐射生物效应与危害防治领域的国际前沿。更重要的是，我们立足于我国在此领域已有的工作基础，拟进一步开展的工作将可能形成新的突破。例如，深化我国在测量生物电磁特性变化与生物组织电磁能量转换过程方面的研究，将原初物理过程与生物效应研究相结合，以活体生物组织电磁特性变化作为机体电磁能量转换与分布指征，揭示健康危害效应的生物物理机制，将可能在解决生物组织吸收剂量方面取得突破；从细胞电磁感受位点与敏感性差异入手，在重要功能基因与蛋白（膜受体、离子通道）等不同层次研究揭示电磁生物效应机制的关键分子事件，将可能阐明细胞电磁辐射感受与敏感性差异的机制；针对敏感器官损伤特点的深入研究，将可能在电磁辐射与多种疾病发生的关联上提出新理论、新观点。因此，通过本项目的研究，将进一步保持我国领先的特色与优势方向，并可能形成新的突破。

④ 微观与宏观结合，提出防治电磁辐射危害的创新策略。由于电磁辐射生物学损伤效应特点和机理尚未阐明，对其危害防治的医学靶点不清，更缺乏危害监测与评估的生物标志物，因此，不可能提出电磁辐射危害的防治的针对性措施与策略。目前国际上对电磁辐射危害防治的主要工作集中在研究物理防护措施，用不同的材料屏蔽或吸收电磁辐射的能量，但在人群水平如何监测与防治电磁辐射的危害仍缺乏研究。本项目研究在开展人群流行病学研究的基础上，获得我国环境与职业电磁辐射健康危害的核心数据，明确电磁辐射健康危害特征与程度，发现电磁健康危害生物标志物，为进一步结合我国对疾病防控的三级预防体制，在宏观上提出针对电磁辐射危害的限制暴露与危害监测的具体措施奠定基础，为国家开展电磁辐射危害防治提供科学依据。

processes of EMF perception, which are difficult to analyze in a unified biological dose dimension for the results obtained by biological effects research.

In order to overcome these deficiencies and technical difficulties in the fields of biology research, a deeper level and a wider range of cross-integration between physics and life sciences are urgently needed. Aiming at the complexity and specialty of the technical conditions of the research subjects, the project implements the technology strategy of integrated physics, biology and medicine to study in-depth the EMF health hazard effects. It has very strong innovation in research ideas, research tools, and research contents.

② Concentrate on the dose-response of the biologically damaging effects, and quantification research of EMF biological damaging effects

First of all, measure with a unified dimension of physics for exposure conditions, find the rules of the complex relationship of frequency band and effect, and simplify it to find the relationship between the spectrum of characteristics of the biological injury effects and physical parameters of EMF; secondly, in the study of biological effects, if uniform biological dose units can be used to characterize the intensity of exposure, EMF damage thresholds in the different levels, such as cell, organ and body, will be determined, which clarify the dose range for EMF exposure, and set the scientific basis for further formulating standards for safe exposure.

③ Combine with our existing features and advantages, to discover the new breakthrough

The scientific issues and research contents of this project are the international frontier of the EMF biological effects and hazards prevention and control. More importantly, based on our existing research in this field, we can possibly make a new breakthrough by further development.

For example, deepening the research in the measurement of changes of EM properties, EMF energy conversion process in biological tissue, combining the primary physical processes and biological effects research, taking the EM properties change of biological tissues in vivo as the indications for EM energy conversion and distribution in the body, revealing the biophysical mechanisms of health hazards effects, we may make the breakthrough in solving absorbed dose in the tissues; …

④ Combine micro and macro, make the innovative prevention strategies for the electromagnetic radiation hazards

…

（三）课题设置

课题1、生物组织电磁能量转换与生物剂量测量研究

预期目标：

① 明确电磁暴露对活体生物组织与细胞电磁特性的影响特点；

② 揭示电磁辐射能量在生物组织的吸收、分布规律，并实现高精度的计算、建模与仿真模拟；

③ 建立生物组织电磁吸收剂量的测量方法。

研究内容：

1. 活体组织与细胞的生物介电特性研究

采用介电电泳及介电谱测量表征方法,研究活体组织与细胞在电磁辐射环境下的介质极化、电导、损耗效应，以及介电频谱特征。从电介质物理的角度，建立电磁辐射与活体组织、细胞相互作用物理模型,建立多频段的不同组织介电特性数据库，提出加速辐照作用下细胞、组织生物效应的介电表征评价方法。

2. 生物组织电磁能量吸收与分布研究

利用与人体电磁参数一致的等效介质和仿真模型,构建高精度电磁谐振腔测试系统,加载不同频率、强度等物理参数的电磁辐射,精确的测量出人体等效部位电磁能量的吸收、耗散及分布值,并实现生物组织电磁能量吸收与分布的仿真模拟。在实验研究基础上,通过理论分析,构建电磁辐射对人体组织作用的生物物理模型，揭示机体电磁辐射能量吸收分布与生物效应的关系。

3．生物组织电磁吸收剂量测量方法研究

用改进的FDTD 和FEM 等计算方法, 在计算生物组织对电磁辐射能量的吸收和耗散规律以及相应的剂量分布的基础上,采用高精度电场、磁场探针、光纤传感器对仿真模型内部剂量分布进行精确的测量。揭示环境电磁辐射参量、生物组织电磁特性与生物体内电磁辐射剂量分布规律的关系,提出电磁辐射生物吸收剂量指标，建立测量方法。

经费比例：14.5%

承担单位：华东师范大学、西安交通大学、电子科技大学

课题负责人：陈树德

学术骨干：乔登江、邱爱慈、庞小峰、钟力生

3.3 Tasks

Task 1: The electromagnetic energy conversion in biological tissues and biological dosimetry study

Targets:

1. Clarify the electromagnetic exposure influence on living tissue and cell's electromagnetic properties;
2. Reveal absorption and distribution rules of the electromagnetic radiation energy in biological tissue, and realize high-precise calculation, modeling and simulation;
3. Establish tissue electromagnetic absorption dosimetry measurement.

Studies:

1. Study dielectric properties of living tissues and biological cells

Use dielectrophoresis and characterization of dielectric spectroscopy measurement methods to study polarization, conductivity, loss effect, and dielectric spectral characteristics of living tissues and cells in the EMF environment. From the dielectric physics point of view, establish a physical model of EMF interaction with living tissue and cells, and establish a multi-band dielectric properties database for different tissues, make dielectric characterization evaluation methods for cells, tissues biological effects under accelerated exposure.

2. Study EM energy absorption and distribution in tissue

Consistent with media which has equivalent electromagnetic parameters of human and simulation model, build a high-precision electromagnetic resonator test system, load EMF with different frequencies, intensities and other physical parameters, accurately measure the absorption, consumption and distribution of EMF in the equivalent body parts, and achieve EM simulation for energy absorption and distribution in tissues. Based on the experimental study and theoretical analysis, build a biophysical model of human tissue under EMF exposure, and reveal the relationship between the biological effects and the electromagnetic energy absorption and distribution in body.

3. Study dosimetry measurement methods of EM energy absorption in tissue

Use the improved calculation methods such as FDTD and FEM, based on the calculation of the EMF energy absorption and dissipation in biological tissues, and the corresponding dose distribution, use high-precision electric fields, magnetic field probes, and optical fiber sensors, to accurately measure the internal dose distribution in the simulation model. Reveal the parameters of environmental EMF, the relationship between EM properties of biological tissue and EMF dose distribution, propose dose absorption index for biology EMF, and establish measurement methods.

Funding ratio: 14.5%

Research groups: East China Normal University, Xi'an Jiaotong University, University of Electronic Science and Technology

Project Leader: Shude Chen

Academic supporters: Qiaodeng Jiang, Aici Qiu, Xiaofeng Pang, Lisheng Zhong

课题2、细胞电磁感受机制与差异性研究

预期目标：

① 明确几类重要功能细胞的电磁辐射敏感性，确定细胞损伤的量效关系，提出损伤阈值；

② 从细胞信号转导途径和重要功能蛋白等方面，研究阐明电磁辐射致细胞损伤的分子机制。

研究内容：

1. 细胞电磁感受位点与机制研究

利用Raman 光谱、红外光谱等光谱探测技术，研究细胞水平电磁辐射能量感受与传递相关的重要细胞微观结构和生物大分子如细胞缝隙连接、表皮生长因子受体、细胞膜脂质双分子层等在外源性电磁暴露后的变化；利用高灵敏的超导量子干涉仪（SQUID）和磁共振成像技术研究电磁辐射对脑中内源磁性颗粒（Fe_3O_4）形成及其分布的影响。利用超弱光子检测技术、电子顺磁共振技术（ESR）以及纳米探针技术等研究电磁辐射对一些特殊酶（如Na^+-K^+-ATPase、F_0F_1-ATPase）的活性、细胞膜结构（如脂筏等）的影响，明确细胞感受电磁辐射的位点与机制。

2. 不同类型细胞对电磁辐射敏感性研究

选择对电磁辐射敏感的神经系统、生殖系统、免疫系统和视觉系统的代表性细胞，如神经系统的神经元和胶质细胞、生殖系统的滋养层细胞和精子、免疫系统的树突状细胞和T 细胞、眼睛的晶状体上皮细胞为研究对象，以指示DNA 双链断裂的早期指标γ-H2AX 焦点形成、细胞增殖与凋亡、细胞周期变化为指标，评价不同种类重要功能细胞对电磁辐射敏感的量效关系，提出不同种类细胞损伤阈值。

3. 细胞电磁辐射敏感性差异的机制研究

从细胞重要功能蛋白表达与抗氧化损伤两个方面，重点探讨细胞电磁辐射敏感性差异的机制。利用蛋白质双向电泳（2-D）技术结合质谱分析不同敏感性细胞的蛋白质表达谱变化，寻找该图谱上蛋白质表达的差异，根据蛋白质表达差异数量与丰度确定细胞对电磁辐射敏感性差异的物质基础。应用电子自旋捕获法（ESR）、电化学法（ECD）、DCFH-DA 探针等技术，检测细胞内氧自由基、羟自由基的生成和抗氧化系统的酶活性变化，比较不同电磁辐射敏感性的细胞内抗氧化系统及其调控的变化。

经费比例：17.5%

承担单位：浙江大学、中国科学院电工研究所、北京工业大学

Task 2: The cell sensitivity in responding to electromagnetic fields and its underlying mechanisms

Targets:

1. Specify the EMF sensitivity of the important functional cells, determine the dose-response relationships, and specify the damage thresholds;
2. Study the molecular mechanisms of cell injury caused by EMF by means of studies in cell signal transduction pathways and the important functional proteins.

Studies:

1. Study in EMF perception at the cellular level and its mechanisms

Techniques of Raman spectroscopy and infrared spectroscopy spectrum detection technology are to be used to test the changes at cellular levels after exogenous EMF exposure in key intracellular micro-structures and biological macromolecules such as cell gap junctions, epidermal growth factor receptor, and cell membrane lipid bilayer, etc., (which are closely related to the perception and transmission of EMF);

Techniques of SQUID (highly sensitive superconducting quantum interference device) and MRI (magnetic resonance imaging) are to be used to study EMF effects on the formation and distribution of endogenous magnetic particles (Fe_3O_4) in the brain.

Techniques such as ultra-low-light detection technology, electron spin resonance (ESR) technology, and nano-probe technology, etc., are to be used to declare EMF effects on activities of some special enzymes (eg, Na +-K +-ATPase, F0F1-ATPase) , the intracellular receptors of EMF and its mechanism .

2. EMF sensitivity of different types of cells

Typical cells in systems sensitive to EMF exposures such as neurons and glial cells in the nervous system, trophoblasts and germ cells in the reproductive system, dendritic cells and T cells in the immune system, and epithelial cells of lens in the visual system, etc., are selected to test biological endpoints of early markers of DNA double-strand breaks, γ-H2AX foci formation, cell proliferation and apoptosis, and changes in cell cycles. These biological endpoints are further studied in dose-response relationships and thresholds of EMF damage.

3. Study in mechanisms of the cell sensitivity difference to EMF

Biological endpoints of the expression of important functional proteins and anti-oxidation are to be studied in the exploration of the mechanism of cell sensitivity differences to EMF.

Techniques of two-dimensional electrophoresis of protein (2-D) technology and mass spectrometry are to be used to analyze the expressions of proteins in cells with different sensitivities to EMF. EMF sensitivities of cells are to be determined by the kinds and abundances of proteins expressed after EMF exposure.

Techniques of ESR (electron spin-trap), ECD (electrochemical detector), and DCFH-DA probe technology are to be used to detect the formations of free radicals (oxygen free radicals and hydroxyl radicals), the activities of enzymes in the anti-oxidative system, the changes and regulations of the intracellular anti-oxidative system after EMF exposure in cells with different EMF sensitivities.

Funding ratio: 17.5%

Research groups: Zhejiang University, Institute of Electrical Engineering Chinese Academy of Sciences, Beijing University of Technology

课题负责人：许正平

学术骨干：宋涛、曾群力、吴水才、戴道锌

课题3、电磁辐射对中枢神经系统的损伤效应及其机理研究

预期目标：

① 确定电磁辐射对认知功能、神经系统发育不可逆性损害的各参数阈值；

② 揭示电磁辐射致大脑认知功能障碍的神经回路和突触损害基础；

③ 揭示电磁辐射致神经系统发育障碍的细胞和分子基础。

研究内容：

1. 电磁辐射对认知功能与神经系统发育不可逆性损害的阈值研究

分别采用神经行为学、神经形态学、神经电生理学、脑功能成像和生物化学等技术，观察不同频率、剂量、时间和空间距离等不同参数的电磁辐射后，大脑认知功能相关主要脑区（新皮层、内嗅皮层和海马等）中主要细胞、核团等各层次功能变化过程，分析与认知功能行为异常的相关性，以此确定电磁辐射对大脑认知功能不可逆性损伤的各参数阈值。观察不同发育时间段（E12.5 到P30），实验动物新皮层、海马、小脑皮层、大脑皮层下白质结构形态和功能的发育变化，检测个体成熟后（P60）相关脑区功能受损的程度，确定电磁辐射对神经系统发育不可逆性损伤的各参数阈值。

2. 电磁辐射致认知功能损伤的神经回路和突触机制研究

采用多通道电活动记录技术，膜片钳记录技术、双光子成像技术和脑功能成像技术等手段，观察电磁辐射后新皮层、内嗅皮层和海马等认知功能相关脑区主要神经回路变化，包括神经回路中各脑区主要神经元信息传送特性、信息整合特性改变、对神经回路电活动振荡的作用及干预能力改变等，分析电磁辐射对神经回路的损害机制；观察电磁辐射损害敏感的认知功能神经回路突触结构和功能的变化，观察突触末梢分叉、突触囊泡循环、树突分枝、数突棘数目和复杂度、关键性功能性受体通道（如电压门控钾、钙通道等）数量和状态、膜被动和主动特性、树突信息整合能力、以及与突触可塑性发生能力密切相关大的关键分子（如synapsin I, 突触相关蛋白25 和突触后密度蛋白95 等）表达与功能的变化，以分析电磁辐射对突触及突触传递损害基础。应用特异的激动剂或抑制剂（包括si-RNA干扰），观察电磁辐射引起的认知功能损伤通过生物体内的自身反应分子获得逆转的可能途径。

Project Leader: Xu Zhengping
Academic supporters: Song Tao, Zeng Qunli, Wu Shuicai, Dai Daoxin

Task 3: The effects of electromagnetic fields on the central nervous system

Targets:

1. Determine the threshold of irreversible damage effects of EMF on cognitive functions and the development of the nervous system;
2. Reveal the biological mechanisms of EMF damage effects on neural circuits and synapses involved with brain cognitive functions;
3. Reveal the mechanisms of EMF effects on developmental retardation in the nervous system at the cellular and molecular levels.

Studies:

1. Study the threshold of irreversible damage in the development of cognitive function, and nervous system due to EM radiation

To determine the threshold levels of irreversible effects on cognitive functions after exposures to various EMF with different frequencies, intensities, periods, and distances, dynamic functional changes in various structures of key cells and nuclei in important brain areas (such as neocortex, entorhinal cortex and hippocampus, etc.), which are responsible for cognitive functions, and their relation with cognitive functions are to be studied using a combination of neurobehavior, neuromorphology, neuro-electrophysiology, cerebral functional imaging and biochemistry approaches.

To determine the threshold levels of irreversible EMF effects on developments of the nervous system, developmental changes (period E12.5-P30) in morphology and functions of white matter of neocortex, hippocampus, cerebellar cortex and cerebral cortex are to be observed in experimental animals.

In addition, seriousness of damages in related brain area is to be examined when animals are mature (P60).

2. Study mechanisms of EMF effects on neural circuits and synapses of cognitive functions

To study the mechanism of EMF effects on neural circuits, techniques of multi-channel electrical activity recording, patch clamp recording techniques, two-photon imaging and cerebral functional imaging and other techniques are to be used to test changes of neural circuits in important brain areas (such as neocortex, entorhinal cortex and hippocampus, etc.) after EMF exposure, including changes of signal transmission between major neurons, signal integration, electrical activity oscillations, and the capacity of intervention.

To study the mechanisms of EMF effects on synapses and synaptic transmission, the following biological effects are to be tested:

- changes of synaptic structure and functions in neural circuits involving with cognitive functions which are sensitive to EMF exposures;
- changes in branches of synaptic terminals, cycling of synaptic vesicles, branches of dentrites, number and complexity of dendritic spines;
- changes in the number and state of the key functional receptor channels (such as voltage-gated potassium, calcium channels, etc.), passive and active properties of membranes, information integration capabilities of dendrites, as well as changes in expressions and functions

3. 电磁辐射致神经系统发育障碍的机理研究

采用神经形态学、生化分子生物学和全胚胎培养等技术，观察不同发育时间段（E12.5 到P30）电磁辐射后，新皮层、海马、小脑皮层、皮层下白质等脑区神经发育中的关键细胞事件，包括神经元轴突导向、树突成熟、细胞极性、神经元迁移、突触形成与成熟、脑内神经干细胞增殖和定向分化变化，并分析上述神经系统发育中细胞事件异常改变与相关脑区的发育性组织结构和行为功能障碍的关系。在此基础上，选择典型细胞事件发生中的相关关键分子（如netrin, Wnt, sonic hedgehog, NATRE, 细胞骨架蛋白等），观察电磁辐射对其表达和功能的影响，并与相关脑区的发育性组织结构和行为功能障碍发生进行相关性分析。

经费比例：15.5%

承担单位：复旦大学、中国人民解放军第三军医大学、华东师范大学

课题负责人：梅岩艾

学术骨干：夏若虹、赵冰樵、胡志安、胡长龙

课题4、电磁辐射的生殖危害效应与机理研究

预期目标：

① 明确电磁辐射和生殖损伤效应之间的频率效应关系、剂量效应关系；

② 明确电磁辐射对性激素代谢、精子发育、受精过程的危害效应与机理。

研究内容：

1. 电磁辐射对性激素代谢的影响与机制研究

应用不同频率电磁辐射暴露的整体动物模型，以观察剂量 - 反应关系为出发点，以下丘脑 - 垂体 - 性腺轴为主线，研究电磁辐射对下丘脑-垂体激素（性腺激素释放激素、卵泡刺激激素、黄体生成素等）、性激素及衍生物（睾酮、脱氢表雄酮、雌二醇、雌酮等）、性激素代谢调控蛋白与关键酶（性激素结合球蛋白、17-α羟化酶、类固醇脱氢酶等）的影响及机制。

of the key molecules (such as synapsin I, synapse-associated protein 25 and the postsynaptic density protein 95, etc.) which are closely related to the plasticity of synapses in synaptogenesis;
In addition, specific antagonists or inhibitors (including si-RNA interference) are to be used to measure adverse EMF effects on cognitive functions caused by auto-reactive molecules.

3. Study the mechanism of EMF effects on developmental disorders of the nervous system
To observe the key intracellular events (including neuron axon guidance, dendritic maturation, cell polarity, neuronal migration, synapse formation and maturation, brain neural stem cell proliferation and changes of directed differentiation) in different developmental periods (E12.5 to P30) of the neural system in the neocortex, hippocampus, cerebellum, cortex, subcortical white matter and other brain regions after EMF exposure, and techniques in neuromorphology, biochemistry molecular biology and whole embryo culture etc., are to be used to test abnormalities in the above mentioned events and their relations with histological structure in development as well as disorders in behavior;
On this basis, relevant key molecules (such as netrin, Wnt, sonic hedgehog, NATRE, cytoskeletal proteins, etc.) in these typical intracellular events are to be tested to see EMF effects on the correlation of their expression with abnormal changes in developmental histological structure of related brain areas and disorders of behavior.

Funding ratio: 15.5%
Research group: Fudan University, Third Military Medical University, East China Normal University,
Project Leader: Mei Yanai
Academic supporters: Xia Ruohong, Zhao Bingaiao, Hu Zhian, Hu Changlong

Task 4: The effects of electromagnetic fields on the reproduction system

Targets:

1. Define the frequency-effect and dose-response between EMF and reproductive damage effects;
2. Define the EMF hazard-effects and the mechanisms on sex hormone metabolism, sperm development, and fertilization.

Studies:

1. Study EMF effects and mechanisms on sex hormone metabolism
Use animal model exposure to different frequencies of EMF, start from the dose-response relationship, followed by the main thread as hypothalamus - pituitary - gonadal axis, study the effects and mechanisms of the hypothalamus - pituitary hormones (gonadotropin-releasing hormone, follicle-stimulating hormone, luteinizing EPO, etc.), sex hormones and derivatives (testosterone, DHEA, estradiol, estrone, etc.), sex hormone metabolism protein and key enzymes (sex hormone binding globulin,17-α hydroxylase, steroid dehydrogenation enzymes etc.).

2. 电磁辐射对精子发育与调控的影响及机制研究

从雄性性腺轴、睾酮等性激素分泌及调控、巨噬细胞旁分泌及调控等环节的改变研究电磁辐射如何影响精子的发生发育；建立体外生精细胞原代培养体系，观察电磁辐射对生精细胞发育各期功能状态的影响;从与生殖细胞发育相关调控通路的多基因关联入手，选择与精子发生相关调控基因、环境应答基因、核受体基因、氧化应激相关基因和激素受体受体为候选基因，进行大样本、大规模SNPs位点分析。研究电磁辐射对调控生殖细胞发育的重要信号转导途径（G 蛋白/酪氨酸蛋白激酶信号转导系统、Wnt/PI3K/GSK3β、JAK/STATs 信号转导系统）的影响，在细胞膜受体、胞浆受体、胞浆信号转导蛋白、核受体与蛋白的激活、转位、失活等不同环节，揭示电磁辐射生殖损伤效应的分子机理与信号转导机制。

3．电磁辐射对受精过程与受精卵发育的影响及机制研究

着重研究以精卵质膜融合为关键步骤的受精过程，围绕精卵识别、精卵结合和精卵质膜融合的三个关键受精环节，研究电磁辐射对精子去整合素金属蛋白酶（ADAM）家族成员、lzumo 蛋白、DE/CRISP1 蛋白和Equatorin、FAP - 1、MA - 24、MH61、FLB1 等精子膜蛋白的表达和精卵质膜融合的影响，观察电磁辐射对顶体反应相关的蛋白及信号传导途径（如G 蛋白耦联的信号传导、受体酪氨酸激酶（RTK）途径）的影响；研究电磁辐射对精子细胞、卵细胞膜表面Ca2+离子通道与胞浆内Ca2+浓度的影响、细胞骨架的重组与分布，以及DNA 甲基化和组蛋白修饰等表观遗传学变化，揭示电磁辐射对受精过程、卵细胞激活的影响及分子机制。

经费比例：17.5%

承担单位：中国人民解放军第四军医大学、中国人民解放军第三军医大学、苏州大学

课题负责人：郭国祯

学术骨干：童建、杨桦、曾丽华、李静

课题5、电磁辐射的遗传效应及机理研究

预期目标：

① 在整体实验动物、重要功能细胞与生物大分子三个层面上，揭示电磁辐射遗传效应特点；

② 从染色体、基因与基因组、DNA 不同水平，明确电磁辐射的遗传损伤位点和表观遗传学机制；

③ 明确电磁辐射是否具有促细胞恶性转化的致癌效应。

2. Study EMF effects and mechanisms of sperm development and regulation

From the changes in the male gonadal axis, testosterone and other sex hormone secretion and regulation, macrophages secretion and regulation etc., study how EMF affects the generation and development of sperm; establish primary culture system in vitro for germ cells, observe EMF impact on function of germ cells during development; start from multiple epistasis relevant to germ cell development in regulating pathway, select spermatogenesis-related genes, such as regulation genes, environmental response genes, nuclear receptor genes, oxidative stress genes and hormone receptor-related gene, as the candidate genes, make large-sample, large-scale analyses of SNPs. Study the EMF effects on important signal transduction pathways related to the regulation of germ cell (G protein/protein tyrosine kinase signal transduction system, Wnt/PI3K/GSK3β, JAK / STATs signal transduction system), reveal the molecular mechanisms and signal of the EMF damage effects in the reproductive transduction mechanism, in various sectors such as: membrane receptors, cytoplasmic receptors, cytoplasmic signal transduction proteins, nuclear receptors and protein activation, translocation, inactivation.

3. Study EMF effects and mechanisms on fertilization and development of fertilized eggs

Research the three main steps in the fertilization process: the sperm-egg recognition, sperm-egg binding and sperm-egg plasma membrane fusion, to study the EMF effects on sperm membrane proteins expression (such as: sperm in ADAM category, lzumo protein, DE/CRISP1 protein and Equatorin, FAP - 1, MA - 24, MH61, FLB1) and sperm-egg plasma membrane fusion, and to observe EMF effect on protein related with the acrosome reaction and signal transduction pathway (such as G protein-coupled signal transduction, receptor tyrosine kinase (RTK) pathway); study EMF effects on Ca2 + ion channels in membrane and intracellular Ca2 + concentration of sperm cells and egg cell, restructuring and distribution of cytoskeleton, as well as the epigenetic changes in DNA methylation and histone modifications, reveal EMF effects on the fertilization and activation of the egg cell, and its molecular mechanisms.

Funding ratio: 17.5%

Research group: Third Military Medical University, China, Fourth Military Medical University, China, Suzhou University

Project Leader: Guo Chen

Academic supporters: Tong Jian, Yang Hua, Zeng Lihua, Li Jing

Task 5: The genetic effects of electromagnetic fields

Targets:

1. Reveal the genetic effects due to EMF, from the three levels of experimental animals, important functional cells and biological macromolecules;
2. Clarify the genetic damage sites and mechanisms of epigenetic damage due to EMF, from different levels such as chromosomes, genes and the genome, and DNA;
3. Clarify whether the EMF has carcinogenic effects on malignant transformation.

研究内容：

1. 电磁辐射遗传物质损伤效应与位点研究

按照遗传毒理学评价国际协调委员会的最新指导原则，在DNA 完整性的改变（形成DNA 加合物、断裂、交联）、DNA 重排和交换、基因突变、染色体畸

变、染色体分离改变等5 个遗传学终点上，对电磁辐射暴露的遗传损伤效应进行系统检测，全面评价遗传效应。在此基础上，有针对性地利用多彩色染色体探针荧光原位杂交、微核细胞组学评价体系、转基因动物等先进技术，评价电磁辐射诱发染色体结构与数量改变、非整倍体形成、基因组缺失与扩增、DNA 断裂与重组、DNA 损伤与修复、微卫星不稳定性和基因组不稳定性等异常改变，研究电磁辐射诱发机体辐射易感基因的突变位点、类型、频率与可能的突变热点，初步描绘电磁辐射所致遗传损伤突变谱，筛选电磁辐射致突变效应的特异损伤位点。

2．电磁辐射的表观遗传效应研究

通过在体与体外细胞模型，对组蛋白修饰酶、染色质重塑复合物（Chromatin remodeling complex），组蛋白变体和DNA 甲基化酶，甲基化DNA 结合蛋白等进行分析，初步阐明电磁辐射致表观遗传学改变的修饰或效应通路。利用定量质谱学分析、全基因组甲基化分析、实时定量PCR 等高通量的测试技术进行转录组分析，重点寻找电磁辐射对基因组甲基化的影响，克隆相关的受甲基化调控的关键基因并分析其作用，初步揭示电磁辐射对表观遗传学影响的特点和分子机制。

3. 电磁辐射诱导细胞恶性转化及机制研究

采用人和动物胚胎性细胞及成体干细胞体外培养技术，评价电磁辐射长期低剂量作用下诱发细胞恶性转化与成瘤性的能力，观察电磁辐射暴露对干细胞生长、增殖、分化、细胞周期、凋亡、迁移、克隆形成和成瘤性及转移潜力等生物学行为的影响，分析细胞染色体、抑癌与促癌基因表达和表遗传学改变，探讨以恶性转化为主要过程的遗传学异常。进一步采用转基因动物模型（Knock in/out），进行重要应答基因的功能研究，阐明电磁辐射致癌效应的分子机制。

经费比例：14.5%

承担单位：中国人民解放军第三军医大学、中国人民解放军第四军医大学、工业和信息化部电信研究院

课题负责人：曹佳

学术骨干：张绍祥、丁桂荣、周舟、巫彤宁

Studies:

1. Study damage effects and sites on genetic material due to EMF

According to the latest guidelines of International Coordinating Committee on genetic toxicology evaluation, from five genetics' endpoints such as: changes in integrity of DNA (the formation of DNA adducts, breaks, or cross-links), DNA rearrangement and exchange, gene mutations, chromosome aberrations, chromosome segregation and changes, comprehensively test the EMF damage effects in genetic, and assess the genetic effects. Based on this, use advanced technologies such as multi-color chromosome probes fluorescence, in situ hybridization, evaluation systems for micro-nuclear cell genomics, and transgenic animals; evaluate EMF-induced abnormal changes in chromosomes: structure and numeric changes, aneuploid formation, genome deletion and amplification, DNA breakage and reorganization, DNA damage and repair, microsatellite instability and genomic instability; study EMF induced mutations of susceptibility gene, such as type, frequency, and hot spots of possible mutation, make initial description of the mutations spectrum due to EMF induced genetic damage, and select specific injury sites of mutation effects caused by EMF.

2. Study EMF epigenetic effects

Based on cell model in vivo and in vitro, analyze histone modification enzymes, chromatin remodeling complexes, histone variants and DNA methylase, methylated DNA binding protein etc., clarify the modifying or effecting pathway of EMF induced epigenetic changes. Using high-throughput measurement techniques, such as quantitative mass spectrometry analysis, genome-wide methylation analysis, real-time PCR technology for transcriptome analysis, mainly find out the EMF effects on the genome methylation, and key genes and their functions, which are clone-related and regulated by methylation, and initially reveal the characteristics and molecular mechanisms of EMF effects on the epigenetic.

3. Study EMF-induced neoplastic transformation and its mechanisms

Use embryonic cells of human and animal, and adult stem cells culture techniques in vitro, evaluate the effects on malignant transformation and tumorigenesis by the long-term low-dose response EMF, observe the EMF effects on the biological behavior such as: stem cell growth, proliferation, differentiation, cell cycle, apoptosis, migration, colony formation, tumorigenicity and metastasis potential, analyze gene expression and epigenetic changes in chromosome tumor-suppressing and tumor-promoting, explore the genetic abnormalities in the main process as malignant transformations. Furthermore, use transgenic animal models (knock in / out), make major response gene function studies, and clarify the molecular mechanisms of the carcinogenic effects due to EMF.

Funding ratio: 14.5%
Research group: Third Military Medical University, China, Fourth Military Medical University, China, Industry and Information Technology Telecommunications Research Institute
Project Leader: Cao Jia
Academic supporters: Zhang Shaoxiang, Ding Guirong, Zhou Zhou, Wu Tongning

课题6、电磁辐射健康危险度与危害监测的应用基础研究

预期目标：

① 通过大样本人群流行病学研究，明确我国电磁辐射健康危害现状，确定职业与环境电磁辐射暴露的健康危险度；

② 揭示电磁辐射健康危害与人群遗传易感性的关联，分析电磁辐射暴露与遗传易感性相互作用的方式，明确独立和联合作用的贡献度；

③ 研究提出电磁辐射危害监测的生物标志物，并验证特异性与灵敏度。

研究内容：

1. 人群电磁辐射健康危害特征与危险度分析

在北京、上海、重庆、西安等城市，选择特定的环境与职业电磁辐射暴露人群，进行多中心大规模的人群流行病学研究。在电磁辐射职业暴露人群开展流行病学现况调查；以职业暴露人群和社区人群为对象，开展病例-对照研究，同时进行环境电磁暴露特征测评与生物剂量测量、人群神经与生殖遗传相关项目检测，从而明确我国职业与环境电磁辐射暴露人群健康危害现状，进一步分析职业与环境电磁辐射暴露与神经与生殖遗传异常的关联度，明确不同条件暴露的危险度。结合我国对疾病防控的三级预防策略，探讨在病因一级预防和早期检诊二级预防中如何在人群水平早期干预与控制电磁辐射的危害，以生物标志物为核心，实现电磁辐射健康危害的监测与评估。在此基础上，建立我国电磁辐射职业与环境暴露人群队列研究，为长期电磁辐射健康危害监测与防护奠定科学基础。

2．电磁辐射健康危害效应与遗传易感性的关联度研究

选择职业与环境电磁辐射暴露人群，以神经系统和生殖功能损伤为靶点，采用具有高通量基因定型能力的ILLUMINA 遗传分析系统，研究关键的环境反应基因（如DNA 损伤修复、氧化应激关键调控基因、自由基代谢相关基因等）在人群中的多态性，通过建立数理模型，进行环境-基因交互作用分析，明确遗传因素和环境因素相互作用模式，探讨电磁辐射所致神经与生殖功能损伤的危险因素和保护因素。将基因多态性、遗传损伤生物标志物、分子突变谱、剂量反应关系以及不同生物材料、检测技术条件的信息整合，建立生物学数据库，初步提出可能作为电磁辐射神经与生殖系统危害效应预测、识别和监测的易感基因。

3. 电磁辐射危害生物标志物研究

在前期研究工作基础上，遴选出能反映电磁辐射健康危害特点而又具有显著的量效反应关系的效应标志物，在人群水平，重点围绕能反映神经系统、生殖系统功能损伤的外周血和体液的细胞学、生化学指标，以及组织器官功能评价的无创性指标与技术筛查生物标志物，并在职业电磁暴露人群进一步验证上述生物标志物监测与评估电磁辐射健康危害的特异性和敏感性。

Task 6: Health risk assessment of electromagnetic fields

Targets:

1. Based on large sample population epidemiological studies, clarify the status of EMF health hazards in China, and define health risk under occupational and environmental EMF exposure;
2. Reveal the relationship between EMF-induced health hazards and population genetic susceptibility, analyze the interaction between EMF exposure and genetic susceptibility, and clarify the contribution in independent and combined effects;
3. Propose the biomarkers for EMF hazards monitoring, and verify its specificity and sensitivity.

Studies:

1. Analyze characteristics and risks of population health hazards due to EMF

In Beijing, Shanghai, Chongqing, Xi'an and other cities, select groups exposed to specific environmental and occupational EMF to build multi-center large-scale epidemiological studies. Carry out epidemiological investigation among people under occupational exposure; take cases within community groups and groups under occupational exposure, make case-control studies, as well as make evaluations of the characteristics of environmental EMF exposure, and assessments in bio-dosimetry, population nervous and reproductive genetics related projects, clarify the status of population health hazards in China due to occupational and environmental EMF exposure, further analyze the correlation between occupational and environmental EMF exposure with abnormalities in nervous and reproductive genetics, and define the risks of different exposures. Combining with the tertiary prevention strategies of China in disease prevention and control, discuss how to early intervene and control EMF hazards in the population level during primary prevention and secondary prevention, to achieve EMF health hazards monitoring and evaluation based on biological markers. On this basis, launch a population cohort study of occupational and environmental EMF exposure in China, establishing the scientific basis for monitoring and protection long-term EMF health hazards.

2. Study correlation degrees of EMF health hazards effects with genetic susceptibility

Select a population exposed to occupational and environmental EMF, set the nervous system and reproductive impairment as the target, use the ILLUMINA genetic analysis system which has high-throughput genotyping capacity, to study polymorphisms of the critical environmental response genes (such as DNA damage repair, oxidative stress key regulatory genes, free radical metabolism-related genes, etc.) in the population, through establishing mathematical models to analyze the interaction between the environment and genes, clarify the mode of interaction between genetic factors and environmental factors, and explore the risk factors and protective factors of EMF introduced damage in nervous and reproductive functions. Integrate the information of genetic polymorphism, genetic damage biomarkers, molecular mutation spectrum, dose-response relationship and different biological materials, experiment with technical conditions, establish biological databases, and initially propose the susceptibility genes for predicting, identifying and monitoring EMF hazard effects in the nervous and reproductive systems.

3. Study biomarkers for EMF hazards

Based on the preliminary studies, select effect markers that can reflect the characteristics of EMF health hazards and with a significant dose-response as well. At the population level, focus on cytological and biochemical markers in the peripheral blood and body fluids which can reflect the damage in the nervous and reproductive systems, and non-invasive indicators for functional

经费比例：20.5%

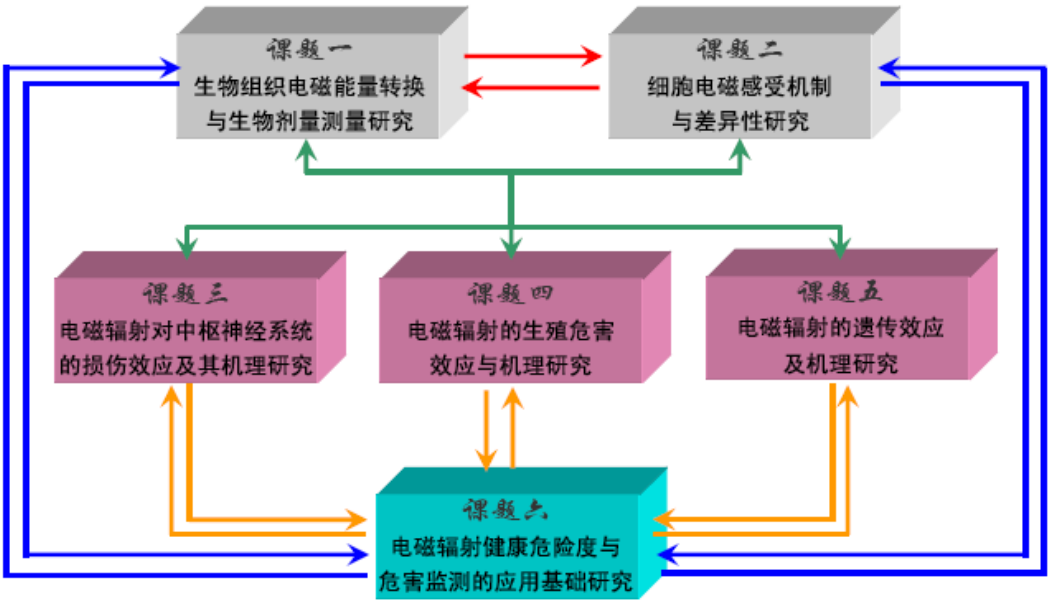
承担单位：中国人民解放军第三军医大学、浙江大学、中国人民解放军军事医学科学院

课题负责人：余争平

学术骨干：余运贤、胡向军、杨国山、孙文均

各课题间相互关系

本项目研究围绕拟解决的关键科学问题，根据研究内容设置了六个既相对独立又在研究内容和预期目标方面相互联系的课题（课题间联系见下图）。课题一“生物组织电磁能量转换与生物剂量测量研究”和课题二”细胞电磁感受机制与差异性研究”是综合采用物理学和生物学的方法研究机体对电磁辐射的响应特点和机制，紧紧围绕电磁辐射能量在生物体内吸收、转换、传递的过程，探索电磁辐射健康危害效应的生物物理机制，并实现与生物医学损伤机制的联系与转换；课题三”电磁辐射对中枢神经系统的损伤效应及其机理研究”和课题四”电磁辐射的生殖危害效应与机理研究”则是从电磁辐射损伤最敏感的器官与系统入手，揭示电磁辐射敏感器官损伤特点与分子机制，明确电磁辐射引起损伤的量效关系，确立损伤阈值；课题五”电磁辐射的遗传效应及机理研究”着重回答长期低强度电磁辐射暴露是否具有遗传效应这一关键科学问题和公众的疑虑，也进一步印证和揭示电磁辐射健康危害机理；课题六”电磁辐射健康危险度与危害监测的应用基础研究”是在前面五个课题从不同层面研究电磁辐射健康危害机理的基础上，回归人群水平，瞄准提出有针对性的防护措施这一目标，研究提出电磁辐射危害监测的生物标志物，揭示我国电磁辐射健康危害现状与特征，确立健康危险度，为我国电磁辐射健康危害的综合防治奠定科学基础。



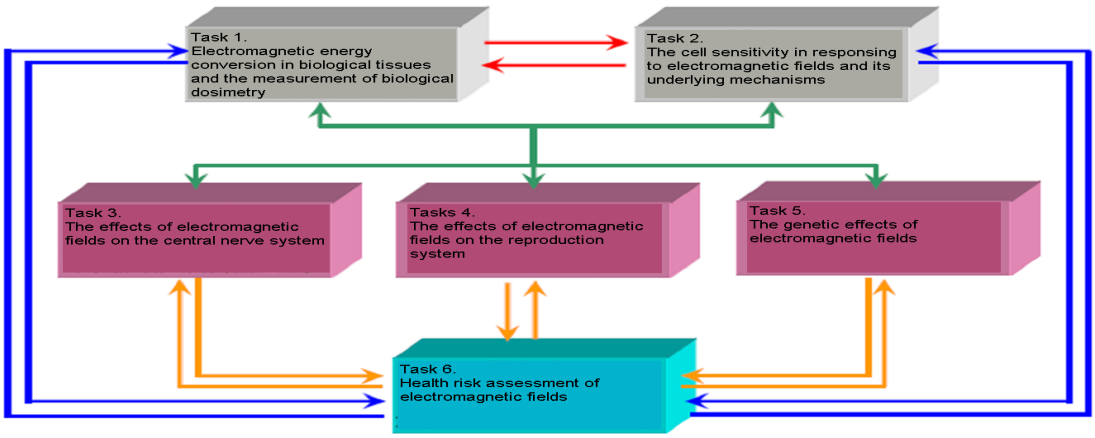
课题间相互联系示意

assessment of tissues organs and biomarkers in screening technology, and further validate sensitivity and specificity of these biomarkers in monitoring and assessing the health hazards in the population under occupational electromagnetic exposure.

Funding ratio: 20.5%
Research group: Third Military Medical University, China, Zhejiang University, Academy of Military Medical Sciences Military, China
Project Leader: Yu Zhengping
Academic supporters: Yu Yunxian, Hu Xiangjun, Yang Guoshan, Sun Wenjun

The relationship between the tasks

The research project focuses on key scientific issues to be solved, which contain six relatively independent tasks but are mutually related by contents and targets (the relationship between these tasks is shown below). Task 1 "The electromagnetic energy conversion of biological tissues and biological dosimetry study" and Task 2 "The cell sensitivity in responding to electromagnetic fields and its underlying mechanisms" study the characteristics and mechanisms of the body responding to EMF, based on methods combining physics and biology, explore the biophysical mechanisms of EMF health effects and understand its relationship and interaction with biomedical injury mechanisms, by focusing absorption, conversion, and transfer processes of EMF energy in vivo; Task 3 "The effects of electromagnetic fields on the central nervous system and its mechanisms" and Task 4 "The effects of electromagnetic fields on the reproduction system" start from the organs and systems which are most sensitive to EMF damage, to reveal the characteristics and molecular mechanisms of the damage in EMF sensitive organs, clarify the dose-response of the damage caused by EMF, and establish the damage threshold; Task 5 "The genetic effects of electromagnetic fields" focuses on the critical scientific issues and public concerns of whether long-term low-intensity EMF exposure has genetic effects, further verify and reveal the mechanism of EMF health hazards; Task 6 "Health risk assessment of electromagnetic fields and research in risk monitoring" is based on the five tasks above to study the mechanisms of EMF health hazards from different levels, aiming to propose a targeted protection method at population level, study and propose biomarkers for EMF hazard monitoring, reveal the status and characteristics of EMF health hazards, clarify the health risk, and establish the scientific basis for integrated control of EMF health hazards.



四、年度计划

年度	研究内容	预期目标
第一年	1．建立统一的模拟职业与环境电磁暴露的动物小鼠、大鼠、家兔等品系标准实验动物模型。 2．研究可用于"电大"问题模拟计算的高效算法，完成新算法的代码设计和理论验证；建立均匀电磁谐振腔和高精度微型天线电磁辐射测量系统。 3．筛选电磁辐射敏感细胞，检测电磁辐射对其 DNA 双链断裂的影响。 4．研究电磁辐射暴露对大鼠等动物认知行为的影响，建立电磁辐射对动物脑区发育与脑功能影响研究的方法、技术。 5．电磁辐射遗传毒性细胞组学分析和染色体组学分析；建立成体干细胞分离和培养方法。 6．开展职业电磁暴露环境测评健康危害和流行病学现况调查，获得电磁健康危害的基本信息。在模拟职业与环境电磁辐射实验动物模型，进行认知功能损伤和生殖功能损害的评价。	1. 建立模拟职业与环境电磁暴露标准化动物模型 2-3 个。 2. 建立可用于"电大"问题模拟计算的高效计算程序和动物（大鼠）体内电磁辐射剂量测量的测试系统。 3. 明确 2-3 种细胞电磁敏感的剂量效应关系。 4. 初步确定电磁辐射导致动物行为学改变的一些参数；建立相关脑区检测神经元环路、突触机制的电生理技术；建立细胞水平研究的技术平台，获得一些正常对照值。 5. 获得电磁辐射致染色体结构和(非)整倍体改变数据；获得电磁辐射作用过程中受甲基化调控的基因数据。 6. 完成 1-2 个代表性行业职业电磁暴露测评工作；初步开展的流行病学调查。 7. 发表 SCI 论文 10-15 篇。

年度	研究内容	预期目标

年度	研究内容	预期目标
第二年	1. 研究活体生物组织和细胞的介电(介质极化、电导)频谱特性及其差异性；设计人体电磁辐射剂量模拟计算程序，并理论验证其正确性、可靠性；利用人体介电参数模拟计算人体体内电磁场分布 2. 研究电磁辐射对一些特殊酶活性、细胞缝隙连接、表皮生长因子受体的影响规律；以电磁辐射敏感细胞为检测对象，研究电磁辐射对细胞周期、凋亡、增殖的影响。 3. 研究电磁辐射对大脑认知功能的影响；电磁辐射对认知功能相关脑区主要神经回路变化，突触可塑性影响；开展电磁辐射大脑皮层电磁辐射和小脑神经元迁移、网络构建等研究；开展电磁辐射对脑内和培养神经元极性、突触成熟等神经生理学研究。 4. 开展电磁辐射对性激素代谢、丘脑-垂体性激素调控蛋白和关键酶分子、精子发育与调控的影响及机制研究。 5. 评价电磁辐射对 DNA 链的作用；对内源性基因突变作用；开展电磁辐射对细胞基因表达谱分析；电磁辐射作用应答基因表观遗传学机制的研究。 6. 进一步开展职业和环境电磁测评，和流行病学研究，在明确健康危害相关候选基因的基础上，开展 2-3 个候选基因的 SNP 分析，基因型检测；在模拟职业与环境电磁暴露损伤实验动物模型，以血清蛋白谱、代谢产物差异的分析、血清酶谱和血激素水平为靶标，筛查生物标志物。	1．获得 5-8 种组织、细胞的基本介电(介质极化、电导)参数；初步获得电磁辐照时人体内体内电磁场分布特征数据。 2．初步揭示细胞膜上 2-3 个重要蛋白质分子(如受体)及特殊膜性结构(细胞缝隙连接)对外源电磁场的反应模式及可能机制。 3．基本确定电磁辐射导致动物行为学改变的量效关系；明确细胞水平神经元损伤的阈值。 4．初步明确电磁辐射对性激素代谢的影响的量效关系。 5．提出 1-2 个电磁辐射致内源性基因突变类型及特点；初步明确电磁辐射致染色体重塑、组蛋白修饰、甲基化的量效关系。 6．完成 1-2 个代表性职业与 1-2 个代表性城市环境的电磁暴露测评工作。初步明确电磁暴露对人体器官、系统危害的特征；建立 SNP 分析和基因型检测的高通量筛选技术平台。 7．发表 SCI 论文 10-15 篇，申请专利 1-2 项。

年度	研究内容	预期目标
第三年	1．研究活体组织、细胞的介电(介质极化、电导)特性与其生物效应的相关性；模拟计算均匀电磁谐振腔内动物（大鼠）体内电磁辐射剂量分布；比对分析大鼠体内电磁辐射剂量分布的模拟结果和实验测量结果。 2．观察电磁辐射对细胞膜脂双分子层以及脂筏结构的影响；检测电磁辐射对细胞蛋白质表达谱变化的影响，鉴定差异表达蛋白质。 3．研究电磁辐射对大脑认知功能损伤的分子机制研究；继续深入探讨对电磁辐射对皮层、海马神经元回路变化，突触可塑性影响的分子机制；研究电磁辐射对大脑皮层和小脑神经元发育、迁移等分子机制。 4．进一步开展电磁辐射对精子发育与调控的影响及机制研究，包括电磁辐射对生殖细胞膜受体、胞浆受体、胞浆信号转导蛋白、核受体与蛋白的激活、转位、失活等不同环节的影响；电磁辐射对受精过程与受精卵发育的影响及机制研究。 5．评价电磁辐射对外源性基因的突变作用；克隆甲基化调控新基因并研究其功能；电磁辐射作用应答基因作用机制的研究；电磁辐射对体细胞及胚胎细胞恶性转化的作用 6．完成职业和环境电磁测评工作，进一步开展流行病学研究，连续积累电磁健康危害的基本信息；研究电磁神经与生殖健康危害的遗传易感性，对检测数据进行建模和统计分析；在职业暴露人群，筛查生物标志物。	1．建立的不同活体组织介电（介质极化、电导）特性数据库；建立动物体内电磁辐射剂量实验测量的方法和技术平台。 2．提出电磁辐射对 3-5 种重要功能细胞损伤阈值与量效关系；确定细胞电磁辐射敏感性差异的相关功能基因 3-5 个和相关蛋白 3-5 个；确定电磁辐射诱导细胞转化的时效和量效关系。 3．在电磁辐射对海马神经元环路、突触可塑性影响方面提出电磁暴露损伤的阈值。 4．揭示电磁辐射生殖损伤相关联的重要信号转导通路；明确电磁辐射对受精过程与受精卵发育的影响量效关系。 5．获得电磁辐射致外源性基因突变作用及特点;阐明 1-2 个电磁辐射应答新基因的功能与调控机制。 6．明确我国职业与环境电磁辐射暴露的特征（频谱分布、强度、暴露模式），建立我国电磁健康危害数据库，并初步在本项目组单位内实现共享;提出 1-2 个电磁健康危害遗传易感基因;提出 2-3 个危害监测评估标志物。 7．发表 SCI 论文 20-25 篇，申请专利 1-2 项。

年度	研究内容	预期目标
第四年	1．研究建立电磁辐射与活体组织、细胞相互作用的物理模型；模拟计算多种辐照方式下的人体内电磁辐射剂量分布。 2．选择一些关键蛋白质分子，进行蛋白质功能分析及相关信号通路研究；应用荧光法结合 DCFH-DA 探针等技术，检测细胞内自由基和抗氧化系统的酶活性变化。 3．运用子宫内电转和皮层电转手段，研究电磁辐射对大脑皮层和小脑神经元发育、迁移等分子机制；电磁辐射对神经干细胞的增生和向神经元、神经胶质细胞及神经小胶质细胞的转化的影响。 4．电磁辐射对精子膜蛋白的表达和精卵质膜融合的影响，观察电磁辐射对顶体反应相关的蛋白及信号传导途径的影响；研究电磁辐射对胚胎发育和子代精神行为的影响及机制。 5．研究电磁辐射致突变作用机制；电磁辐射致表观遗传学改变调控基因功能研究；电磁辐射致癌作用机制的研究。 6．选择 1-2 个职业电磁暴露代表性行业，进行规范的流行病学研究设计，建立我国较大样本、长时间的流行病学对列研究。进一步研究电磁神经与生殖健康危害的遗传易感性，对检测数据进行建模和统计分析；进一步在实验动物模型和职业暴露人群筛查生物标志物。	1. 建立电磁辐射与活体组织、细胞相互作用生物物理模型，揭示生物机体对电磁辐射的响应特点和机制；建立基于活体组织介电特性数据的高精度人体电磁仿真模型。 2. 明确 2-3 个重要功能蛋白变化与电磁辐射生物学效应的关系，研究阐明细胞电磁辐射敏感性差异与抗氧化系统的关联。 3. 明确电磁辐射导致神经干细胞增殖分化影响的规律，明确电磁辐射对神经发育损伤的量效关系。 4. 初步揭示电磁辐射对受精过程、卵细胞激活的影响及分子机制；初步明确电磁辐射对不同阶段胚胎发育和子代个体产生危害的敏感阶段、损伤特点。 5. 揭示电磁辐射致基因突变的分子机制；阐明相关功能基因甲基化对电磁辐射效应的影响及调控。 6. 明确我国职业与环境电磁辐射暴露与神经与生殖健康危害的关联度与危险度；明确神经与生殖健康危害遗传易感基因;提出 3-5 个危害监测评估指标。 7. 发表 SCI 论文 20-25 篇，申请专利 2-3 项。

年度	研究内容	预期目标
第五年	1．研究加速辐照条件作用下细胞、组织生物效应，及其介电特性的变化规律；通过比对、分析实验测量和数字模拟结果，建立一种基于外部电磁场测量和体内电磁辐射剂量模拟计算相结合的定量检测生物组织电磁吸收剂量的方法与技术平台。 2．开展多通道电活动记录电磁辐射损害敏感的神经回路机制的研究；开展培养大鼠海马脑片与认知相关的候选基因干扰的研究；继续电磁辐射对大脑皮层和小脑神经元发育、迁移等分子机制的深入探讨；电磁辐射对调控神经干细胞迁移的因子及对神经营养因子的作用，以及出现的差异表达信号分子研究。 3．进一步研究电磁辐射对精子细胞、卵细胞膜表面 Ca2+离子通道与胞浆内 Ca2+浓度的影响、细胞骨架的重组与分布，进一步研究电磁辐射对胚胎发育和子代精神行为的影响。 4．评价电磁辐射对表观遗传学调控中关键的酶/蛋白的影响;分析电磁辐射致癌过程中关键的信号通路分析。 5．将遴选到的遗传易感基因和敏感标志物在职业电磁暴露人群进一步验证，评价这些上述生物标志物监测与评估电磁辐射健康危害的特异性和敏感性。确立我国大样本流行病学对列研究方案，开展暴露特征与健康危害的监测与评估。 6．进行本课题的研究工作总结，撰写发表学术论文和完成总结报告	1. 提出加速辐照作用下细胞、组织生物效应的介电表征评价方法；建立定量检测生物组织电磁吸收剂量的方法与技术平台。 2. 揭示电磁辐射对脑内神经系统发育可塑性的影响及其机制； 阐明电磁辐射引起的中枢神经系统发育功能改变的关键细胞事件和关键信号分子。 3. 明确电磁辐射对受精过程、卵细胞激活的影响及分子机制；明确电磁辐射对不同阶段胚胎发育和子代个体产生危害的损伤特点、关键分子环节。 4. 揭示电磁辐射致表观遗传学改变的机制和作用的主要信号通路。 5. 建立我国职业电磁暴露健康危害大样本流行病学研究；初步提出电磁辐射危害监测评估的指标。 6. 全面完成本课题的总体目标，并完成课题总结与结题。 7. 发表 SCI 论文 15-20 篇，申请专利 3-4 项。