NTP
National Toxicology Program

National Toxicology Program
Cell Phone RFR Project Update

Virtual GLORE 2020

November 9-12, 2020

NTP Cell phone RFR research program

Moving beyond the cancer studies

Additional studies provide an opportunity to…

- Further characterize RFR-mediated toxicity and carcinogenicity
- Address issues raised during peer review of RFR bioassay
- Probe potential mechanisms for identified RFR-induced effects
- Investigate RFR-induced DNA damage and explore effect exposure on DNA repair activity
- Establish biomarkers of exposures/toxicity to apply to studies of newer and emerging RFR-based communication technologies

Investigative Studies

Goals:

- Address critical knowledge gaps in the association between RFR exposure and toxicity/carcinogenicity
- Clarify the interaction between RFR and biological tissues and the factors that affect these interactions
- Provide additional information for interpretation of RFR data for risk assessment in humans

The NTP cell phone RFR research program

- Phase 1 – The Bioassay Studies
  - Thermal pilot studies
  - 28-Day repeat exposure studies
  - 2-Year toxicology and carcinogenicity studies

Summary of RFR bioassay results

- Mice
  - Positive comet assay for frontal cortex in males (GSM/CDMA) and blood in females (CDMA)
- Rats
  - Greater **survival** in all groups of RFR exposed males compared to controls (GSM/CDMA)
  - Positive comet assay in hippocampus; equivocal in frontal cortex of males (CDMA)
  - Perinatal effects (gestation and lactation)
    - SAR-dependent decrease in **body weights** of dams and pups
    - Decreased pup **survival** at higher exposures tested
  - Increased incidences of malignant schwannomas of the **heart** (GSM/CDMA), malignant gliomas in the **brain** (GSM/CDMA), and pheochromocytomas in the **adrenal medulla** (CDMA)

The NTP cell phone RFR research program

- Phase 1 – The Bioassay Studies
  - Thermal pilot studies
  - 28-Day repeat exposure studies
  - 2-Year toxicology and carcinogenicity studies
- Phase 2 – Investigative Studies
  - Series of targeted studies addressing specific issues regarding the interaction between RFR exposure and biological tissues

Phase 2: Areas of study

- Stress and behavior
- Organ-specific evaluations (heart, brain, adrenal)
- Exposure factors
- The role of heat in RFR-induced effects
- DNA damage and repair
- Evaluate newer 3G/4G technologies, potentially 5G

Progress on Phase 2

- Design of chambers by IT'IS Foundation to accommodate NTP specifications for Phase 2 studies
- Construction of chambers and initial testing by IT'IS Foundation
- Installation of chambers at the contract lab and the establishment of the new exposure facility
- Third-party validation of chamber RF exposures by National Institute of Standards and Technology (NIST)
- Evaluation of background RF exposure in NTP RFR exposure facility
  - Established surveillance program for measuring background and chamber RF

Phase 2 exposure system

General characteristics

- Facility: Two room(s) – one for chambers and one for generation system
- RFR fields: Signal generator → Amplifier → Antenna → Fans for homogeneity in chambers
  - Same design as the facility in bioassay studies (Chicago, IL, USA)
- System: Four chambers (n=10 rats or mice)
  - Environmental monitoring: Temp, humidity, lighting, air flow, noise
  - Equipped with video cameras with nighttime recording capabilities
- Exposures:
  - GSM/CDMA modulations; 900 MHz (rats) and 1900 MHz (mice) frequencies
  - Capacity to generate 3G and 4G modulated signals up to 2700 MHz (chambers may need modifications for different frequencies)

NTP is continuing to work on Phase 2

- Developing of SOPs
- Conducting exposure system performance testing
  - Preliminary experiments (data loggers, video cameras, temperature chips, etc)
- Establishing data handling methods
- **Working out kinks and gearing up to conduct studies**

Phase 2: First set of studies

- Test/validate the performance of the new chambers with live animals
  - Demonstrate a known, robust RFR-mediated effect
- “Bridge the gap”
  - Between the original chambers and the new chambers
  - Between RFR Bioassay and Phase 2 RFR Studies
- Confirm DNA damage
- Investigate behavior, startle response, visible signs of stress

Study endpoints

- Measure SAR-dependent change in body temperature
  - Validate biological effects of RFR exposure in new chambers
  - Validate data loggers; compare to previously-used implanted chips
- Comet Assay
  - Frontal cortex, hippocampus, cerebellum, liver, and heart
- Evaluate activity/reaction to RFR exposure with video cameras
  - Is a startle-response associated with initiation/cessation of exposures?
  - Qualitative evaluation of behavior/activity during exposure and non-exposure periods

Study designs

- Study #1:
  - Aged male rats (20 weeks of age)
  - Exposure to 0 (room and sham control), 3, 6, or 9 W/kg **CDMA** for 5 days
  - n=10 per group
- Study #2:
  - Aged male rats (20 weeks of age)
  - Exposure to 0 (room and sham control), 3, 6, or 9 W/kg **GSM** for 5 days
  - n=10 per group
- Study #3:
  - Aged female rats (20 weeks of age)
  - Exposure to 0 (room and sham control), 3, 6, or 9 W/kg **CDMA** for 5 days
  - n=10 per group
- Study #4:
  - Aged female mice (20 weeks of age)
  - Exposure to 0 (room and sham control), 2.5, 5, or 10 W/kg **CDMA** for 5 days (Alternate: 0, 5, 10, 15 W/kg)
  - n=10 per group

RFR 2.0: Areas of study

- Stress and behavior
  - Evaluate impact of noise (mechanical or signal generated)
  - Does behavior change at the initiation or cessation of exposure to RFR?
- Organ-specific evaluations (heart, brain, adrenal)
  - Further investigation of the heart (unexpected target organ and most robust finding)
- Exposure factors
- The role of heat in RFR-induced effects
  - RFR-induced temperature changes during daytime vs nighttime hours
  - Evaluate the “kinetics” of temperature changes over time within 10-min exposure and non-exposure periods
- DNA damage and repair
  - Comet assay in brain, liver, and heart
- Evaluate newer 3G/4G technologies (maybe 5G?)

What's up next?

- Genetic toxicity studies
  - Developing tiered strategy to evaluate RFR-mediated DNA damage
  - Endpoints for different types of DNA damage
- Gene expression studies
  - Further evaluate gene expression changes observed in bioassay
- Studies to evaluate 3G and 4G-LTE modulated signals and frequencies
- DNA repair studies
- Studies to evaluate cardiac parameters
- Consider utilizing *in vitro* exposure system to further characterize genotoxicity and evaluate effect of higher frequencies (> 6 GHz)

NTP
National Toxicology Program

Questions and Discussion

National Institute of Environmental Health Sciences
Research Triangle Park, North Carolina, USA

Thank You!