NTP
National Toxicology Program

# Cell Phone Radiofrequency Radiation (RFR) Project: Investigative Studies

Michael Wyde, PhD
Toxicology Branch
National Institute of Environmental Health Sciences

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# Goals for Investigative Studies

- Further clarify and fill knowledge gaps in the NTP studies on RFR
- Address issues/criticisms raised during the peer review
- Probe potential mechanisms for RFR-induced effects
- Confirm RFR-induced DNA damage in the brain of rats and mice
- Establish biomarkers of exposures to apply to studies of newer and emerging RFR-based communication technologies

# Summary of Draft Results – NTP Studies on RFR

## B6C3F1 Mice studies

- Equivocal evidence of carcinogenic activity in male and female mice for both GSM and CMDA modulations
- Positive comet assay for frontal cortex in males (GSM and CDMA) and blood in females (CDMA only)

| GSM Males | | CDMA Males | |
|---|---|---|---|
| **Organ** | **Lesion** | **Organ** | **Lesion** |
| Skin | Malignant Fibrous Histiocytoma | Liver | Hepatoblastoma |
| Lung | Alveolar/Bronchiolar Adenoma or Carcinoma (combined) | ----- | ----- |
| **GSM Females** | | **CDMA Females** | |
| **Organ** | **Lesion** | **Organ** | **Lesion** |
| All organs | Malignant Lymphoma | All organs | Malignant Lymphoma |

# Summary of Draft Results – NTP Studies on RFR

## Hsd: Sprague Dawley rat studies

- Some evidence of carcinogenic activity in male rats for both GSM and CMDA modulations based on increased incidences of malignant schwannomas of the **heart**
- Greater survival in all groups of exposed **males** compared to controls
  - Lower survival in control group attributed to high severity of chronic progressive nephropathy
- Perinatal effects (gestation and lactation)
  - SAR-dependent decrease in body weights of dams and pups
  - Decreased pup survival at higher exposures tested
- Comet assay results:
  - Positive in hippocampus; equivocal in frontal cortex of males (CDMA only)

# Summary of Draft Equivocal Neoplastic Findings

| GSM Males | | CDMA Males | |
|---|---|---|---|
| **Organ** | **Lesion** | **Organ** | **Lesion** |
| Brain | Malignant Glioma | Brain | Malignant Glioma |
| Brain | Meninges, Granular Cell Tumor (Benign and Malignant) | Liver | Hepatocellular Adenoma or Carcinoma (combined) |
| Pituitary Gland | Pars Distalis, Adenoma (Includes multiple) | Pituitary Gland | Pars Distalis, Adenoma (Includes multiple) |
| Prostate | Adenoma or Carcinoma (combined) | | |
| Adrenal Medulla | Benign, Malignant or Complex Pheochromocytoma (combined) | | |
| Islets, Pancreas | Adenoma or Carcinoma (combined) | | |
| **GSM Females** | | **CDMA Females** | |
| **Organ** | **Lesion** | **Organ** | **Lesion** |
| | | Brain | Malignant Glioma |
| | | Adrenal Medulla | Benign, Malignant or Complex Pheochromocytoma (combined) |

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# Filling the Knowledge Gaps

- Stress and Behavior
  - Issues:
    - Increases in pheochromocytomas and other neuroendocrine changes suggest a potential stress response
    - Potential impact of noise (mechanical or signal generated) should be further investigated
  - Some specific questions raised:
    - Does the animal's behavior change at the initiation or cessation of exposure to RFR?
    - Are there behavioral changes during exposure that reflect increased stress?
    - Is food consumption affected by RFR exposure?
  - Proposed areas of research
    - Measure serum stress hormones
    - Record video animals during exposure periods (behavior, activity)
    - Perform functional observational battery
    - Measure food consumption
    - Measure gene expression in multiple tissues - evaluation of stress-responsive genes
    - Investigate potential effects on the hypothalamic-pituitary-adrenal axis and sympathetic nervous system

# Filling the Knowledge Gaps

- Organ-specific evaluations
  - Issues:
    - As an unexpected target organ and the most robust finding in the NTP studies, the impact of RFR exposure on the heart requires further investigation
    - Brain tumors considered equivocal, peer review panel recommended “some evidence”
    - Adrenal gland considered equivocal, peer review panel recommended “some evidence”
  - Some specific questions raised:
    - Why are glial cells affected in the heart and brain?
  - Proposed areas of research
    - Evaluate cardiac parameters during exposure
    - Evaluate RFR-induced changes in gene expression in the heart, brain, and adrenal gland
    - Evaluate protein/enzyme expression as markers of damage or mechanisms of RFR-induced effects in target organs

# Filling the Knowledge Gaps

- Exposure factors
  - Issues:
    - Frequency-dependent and/or modulation-dependent
    - Intermittency of exposure
  - Some specific questions raised:
    - What impact does the length of the exposure on/off cycling (10 minutes) have on the RFR response?
    - Since both are RFR at the same frequency, can you combine GSM and CDMA exposure data?
  - Proposed areas of research
    - Comparative studies evaluating cycles of various lengths (5/5, 15/15, 20/20, etc.)
    - Co-exposure or alternating exposure to GSM and CDMA modulations

# Filling the Knowledge Gaps

- The role of heat in RFR-induced effects
  - Issues:
    - Contribution of heat and disruption of thermoregulatory process to RFR-induced effects
    - Some suggest that heating is the only mechanism by which RFR can induce a biological effect
  - Some specific questions raised:
    - Are effects caused by constant challenge to thermoregulatory system?
    - Are daytime body temperature measurements reflective of body temperature during animals' nighttime period of high activity?
  - Proposed areas of research
    - Studies comparing changes observed during exposure to RFR and similar heating by another (non-RFR) source
    - Comparative measurement of temperature during nighttime period of awake hours and daytime hours of animal inactivity

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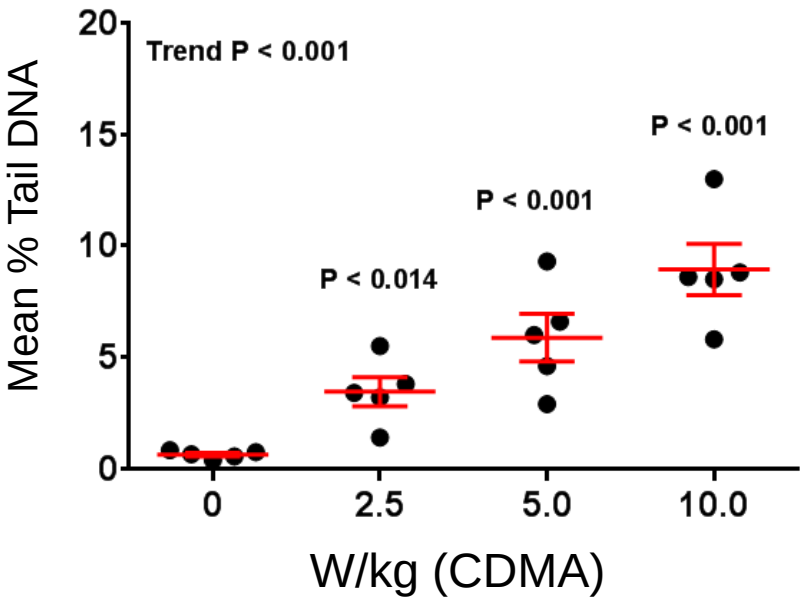
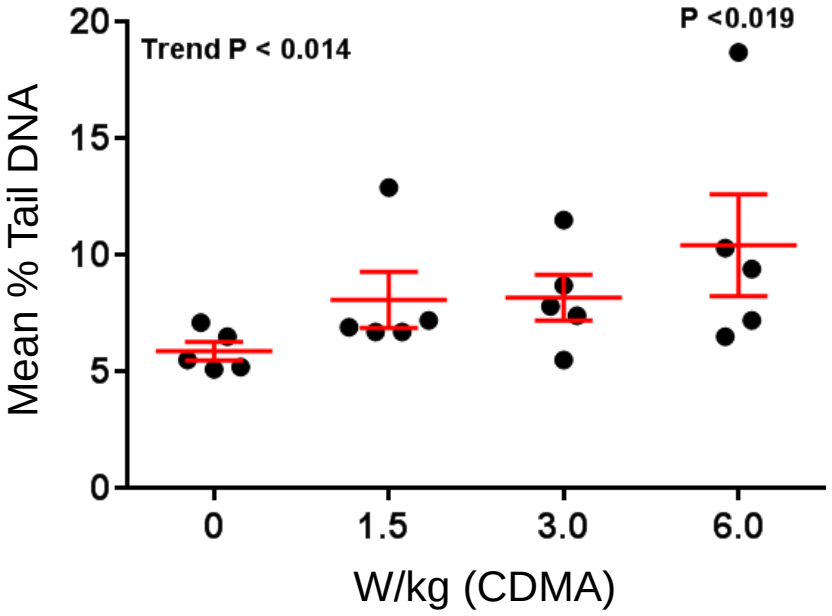
# Confirm DNA Damage Results

- Replicate previously observed comet data to confirm DNA damage effects
  - No historical experience for comet assay in these sub-regions of the brain
  - Low sample size (n=5), high interindividual variability (responders vs non-responders) may have confounded interpretation

**Male Mouse Frontal Cortex**




**Male Rat Hippocampus**



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- Conduct more robust and more targeted assays for DNA damage
- Evaluate activity and expression of DNA repair enzymes

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# Applying Knowledge to Newer Technologies

## Mobile Wireless Networks - Evolution

| 1G | 2G GSM | 3G UMTS | 4G LTE | 5G 5G |
|---|---|---|---|---|
|  |  |  |   |     |
| 1980's | 1990's | 2000's | 2010's | 2020's |
| Basic analogue voice<br>No IP | Digital voice<br>No IP | Digital voice<br>WWW, multimedia | Voice over IP<br>HD Video | Voice over IP<br>VR, V2X, IoT |
| 0 kbit/s | 14kbps | 2Mbps | 300Mbps | 1Gbps |
| One network for voice | One network for voice | One network for voice<br>Other network for IP | One network for IP | One network for IP |
| NMT, AMPS, TACS | GSM, IS-95<br>2.5G (GPRS, EDGE) | UMTS, CDMA2000<br>3.5G (HSDPA, HSUPA, HSPA+, LTE) | LTE-Advanced<br>4.5G (LTE-Advanced Pro) | LTE-Advanced Pro<br>NR |

Image source: https://www.quora.com/What-are-the-differences-between-1G-2G-3G-4G-and-5G

GRANDMETRIC
NETWORK & WIRELESS... STAY CONNECTED.


Image source: http://www.itilam.com/2016/04/what-is-difference-between-3g-4g-e-g-h-h.html

# Applying Knowledge to Newer Technologies

- Newer technologies utilize different modulation schemes
- 5G will utilize higher frequencies (3.1 GHz to 40 GHz)

| Generation→ Features↓ | 1G | 2G | 3G | 4G | 5G |
|---|---|---|---|---|---|
| Deployment | 1970 – 1980 | 1990 - 2001 | 2001-2010 | 2011 | 2015-20 onwards |
| Data Rates | 2kbps | 14.4-64kbps | 2Mbps | 200 Mbps to 1 Gbps | 1Gbps and higher |
| Technology | Analog Cellular Technology | Digital Cellular Technology: Digital narrow band circuit data Packet data | Digital Broadband Packet data: CDMA 2000 EVDO UMTS EDGE | Digital Broadband Packet data: WiMax LTE Wi-Fi | wwww Unified IP seamless combination of broadband LAN PAN MAN WLAN |
| Service | Analog voice service No data service | Digital voice with higher clarity SMS, MMS Higher capacity packetized data | Enhanced audio video streaming video conferencing support Web browsing at higher speeds IPTV support | Enhanced audio, video streaming IP telephony HD mobile TV | Dynamic Information access, Wearable devices with AI Capabilities |
| Multiplexing Switching | FDMA | TDMA, CDMA | CDMA | CDMA | CDMA |
| Core Network | PSTN | PSTN | Packet N/W | Internet | Internet |
| Standards | MTS AMTS IMTS | 2G:GSM 2.5:GPRS 2.75:EDGE | IMT-2000 3.5G-HSDPA 3.75G:HSUPA | Single unified standard LTE, WiMAX | Single unified standard |
| WEB Standard | | www | www(IPv4) | www (IPv4) | wwww (IPv6) |
| Handoff | Horizontal only | Horizontal only | Horizontal & Vertical | Horizontal & Vertical | Horizontal & Vertical |
| Shortfalls | Low capacity, Unreliable handoff, Poor voice links, Less secure | Digital signals were reliant on location & proximity, required strong digital signals to help mobile phones | Need to accommodate higher network capacity | Being deployed | Yet to be implemented |

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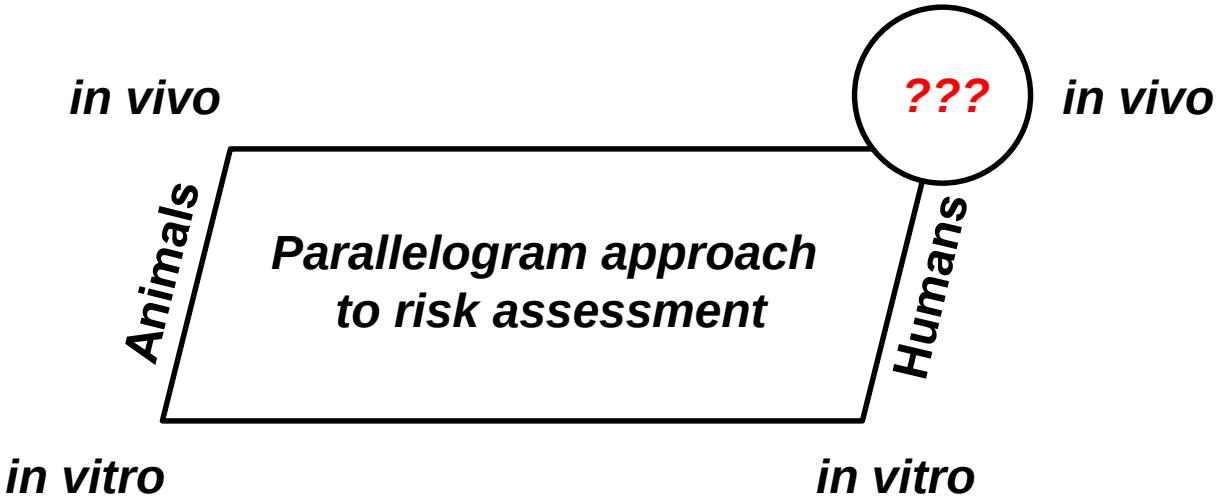
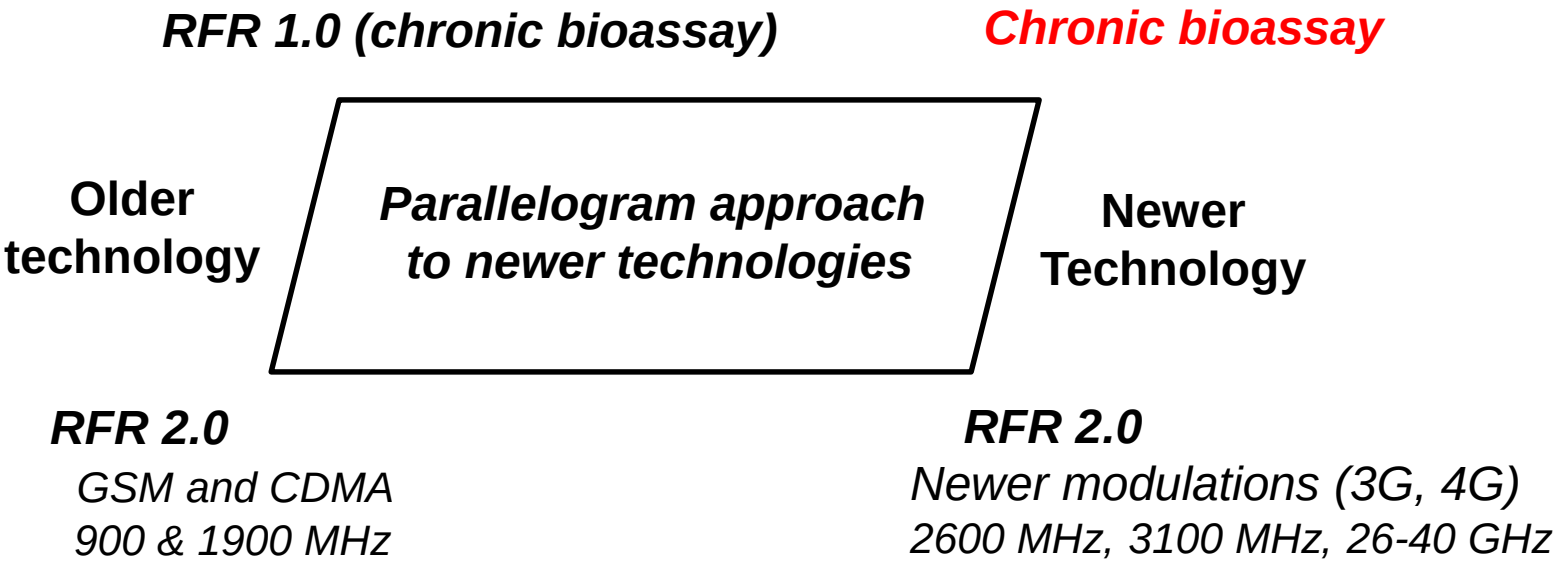


# Applying Knowledge to Newer Technologies

- Newer technologies utilize different modulation schemes
- 5G will utilize higher frequencies (3.1 GHz to 40 GHz)
- RFR 2.0 can bridge the gap between older and newer technologies



# Questions?


Image sources: https://funalive.com/articles/the-evolution-of-cell-phones_W3M.html
http://fixmytouchkelowna.com/the-evolution-of-the-cell-phone/ (edited)