NTP
National Toxicology Program

Cell Phone Radiofrequency Radiation (RFR) Project: Investigative Studies

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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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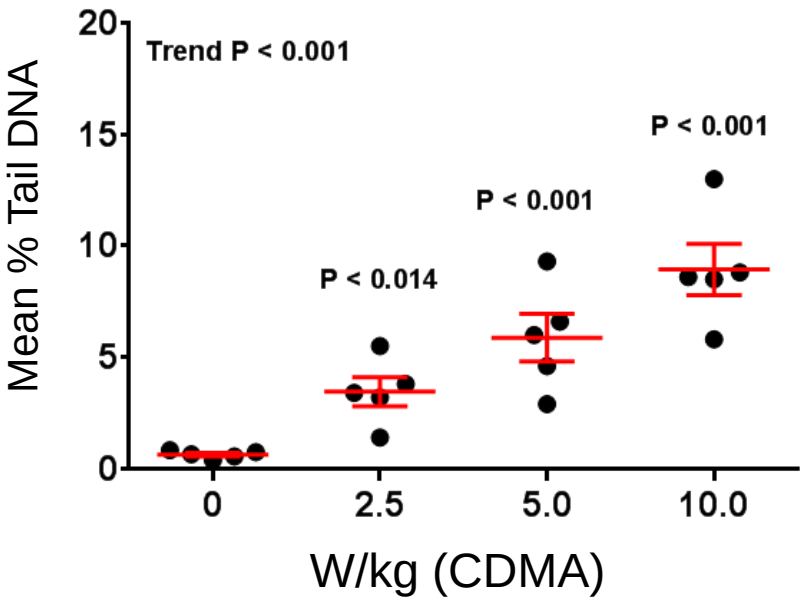
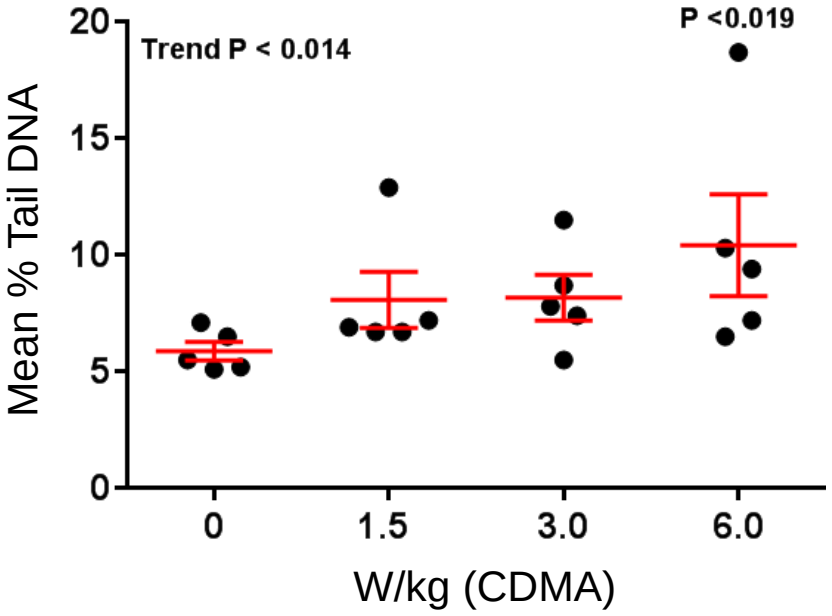
Confirm DNA Damage Results

- 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



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
- 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 No IP	Digital voice No IP	Digital voice WWW, multimedia	Voice over IP HD Video	Voice over IP VR, V2X, IoT
0 kbit/s	14kbps	2Mbps	300Mbps	1Gbps
One network for voice	One network for voice	One network for voice Other network for IP	One network for IP	One network for IP
NMT, AMPS, TACS	GSM, IS-95 2.5G (GPRS, EDGE)	UMTS, CDMA2000 3.5G (HSDPA, HSUPA, HSPA+, LTE)	LTE-Advanced 4.5G (LTE-Advanced Pro)	LTE-Advanced Pro 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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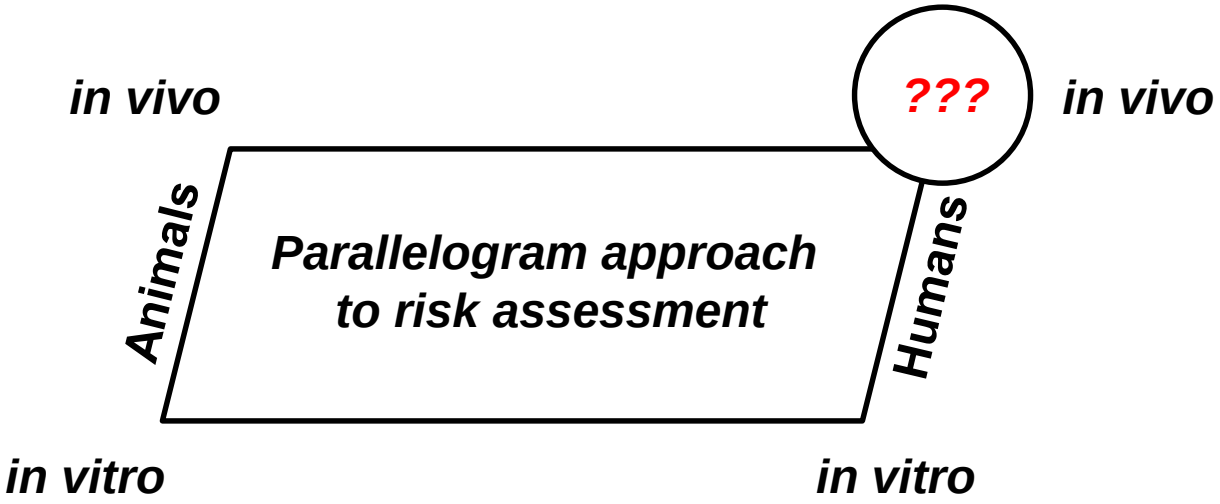
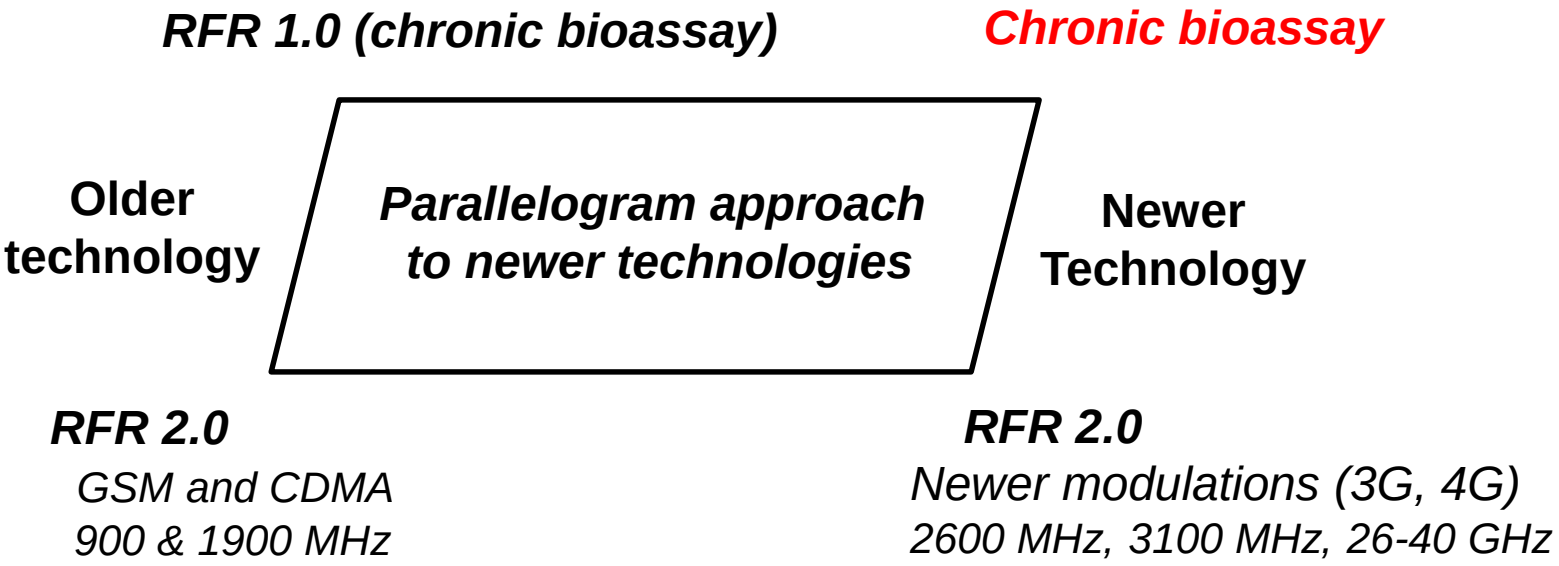


Applying Knowledge to Newer Technologies

- 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)