



National Institute of Environmental Health Sciences
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Partial Results of NTP Carcinogenicity Studies of Cell Phone Radiofrequency Radiation in Rats

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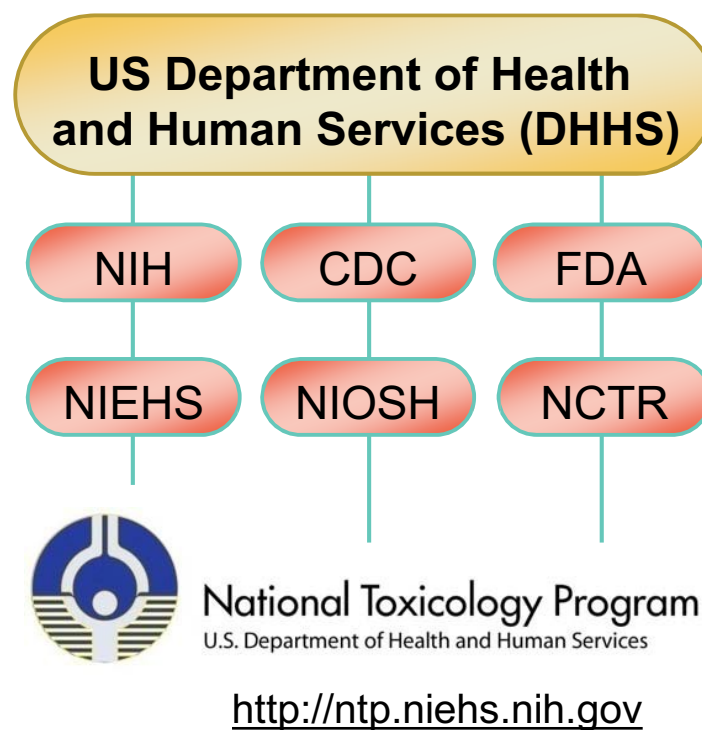
**National Institute of Environmental Health Sciences
National Toxicology Program**

January 23, 2017 ♦ Jerusalem, Israel



The US National Toxicology Program (NTP)

- **Interagency program**
 - Established in 1978
 - Headquartered at NIEHS
- **Research on “nominations”**
 - Thousands of agents evaluated in comprehensive toxicology studies
 - Results communicated through technical reports, scientific publications, and the web
- **Analysis activities**
 - Report on Carcinogens
 - Office of Health Assessment & Translation
 - NTP Interagency Center for the Evaluation of Alternative Toxicological Methods



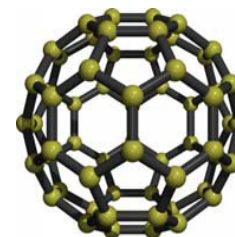
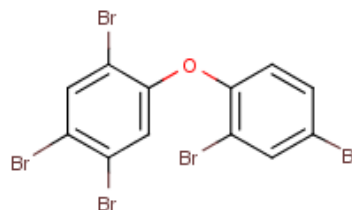
The mission and goals of the NTP

- *Mission:*
 - Evaluate agents of public health concern applying tools of modern toxicology and molecular biology
- *Goals:*
 - Coordinate toxicological testing programs within the Department of Health and Human Services
 - Develop testing methods that reduce, refine, or replace the use of animals
 - Generate data to strengthen scientific knowledge about potentially hazardous substances
 - Communicate this information to health regulatory and research agencies, scientific and medical communities and the public



Current areas of research emphasis

- Botanicals
- Combination AIDS therapeutics
- Complex occupational exposures
- Endocrine active compounds
- Flame retardants
- Food and drinking water contaminants
- Green chemistry
- Industrial chemicals
- Nanoscale materials
- Persistent environmental contaminants
- Personal care products
- **Radiofrequency radiation**



Numbers of substances studied

- Chronic rodent cancer bioassays ~650
- Genetic toxicity ~3000
- Immunotoxicity ~150
- Reproductive/developmental ~400
- General toxicity/other ~900

- How many chemicals are in commerce?
- TSCA inventory ~85,000
- Chemical industry ~ 7,500
- What about everything else? ~ ?



Value of rodent toxicology and cancer studies

- Rats and mice are the principal species used
- Basic biological processes conserved across species
- Two-year exposure covers majority of lifespan
- Every agent known to cause cancer in humans has been shown carcinogenic in animals when adequately tested
- Almost one-third of known human carcinogens were identified following first findings in rodent studies

Background

- U.S. Food and Drug Administration (FDA) nominated cell phone radiofrequency radiation (RFR) emissions for toxicology and carcinogenicity testing
- Specific concern raised for cell phone RFR exposure to the head
- Epidemiology studies demonstrate a potential increase in glial cell tumors in the brain and vestibular schwannomas (acoustic neuromas) may be associated with cell phone usage
 - Inconsistent results, confounding factors, biases, and long latency periods
- Studies in laboratory animals have not associated exposure to RFR with an increase in tumors at any site
 - Study inadequacies and limitations
 - Physical and logistical challenges inherent in testing RFR
- IARC 2B classification – *Possibly carcinogenic to humans*

The NTP RFR reverberation chambers

Empty Chamber



Cage Racks

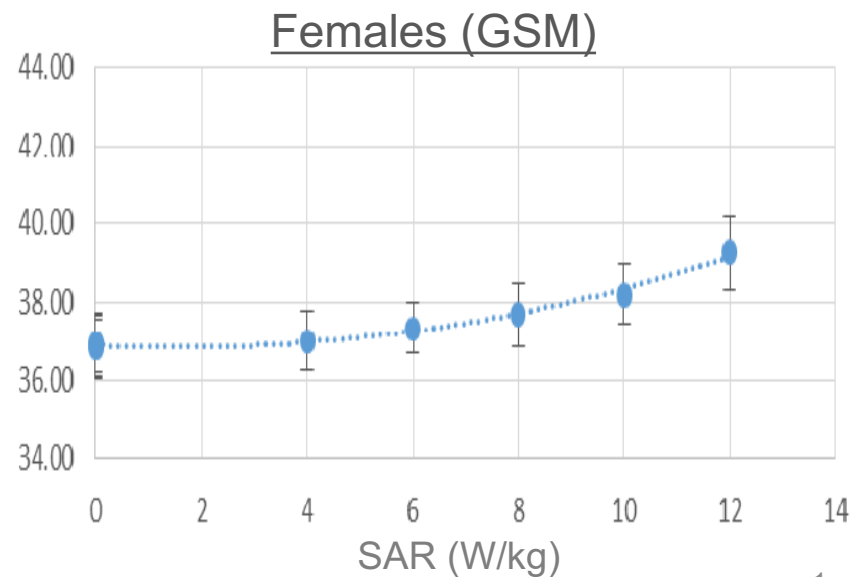
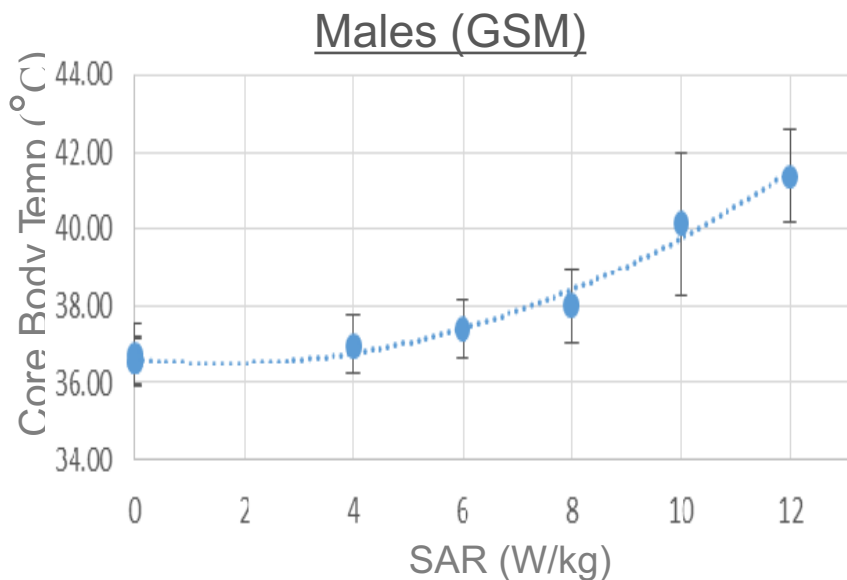


Cell phone RFR research program

- Three-phase toxicology and carcinogenicity studies in Harlan Sprague Dawley rats and B6C3F₁ mice
 - **5-day thermal pilot** studies at SARs of 4-12 W/kg in young and aged rats and mice and pregnant rats (10 studies)
 - **28-day prechronic** toxicology studies
 - **2-year** toxicology and carcinogenicity studies
- In all studies, daily exposure to RFR in reverberation chambers for ~9 hours (18 hr 20 min per day in 10 min on/10 min off cycles)
 - Rats exposed to GSM- or CDMA-modulated signals at 900 MHz
 - Mice exposed to GSM- and CDMA-modulated signals at 1900 MHz

5-day thermal pilot studies

- Determined if animal size (young and aged) or pregnancy status affect RFR thermal effects
 - Measured body temperature, body weight, and survival
- Body temperatures collected via implanted microchips at multiple time points over 5 days
 - A body temperature increase of 1°C was considered an upper tolerable, thermal limit



2-Year cancer study summary

- Body weights at birth and throughout lactation in rat pups exposed *in utero* tended to be lower than controls
- In general, survival was greater in all groups of GSM or CDMA RFR-exposed rats compared to controls
- Increased incidence of schwannoma was observed in the hearts of male rats
 - Significant SAR-dependent positive trend (GSM and CDMA)
 - Significant pair-wise increase at 6 W/kg (CDMA)
- There was a significant SAR-dependent trend for increased gliomas in the brain of rats exposed to CDMA-modulated RFR
- Incidences of heart and brain lesions were not significantly different in female rats

Cell Phone Radiation: GSM

<https://ntp.niehs.nih.gov/testing/status/agents/ts-08013.html>

Cell Phone Radiation: CDMA

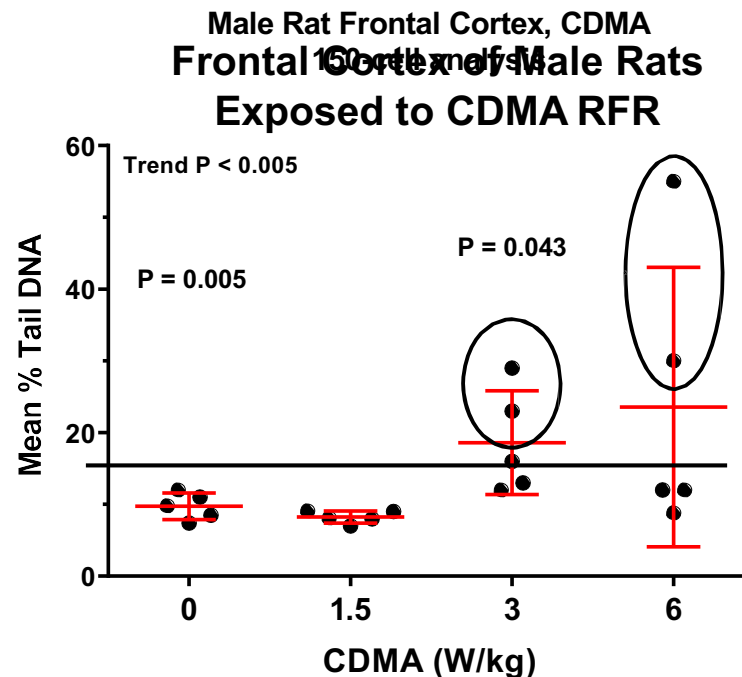
<https://ntp.niehs.nih.gov/testing/status/agents/ts-08015.html>

Conclusions

- Hyperplastic lesions and glial cell neoplasms of the heart and brain in male rats are considered likely the result of whole-body exposures to GSM- or CDMA-modulated RFR.
 - Higher confidence in the association between RFR exposure and the neoplastic lesions in the heart than in the brain.
- Exposure of female rats to GSM- or CDMA-modulated RFR resulted in no biologically significant effects in the brain or heart.
- Full rat and mouse histopathology tables expected for public release by November, 2017
- Draft NTP Technical Report is anticipated to be peer reviewed at a public meeting in early 2018

Genetic toxicology results in rats and mice

- Micronucleus assay
 - No significant increases in micronucleated red blood cells in rats or mice
- Comet assay
 - Mixed results in different tissues and brain regions in rats and mice
 - Responders vs. non-responders



Comet assay summary for rats and mice

		MALE					FEMALE				
RATS	CDMA	Frontal Cortex	Cerebellum	Hippocamp	Liver	Blood	Frontal Cortex	Cerebellum	Hippocamp	Liver	Blood
	GSM	Frontal Cortex	Cerebellum	Hippocamp	Liver	Blood	Frontal Cortex	Cerebellum	Hippocamp	Liver	Blood
MICE	CDMA	Frontal Cortex	Cerebellum	Hippocamp	Liver	Blood	Frontal Cortex	Cerebellum	Hippocamp	Liver	Blood
	GSM	Frontal Cortex	Cerebellum	Hippocamp	Liver	Blood	Frontal Cortex	Cerebellum	Hippocamp	Liver	Blood

Yellow

Statistically significant trend and pairwise SAR-dependent increase

Blue

Statistically significant trend or a pairwise increase

Green

Not significantly different, but increased in 2 or more treatment groups

What US Government Agencies Are Concerned With RFR?

- **Federal Communications Commission (FCC)**
 - Cell phone devices are required to meet exposure guidelines set by the FCC
 - Based on acute effects from higher levels of exposure, and may not be protective against chronic, lower levels of exposures
- **Food and Drug Administration (FDA)**
 - FDA jurisdiction for any health-related issues under the 1968 Radiation Control for Health and Safety Act
 - Cannot mandate the cell phone industry to provide data on health effect
- **Other agencies have interest**
 - National Cancer Institute (NCI), Environmental Protection Agency (EPA), National Institute for Occupational Safety and Health (NIOSH)

What are next steps?

- **Smaller scale exposure facility under development**
 - Chamber design and exposure capabilities similar to original study
 - Verification of exposure characteristics provided by NIST
 - Provides capability to:
 - discover molecular events induced by RFR (e.g. oxidative stress)
 - replicate and expand genetic toxicity findings and assays (DNA repair processes of particular interest)
 - examine early molecular changes in heart
 - explore thermal effects when not induced by RFR (other heat sources)
 - study other frequencies and modulations
 - evaluate newer technologies (4G, LTE, 5G, etc.)

Acknowledgements/Collaborations

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Thank You!

Questions?



**National Institute of
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National Toxicology Program
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**National Institute of
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Superfund Research Program



The NTP RFR exposure facility

