Exploring the Mechanisms of the Radioadaptive Response

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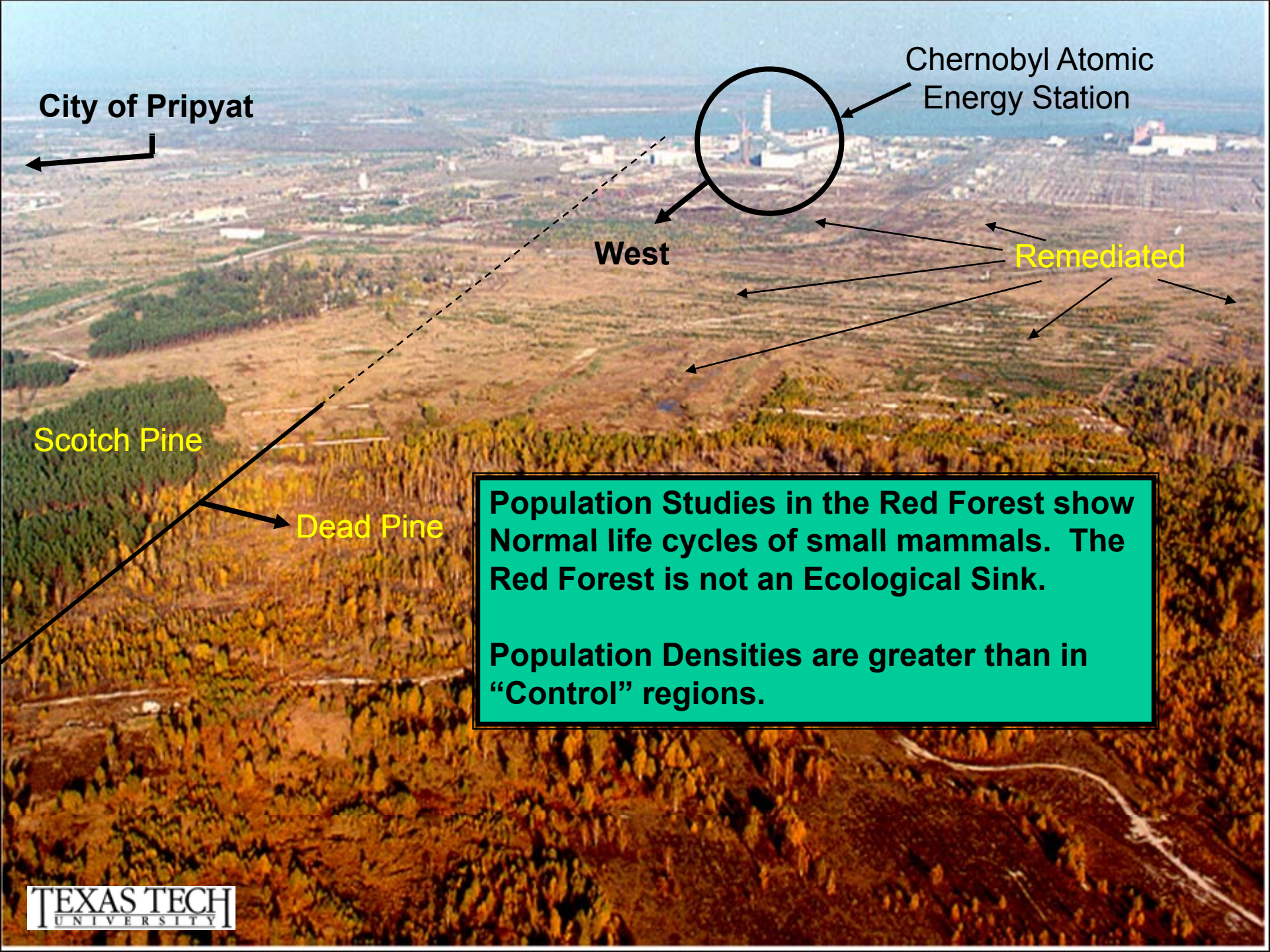
Overview

- Brief History of Studies at Chernobyl
- Specific Aims of Radioadaptive Experiments
- Experimental Design
- Results
- New Directions

Bank vole – the All-time radiation winner!


City of Pripyat
Chernobyl Atomic Energy Station
West
Remediated
Scotch Pine
Dead Pine
Population Studies in the Red Forest show Normal life cycles of small mammals. The Red Forest is not an Ecological Sink.
Population Densities are greater than in "Control" regions.
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Specific Aims:

- To characterize transcriptional responses as a function of dose, dose rate and duration of exposure

Specific Aims:

- To investigate radio-adaptive response in inbred strains of mice continuously exposed to the Chernobyl environment

Specific Aims:

- To investigate variation in response as a function of priming dose, dose rate and duration of exposure

Specific Aims:

- To archive tissues and nucleic acids as a resource for future studies

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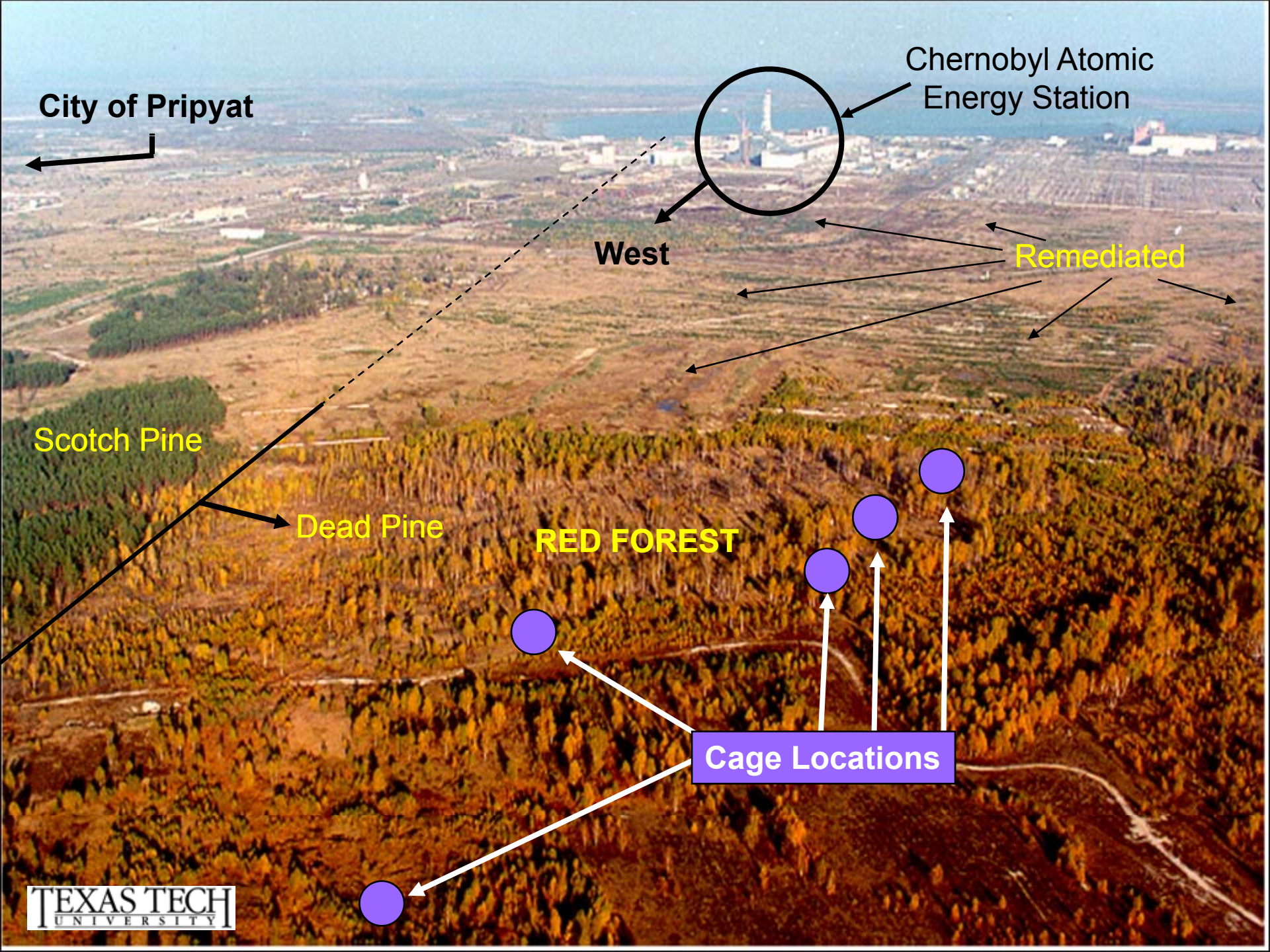
City of Pripyat
Chernobyl Atomic Energy Station
West
Remediated
Scotch Pine
Dead Pine
RED FOREST
Cage Locations
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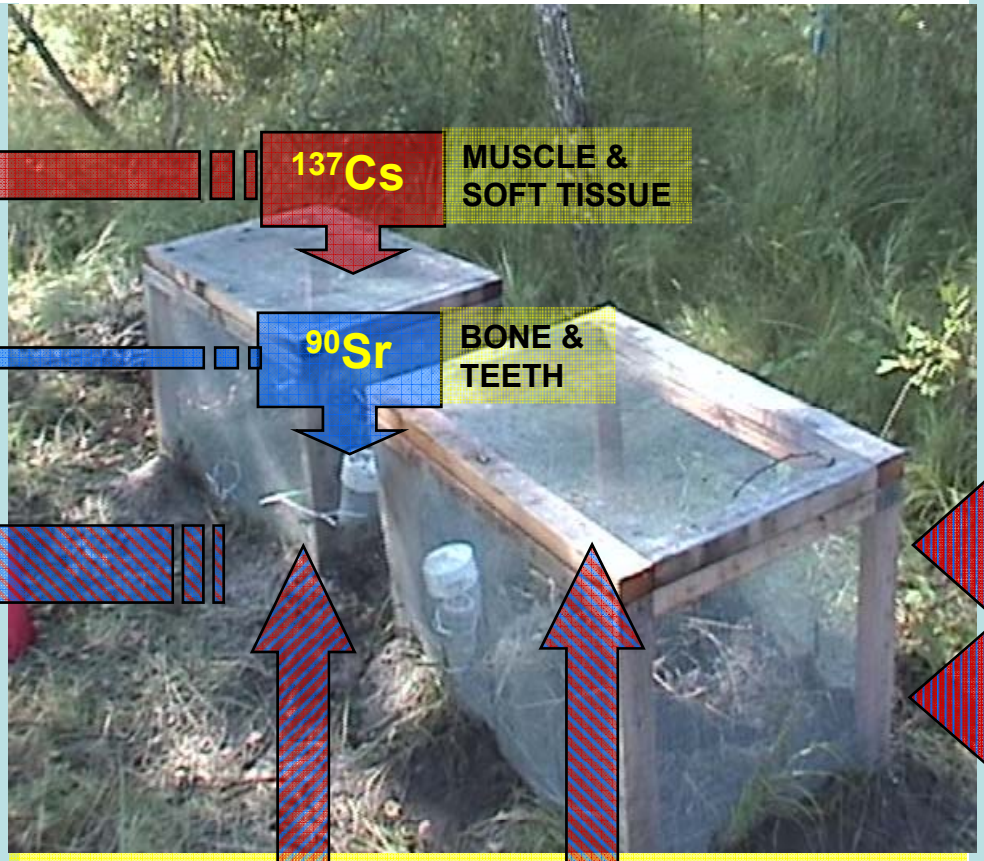

LOSSES

γ-photons
Not absorbed

β-particles
Not absorbed

Egestion &
Urination

^{137}Cs MUSCLE & SOFT TISSUE

^{90}Sr BONE & TEETH

INTERNAL EXPOSURE

INHALATION
Aerial particles

INGESTION
Food & particles

Airborne Particles

Soil & Vegetation

EXTERNAL EXPOSURE

Experimental Enclosures in the Red Forest

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Experiments & Environmentally Relevant Radiation Exposure Groups

- Areas in the Red Forest were identified in which a total absorbed dose of 10 cGy could be achieved.

Mus musculus, BALB/c mice (N=10, male) were placed in enclosures at each field site for 10, 20, or 45 days.

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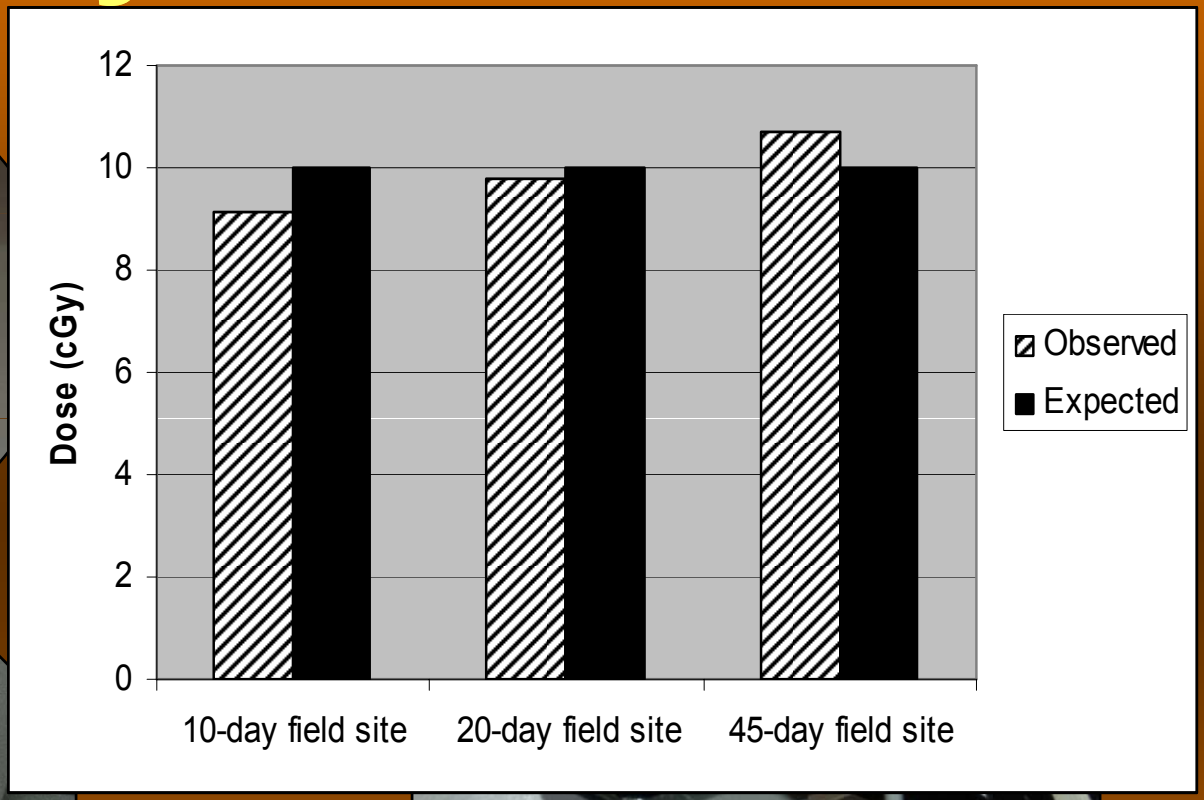
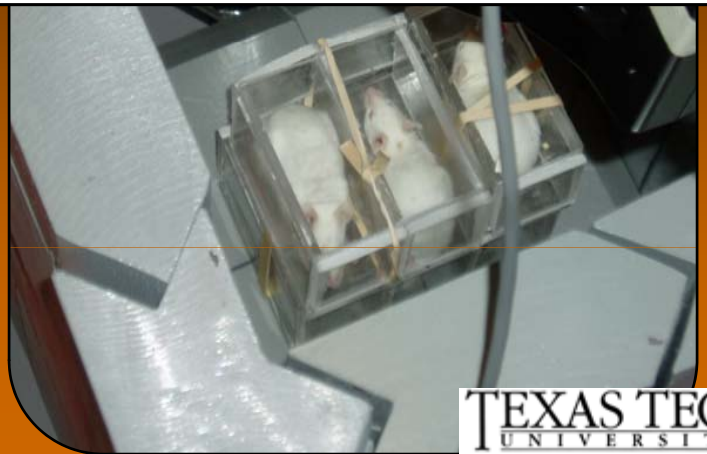
Dosimetry





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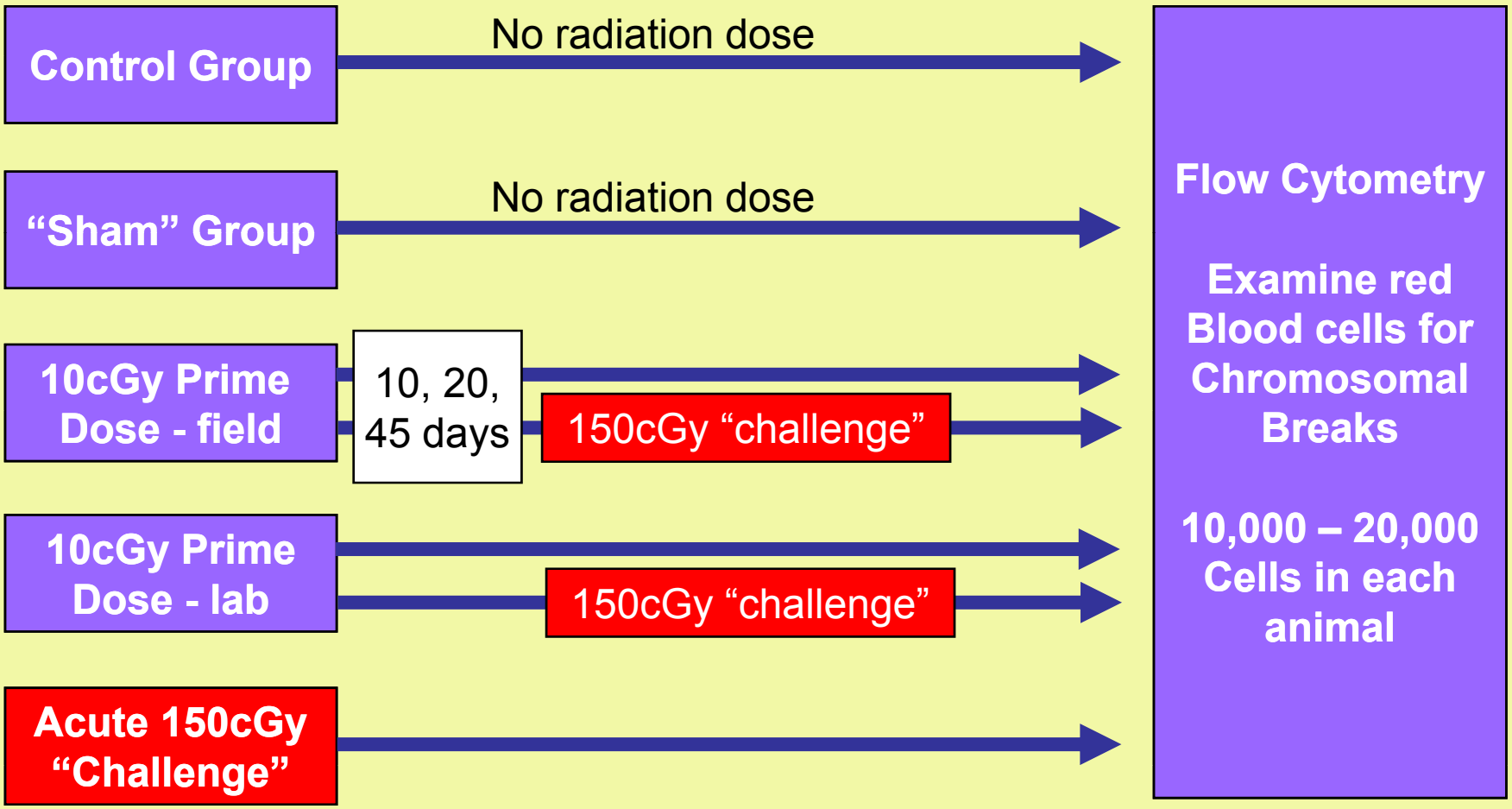
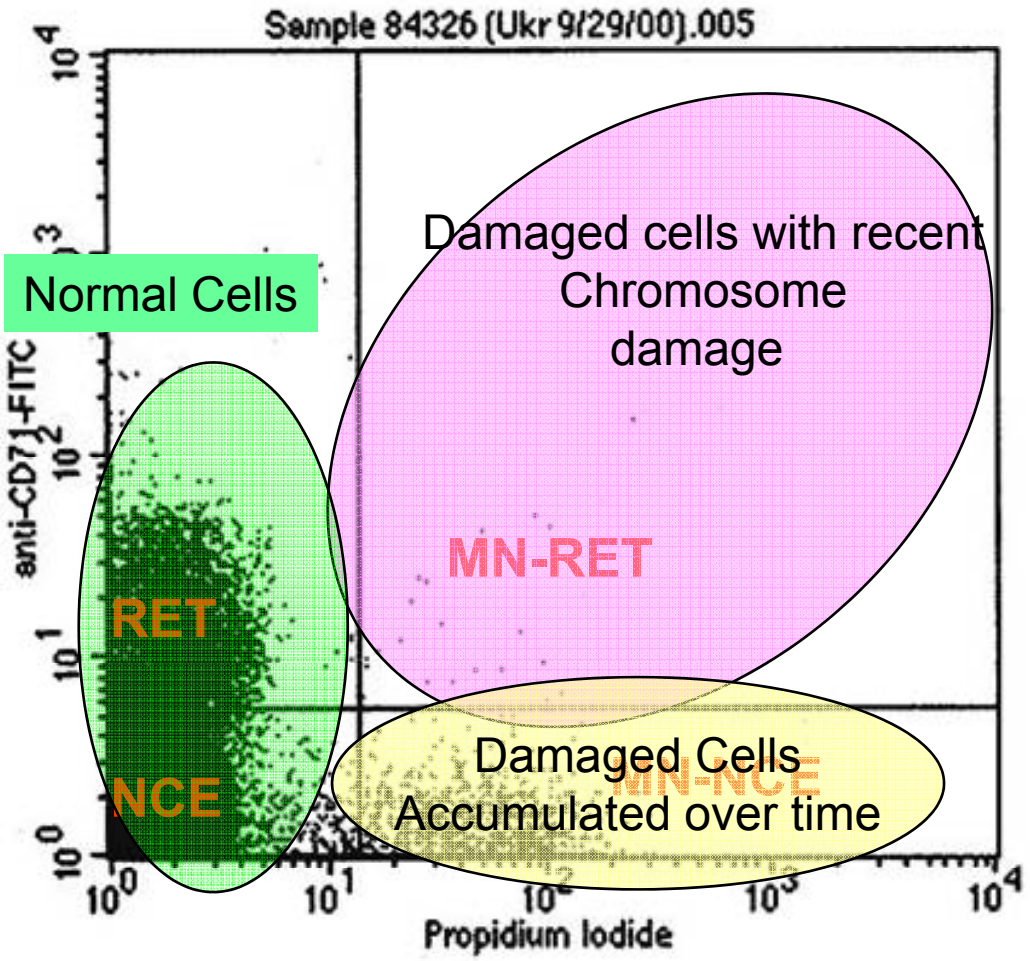
BALB/c Experimental Design



MicroFlow® micronucleus assay



- Enumerates MN in peripheral blood reticulocytes
- 10-20,000 reticulocytes analyzed per blood sample

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Overview

- Define Radioadaptive Response
- Units of Radioactivity
- Objectives of Radioadaptive Experiments
- Experimental Design
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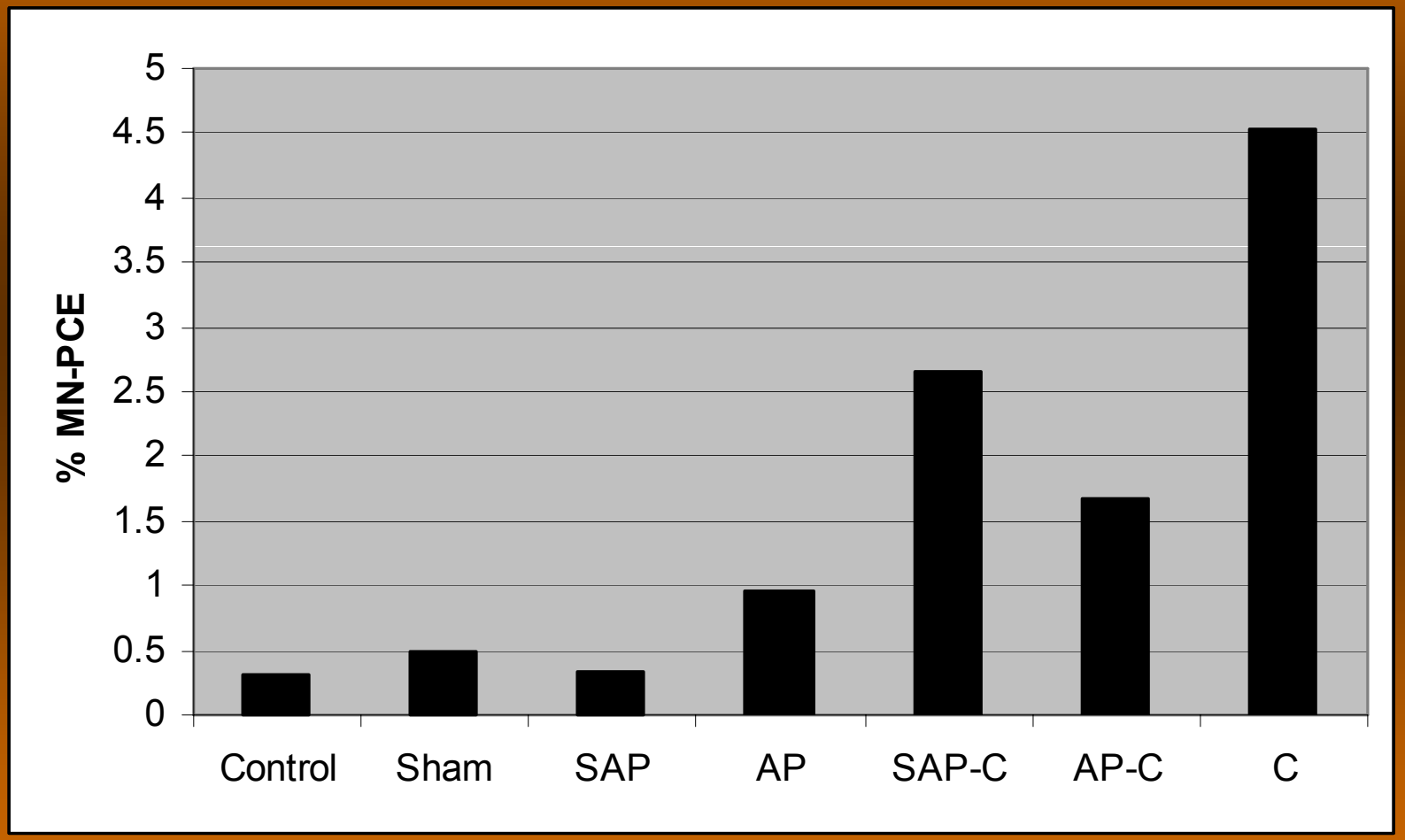
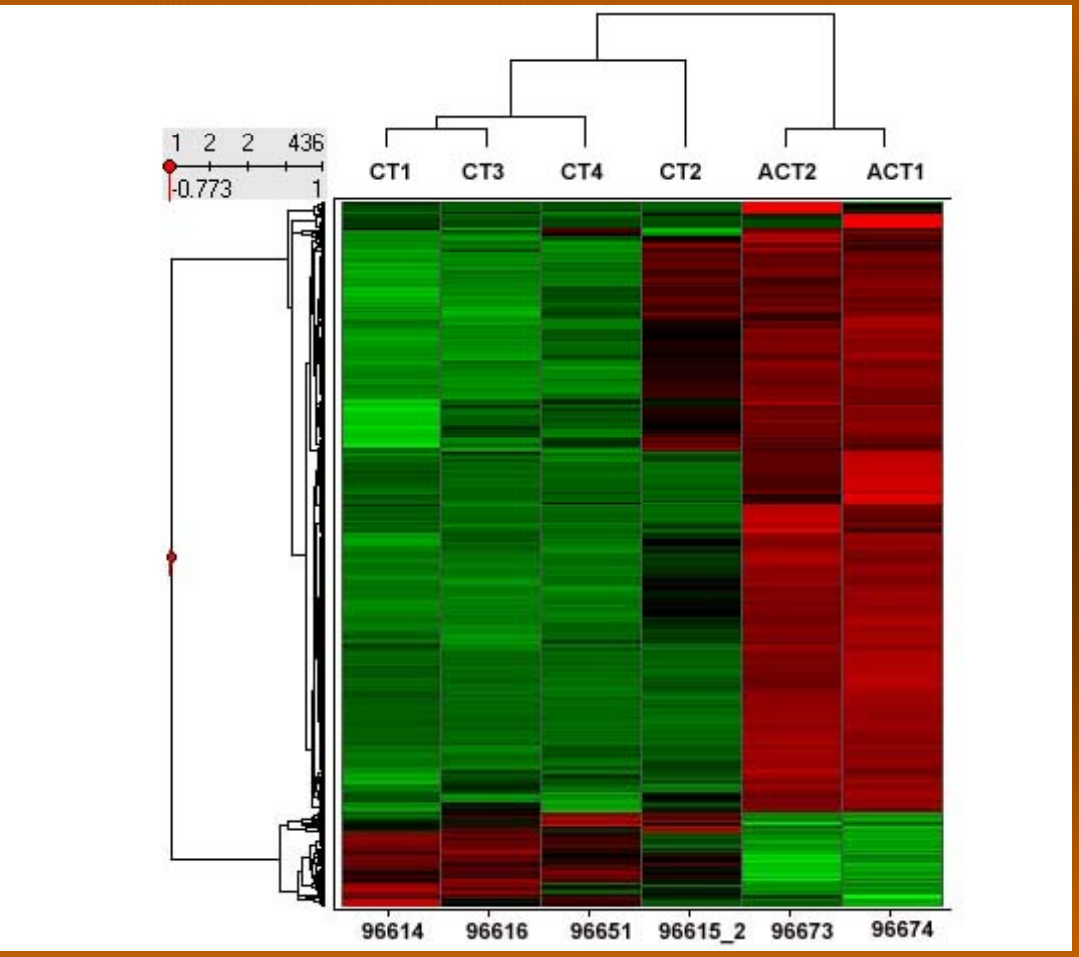
MN-RET frequencies



Expected and Observed Mean MN-RET Frequencies

Group	Expected % MN-RET	Observed % MN-RET	Reduction
SAP + 1.5 Gy	4.86	2.65	45%
AP + 1.5 Gy	5.49	1.68	69%

Gene Chip Analysis



Heat Map comparing controls to 45d exposed

Total RNA wa isolated from liver, RNA from each mouse was then hybridized to its own Affymetrix GeneChip Mouse Genome 430 2.0 Array®

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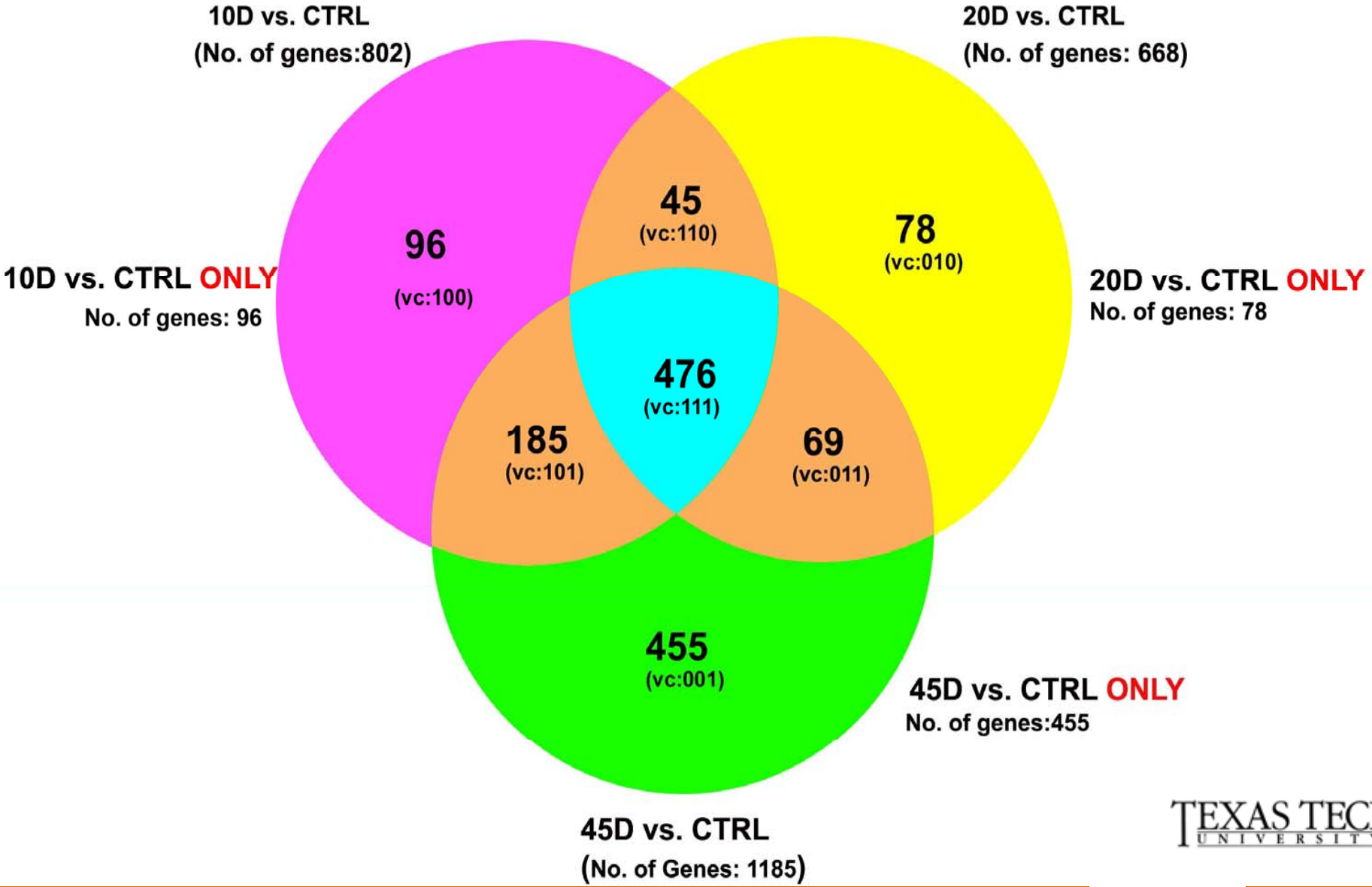
Differentially Expressed Genes



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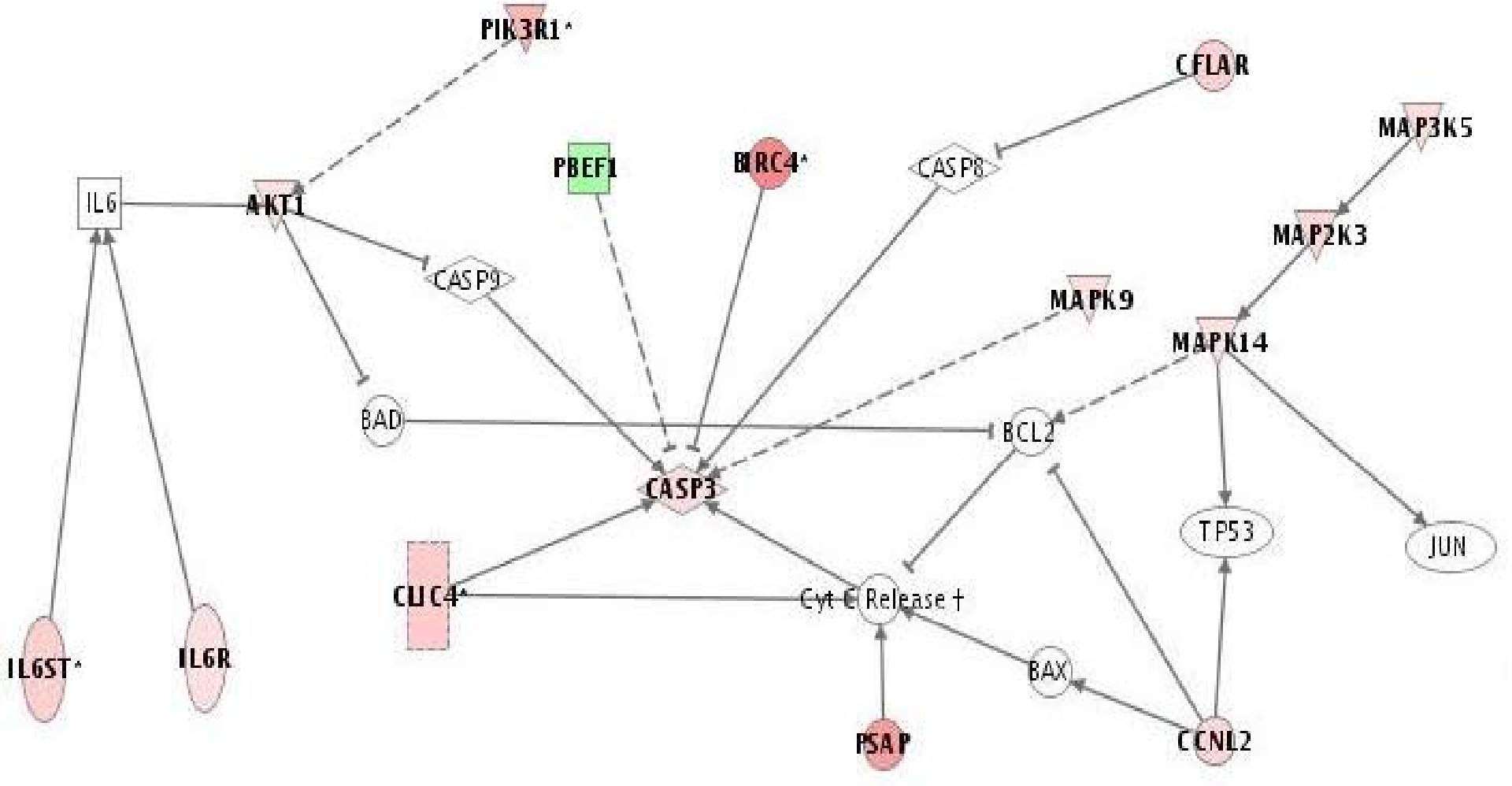
Biological network suggested by IPA ver. 4.1 in which several genes products involved in apoptosis are present. Many of these are differentially transcribed in all exposed animals in comparison to unexposed animals thus possibly representing a signature of low-dose rate exposure.



Future Directions for Chernobyl Research

- Principal Components Analysis (PCA) on genomics datasets.
- Transcriptomic analysis from skeletal muscle tissue (a subset of the same mice used in the liver analyses).
- Real-time PCR array (n = 41 transcribed genes) Molecular Genomics Core facility (UTMB) to validate a subset of genes in the genechip arrays.

Future Directions for Chernobyl Research

- Genetic Susceptibility
- *In utero* exposures
- MN origin
- SEM for Metals Analysis
- Evaluate trans-generational responses (mutational load)

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