"You Want to Irradiate What?"

Why Biologists Should Come to Love Their Dosimetrists

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Scientific Director

AFRRI/USU

Opinions expressed are these of the speaker and do not represent official policy for USU/DoD.

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Scientific Program

Prophylaxis → **Therapy** → **Survival**

Protection

- Candidate screening
- Drug evaluation

Assessment
Biodosimetry

- Cellular and Molecular markers
- Automation

Treatment

- Drug evaluation
- Metal toxicity

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AFRRI's Radiation Countermeasures Program

- Integrating basic and applied research
- 75% of research funds come from competitive extramural sources (NIH, NASA, DTRA, DMRDP, CDMRP, etc)
- Focus on radiation countermeasure candidates with realistic chance of success (route, toxicity, etc)
- High throughput radiation sources (photons, neutrons)
- Coordination between industry, academia, regulatory agencies

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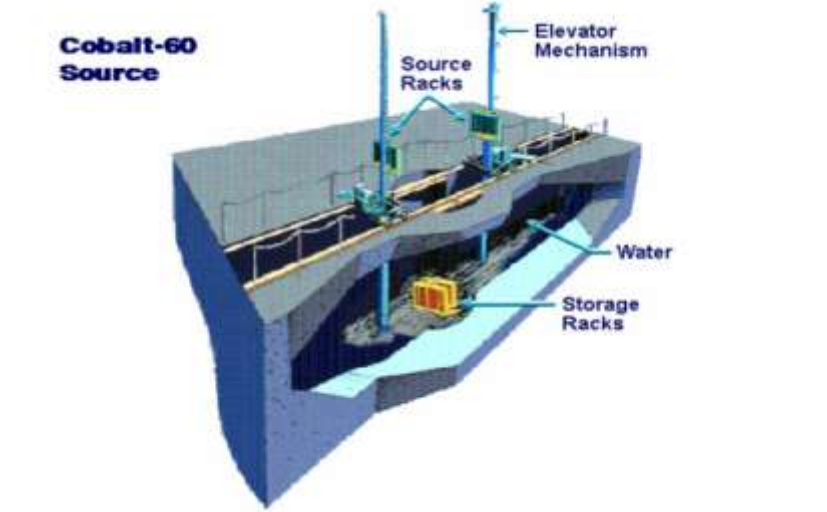
Cobalt-60 γ-Irradiation

- **Average γ-ray energy: 1.25 MeV**
- **Over 165 kCi (9/8/2011) total activity:**
  - **15 kCi (older source)**
  - **150 kCi (newer source)**



- **Each source consists of a pair of planar arrays (bilateral irradiation)**
- **Maximum dose rate to water: 6 kGy/h**
- **Most commonly used dose rate to water: 0.6 Gy/min**
- **Targets: cells, mice, rats, pigs, spores, non-human primates**

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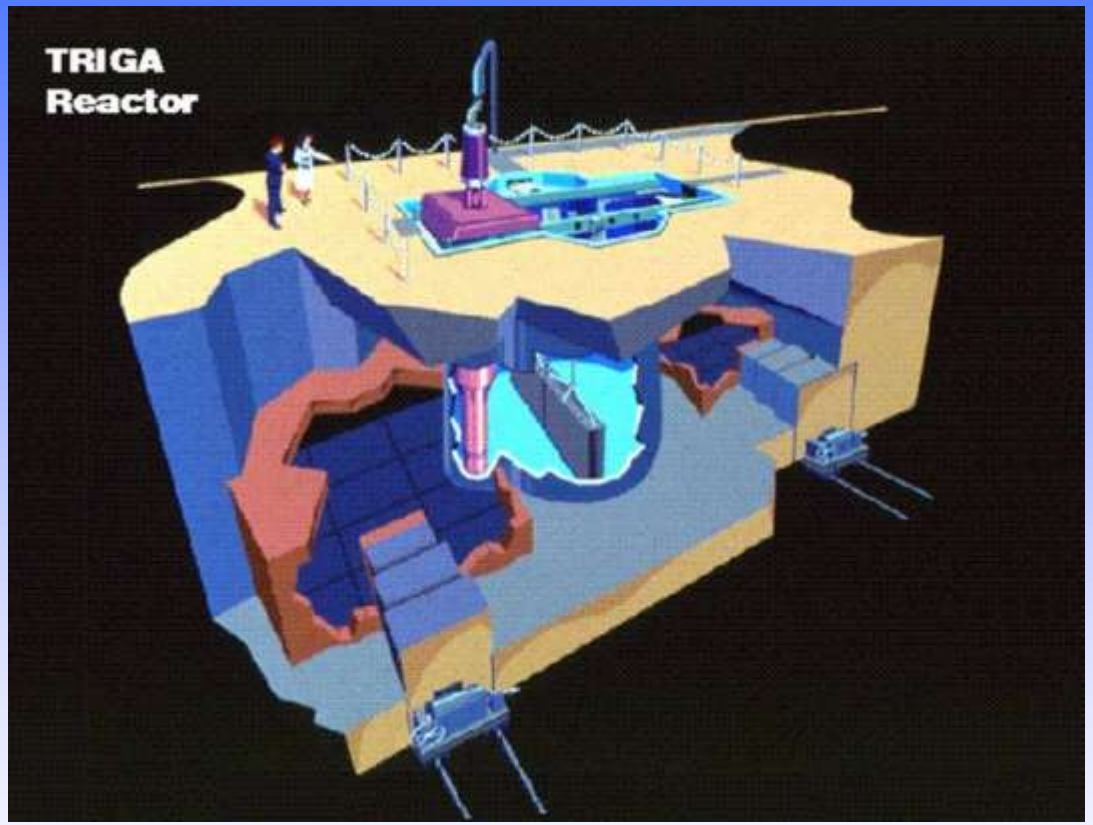
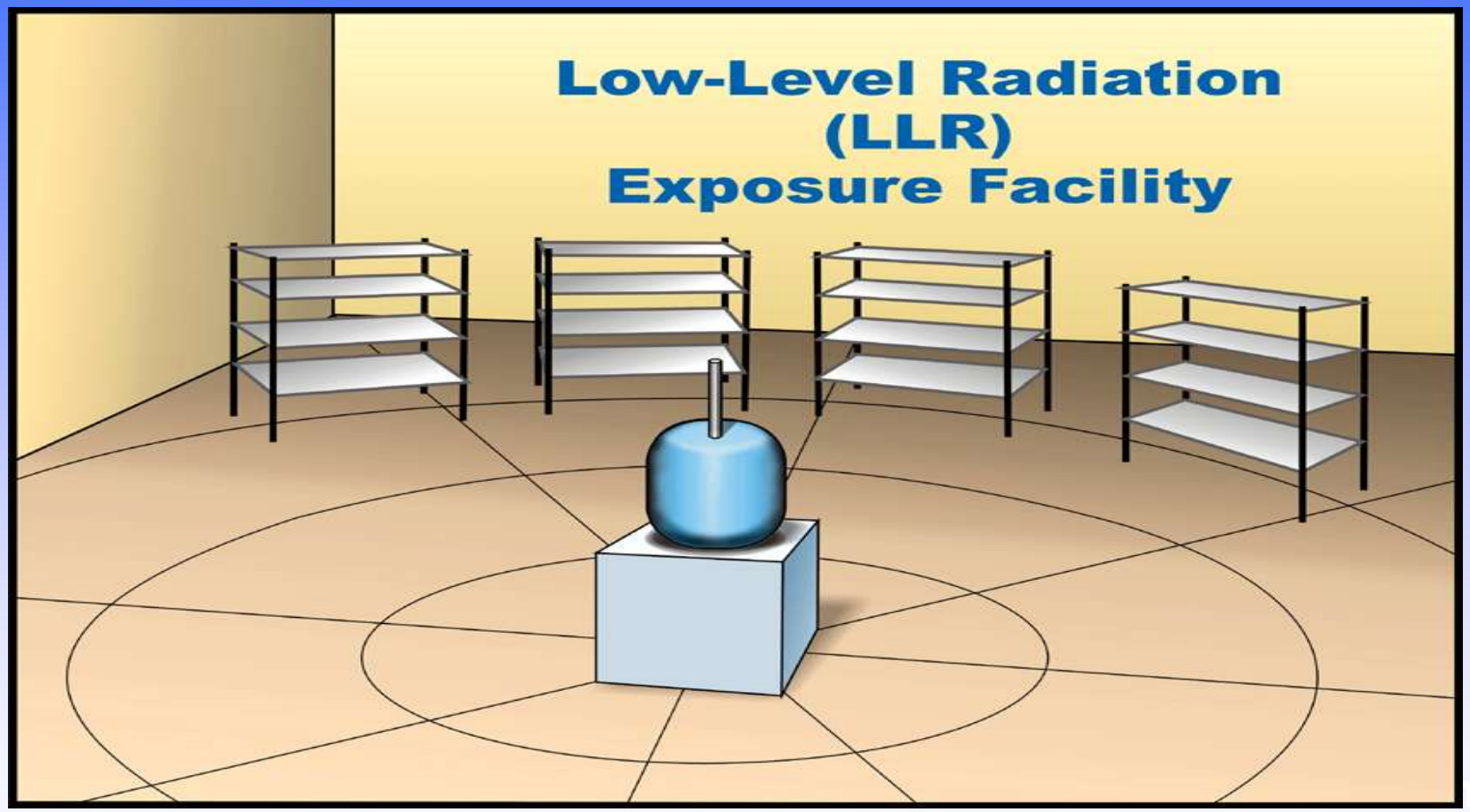
AFRRI TRIGA Reactor



- Mixed field (neutron & gamma)
- Steady state (max. power 1 MW) or pulsed mode (max. power 4,000 MW)
- Higher RBE for mixed field than gamma or x-ray
- Targets: cells, mice
- Most commonly used irradiation parameters: 0.6 Gy/min, 69 kW, 66% neutron

Delivers chronic radiation doses to biological samples to study early and late effects



doses to biological samples
to study early and late effects

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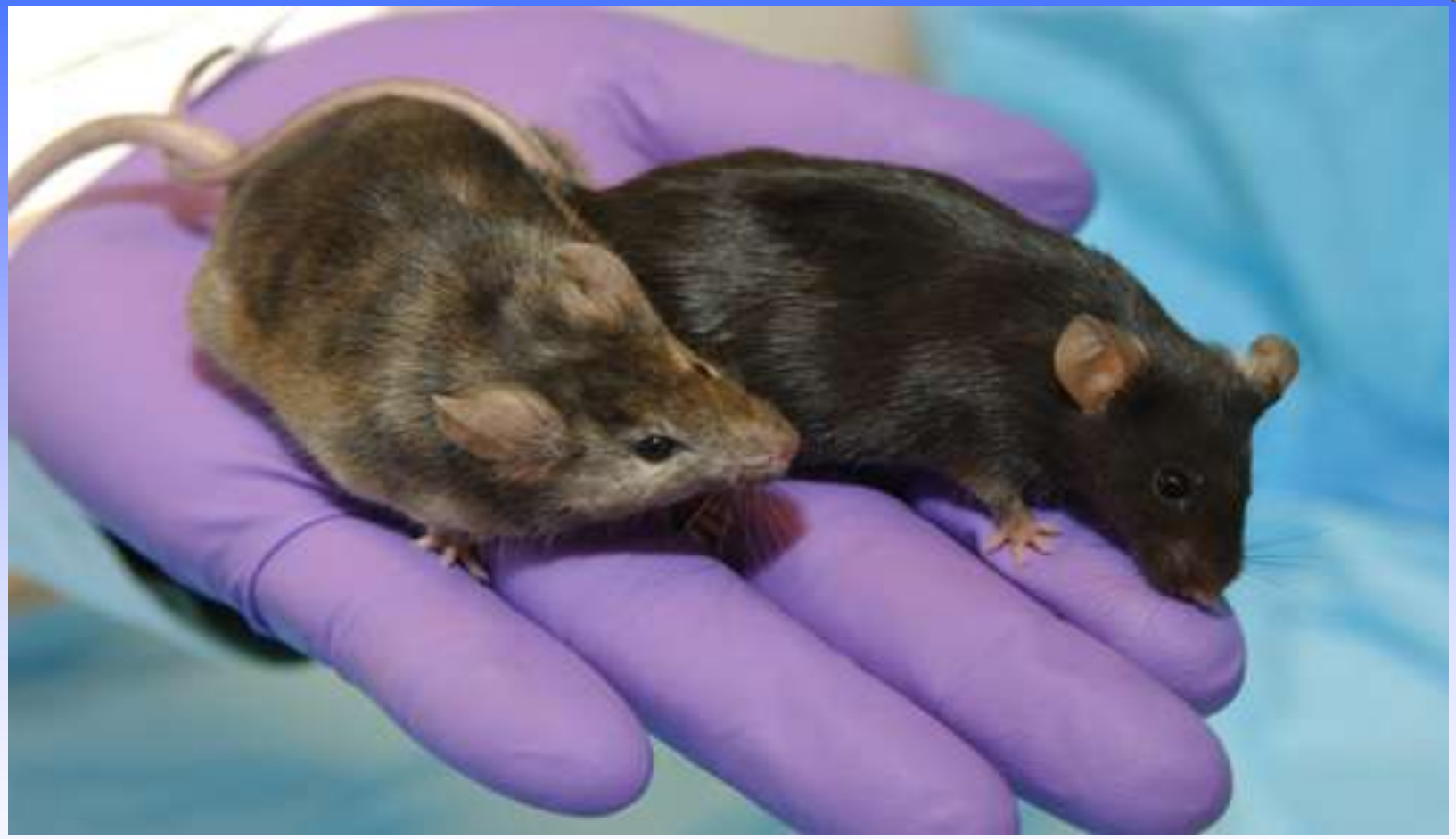
The Mouse



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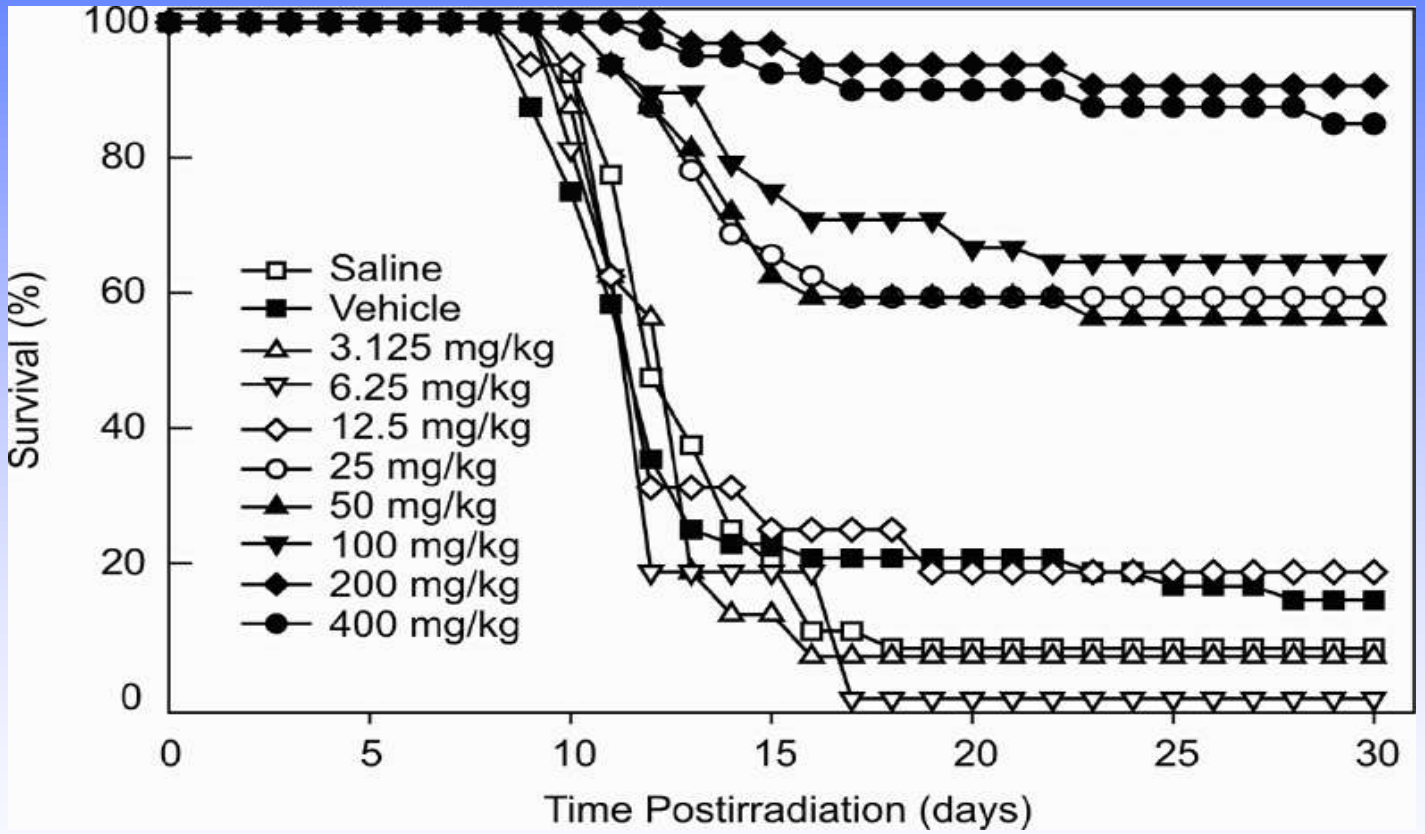
Genistein (BIO300): Conceived, patented, initiated, developed by AFRRI. AFRRI recruited private company to aid advanced development. Small molecule anti-apoptotic kinase inhibitor (PI: Michael Landauer) IND: 2007

Survival in Mice

Genistein administered sc 24 h before irradiation



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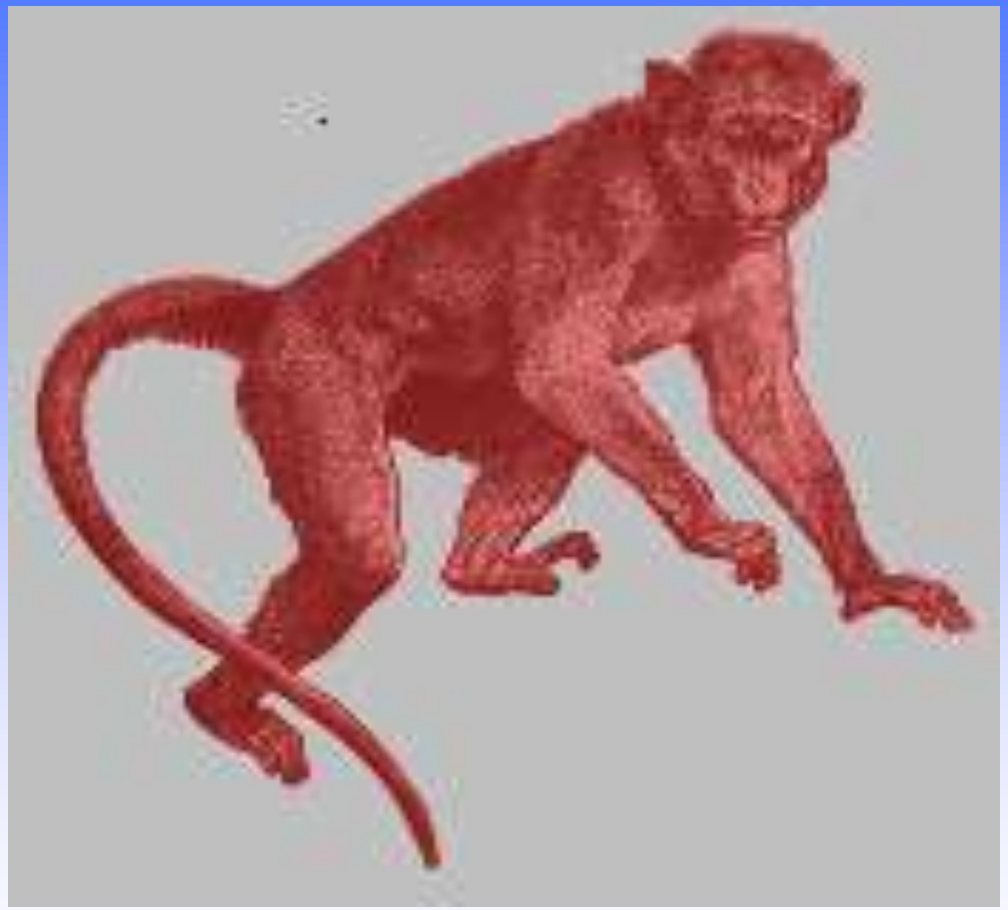
Non-Human Primate



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Gottingen Minipig

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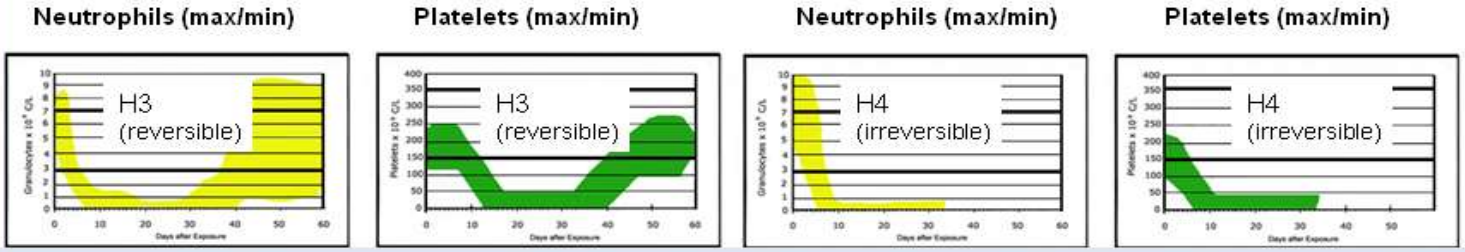
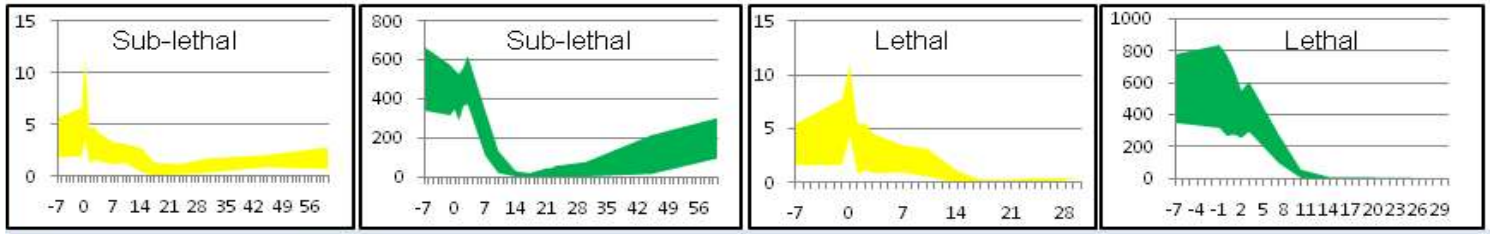
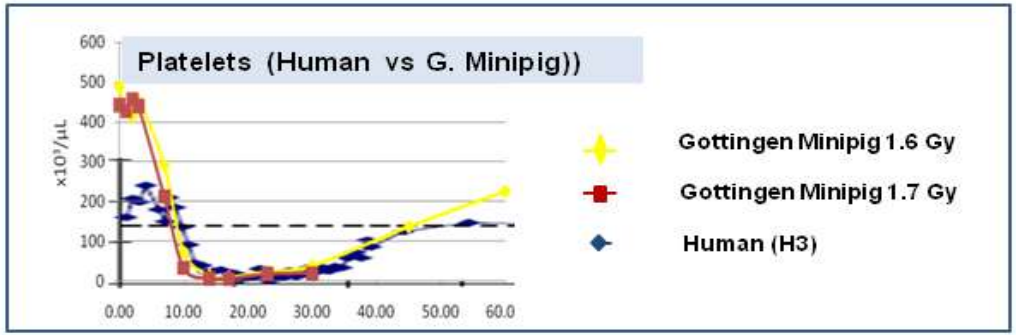
Humans and Gottingen minipig



Humans (Radiation effects on blood counts. Radiation Emergency Medical Management, www.remm.nlm.gov/rad_bloodcounts.htm)



Gottingen minipig (AFRRI)



Maria Moroni, Mark Whitnall, Radiat Res 176: 89-101, 2011; PLoS One in press, 2011

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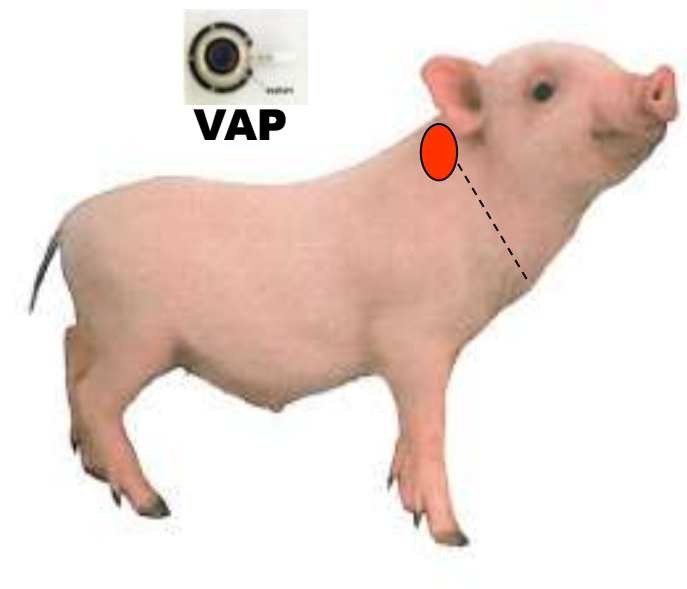
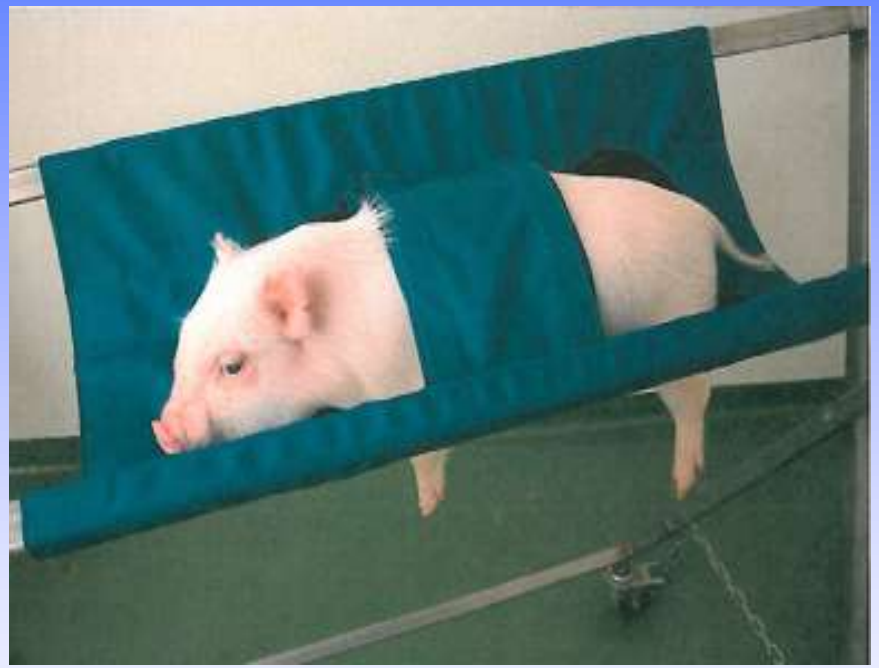
Minipig Blood Collection





Sling: for blood draws from Vascular Access Port (VAP)

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The Ferrett

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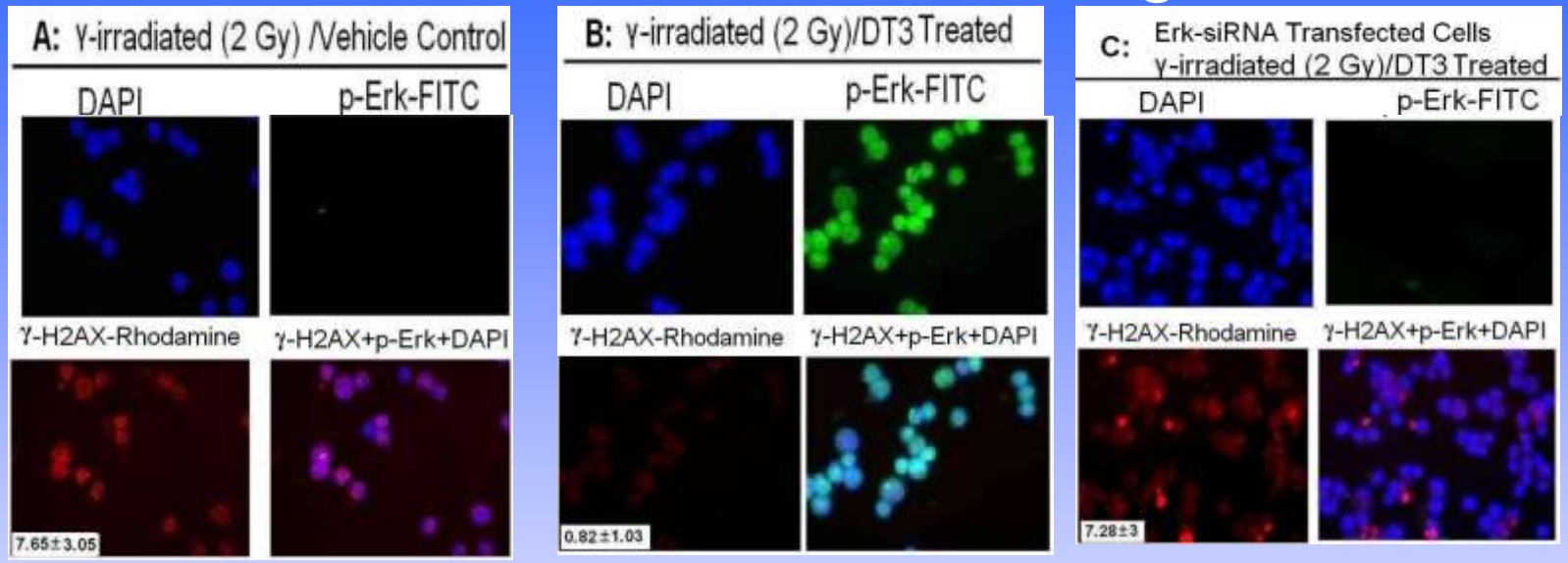
Delta-tocotrienol (DT3) induced Erk phosphory-lation in γ-irradiated CD34+ cells and protected cells from radiation-induced DNA-damage



CD34+ cells: Human hematopoietic stem and progenitor cells

Red: γ-H2AX, marker for DNA double strand breaks
Green: phospho-Erk: protein kinase intracellular signaling molecules
Blue: DNA stain (cell nucleus) – DAPI

Inhibition of Erk expression with siRNA blocked p-ERK and restored γ-H2AX foci

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