Heavy charged particles as an effective tool for solving of fundamental and applied tasks in modern biology

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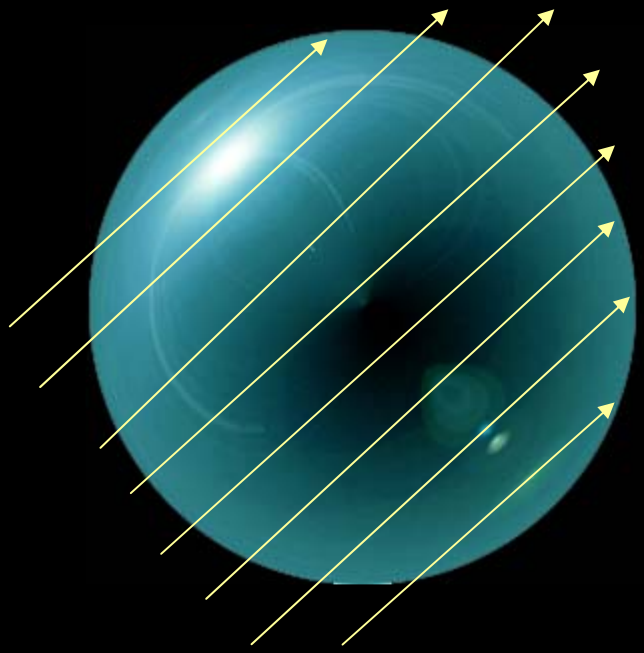
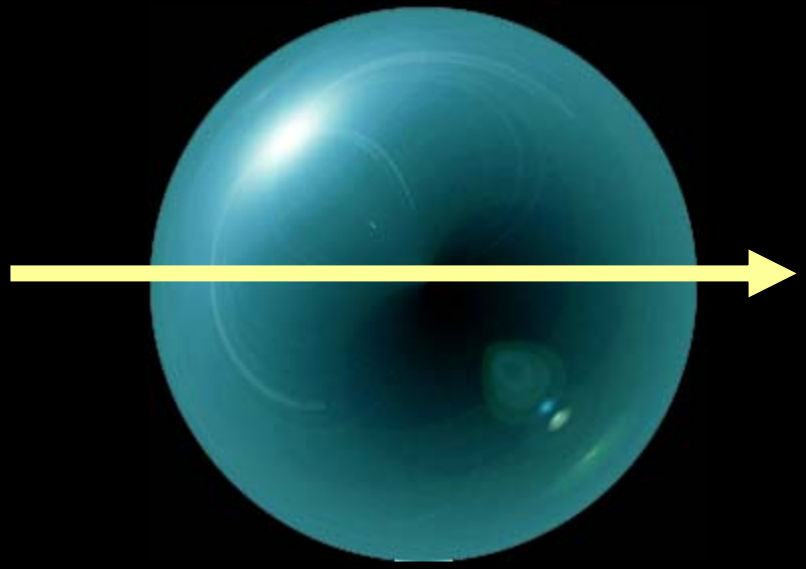
The dose distribution of radiation in matter

1 unit of the dose



X-rays

1 unit of the dose



Fe ion

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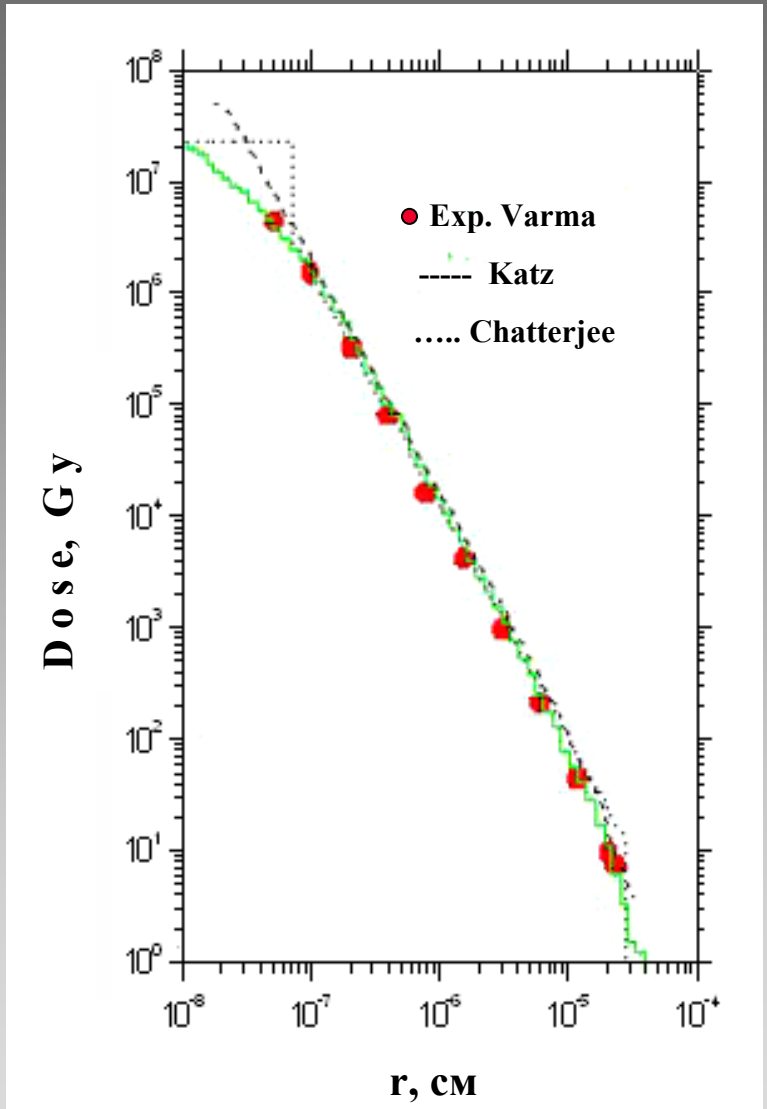

Radial dose distribution in track of heavy ion (^{12}C, 2,57 MeV/u)

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What fundamental biological problems can be solved at use of the accelerated heavy particles?

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A.
Radiation Genetics

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The JINR accelerators

Accelerator	Particles	Energy (up to)	Lab
Phasotron	Protons	660MeV	LNP
U-200	Heavy ions	10MeV/amu	LNR
U-400M	Heavy ions	50 MeV/amu	LNR
Sinchrophasotron	Protons, Heavy ions	10 GeV/amu	LHE
Nuclotron	Protons, Heavy ions	5 GeV/amu	LPHE

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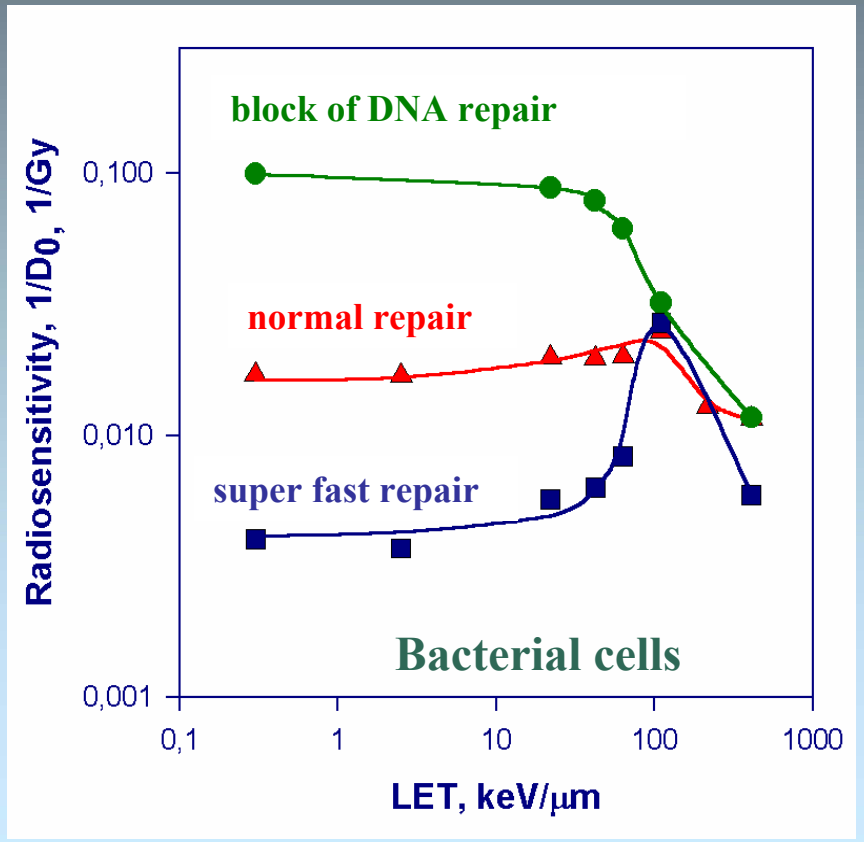
The RBE problem was solved at the Flerov Lab accelerators



DNA repair capacity **of the living cells determines the type of RBE on LET dependence**

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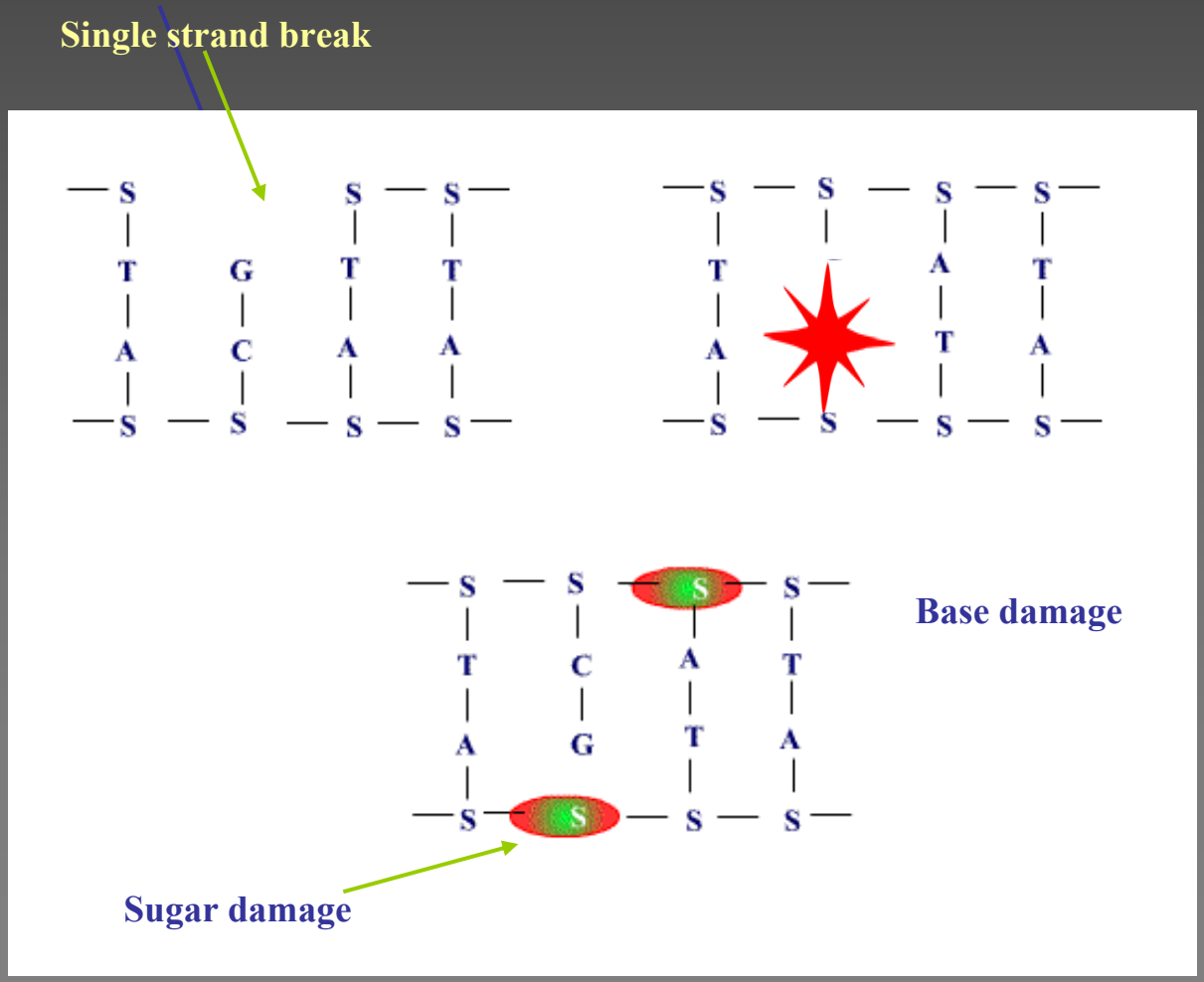
Single DNA damages



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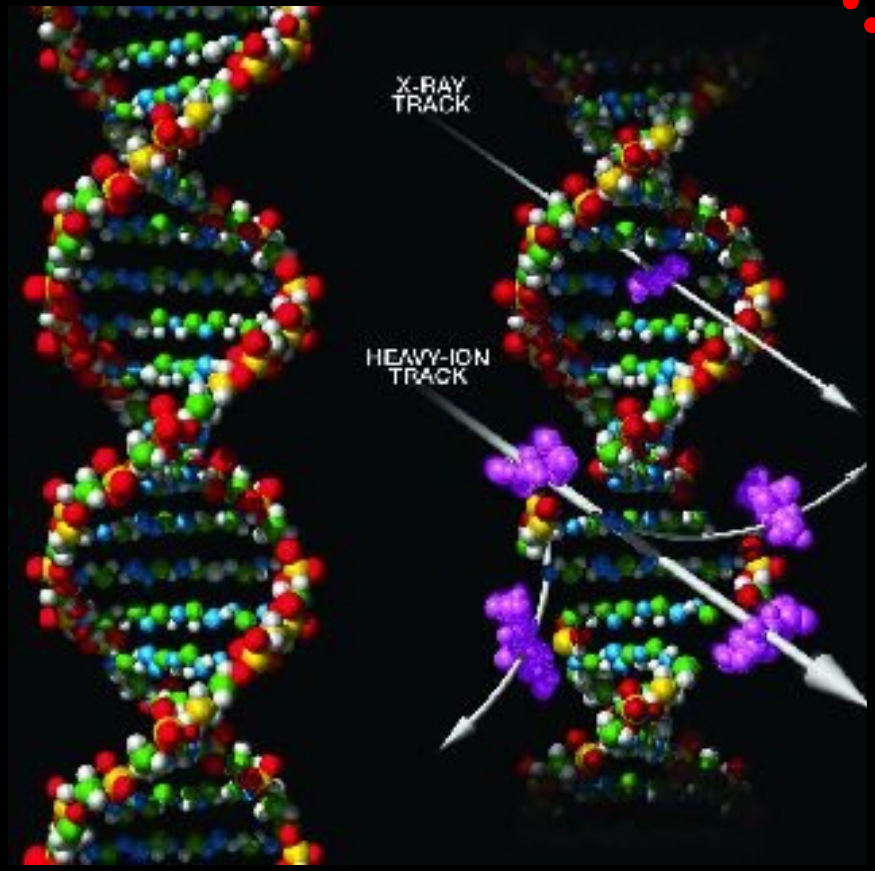
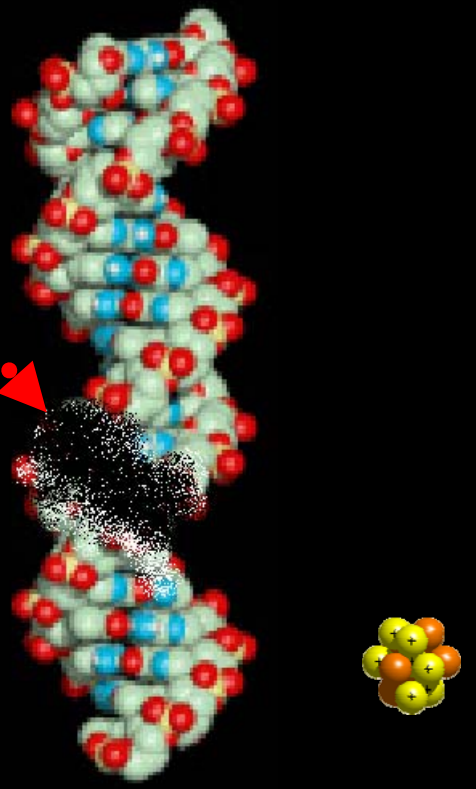
Clustered DNA damages

Fragment of DNA





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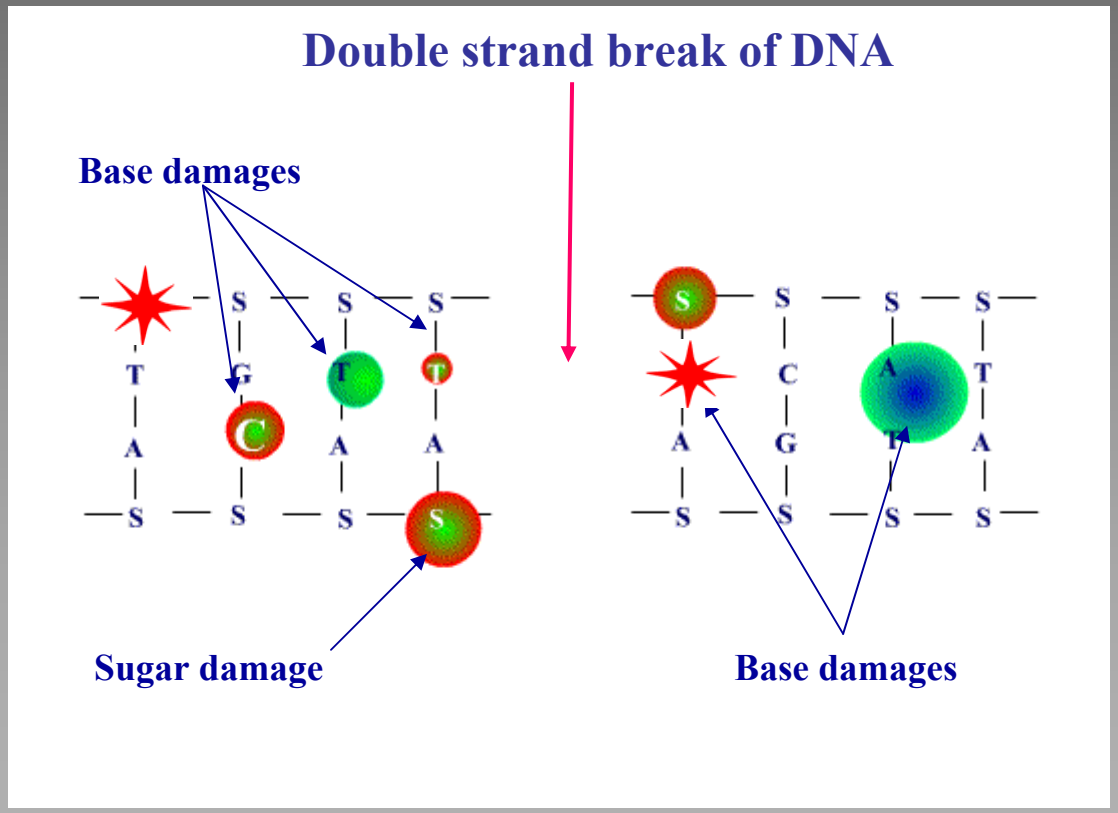
Clustered DNA damages



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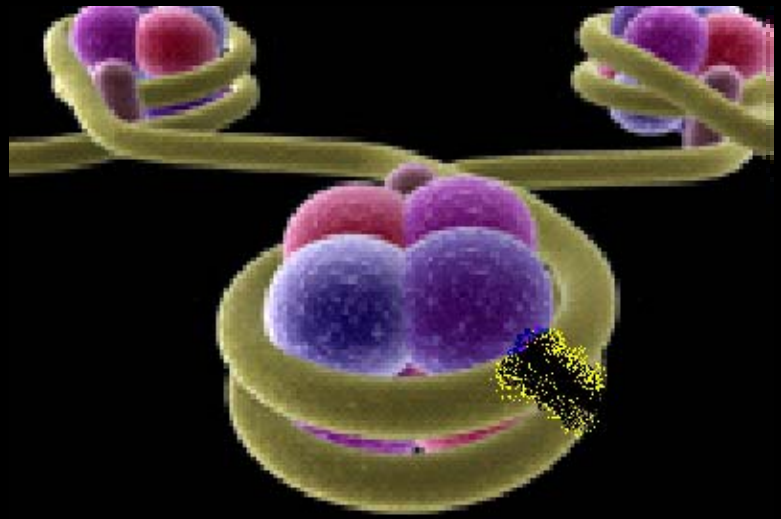
Clustered DNA damages in nucleosome



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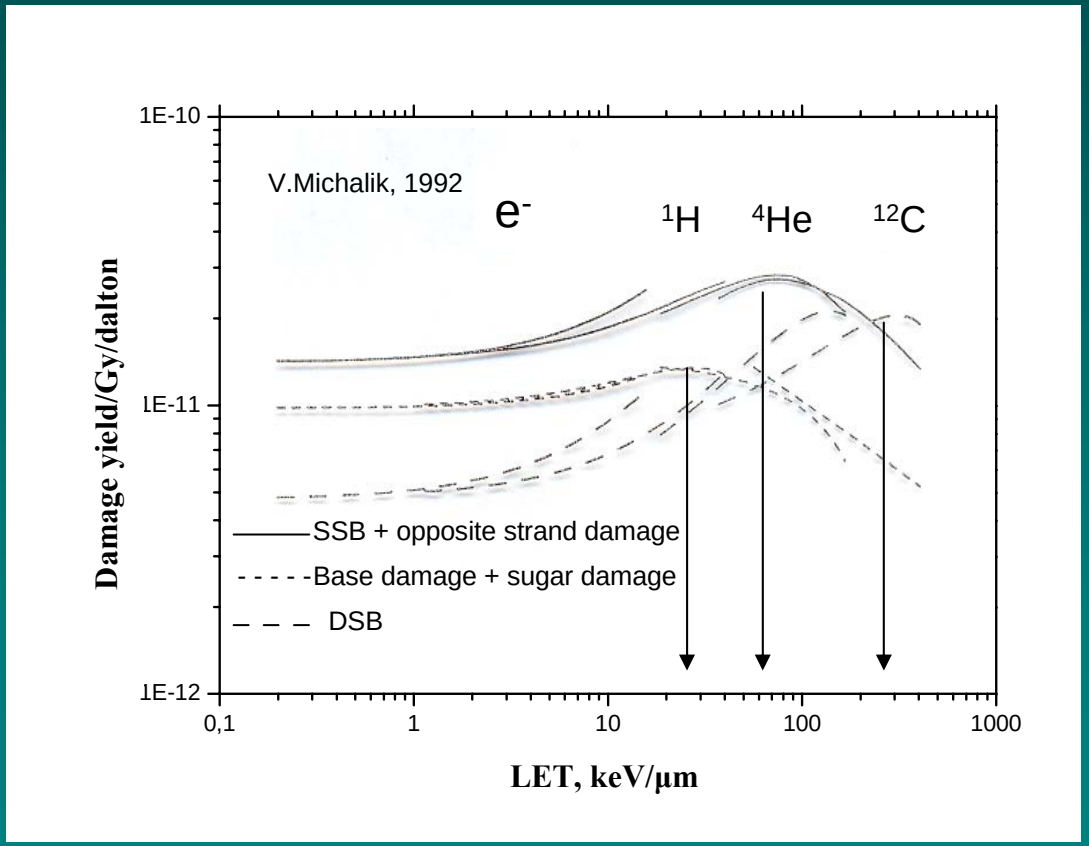
Yield of clustered damages on both DNA strands versus LET



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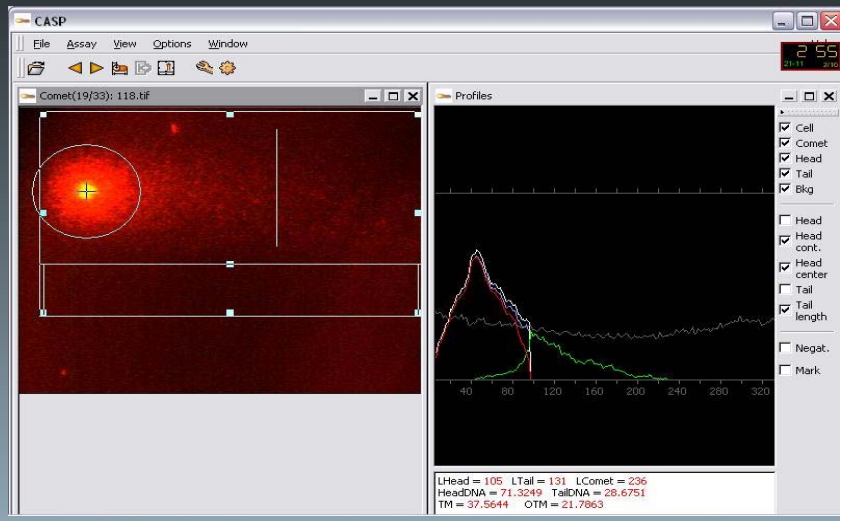
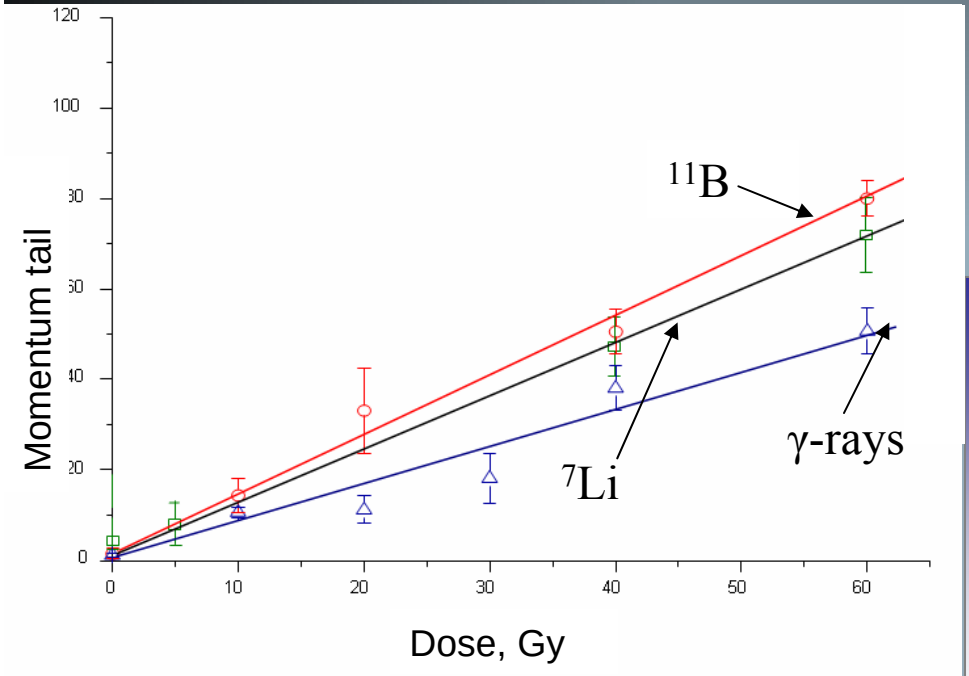
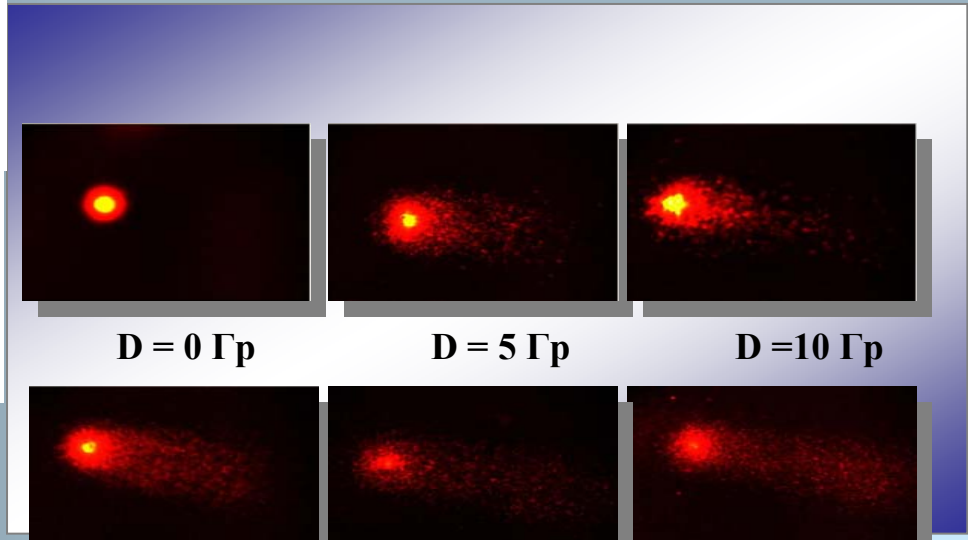
“Comet assay” for detection of DNA lesions







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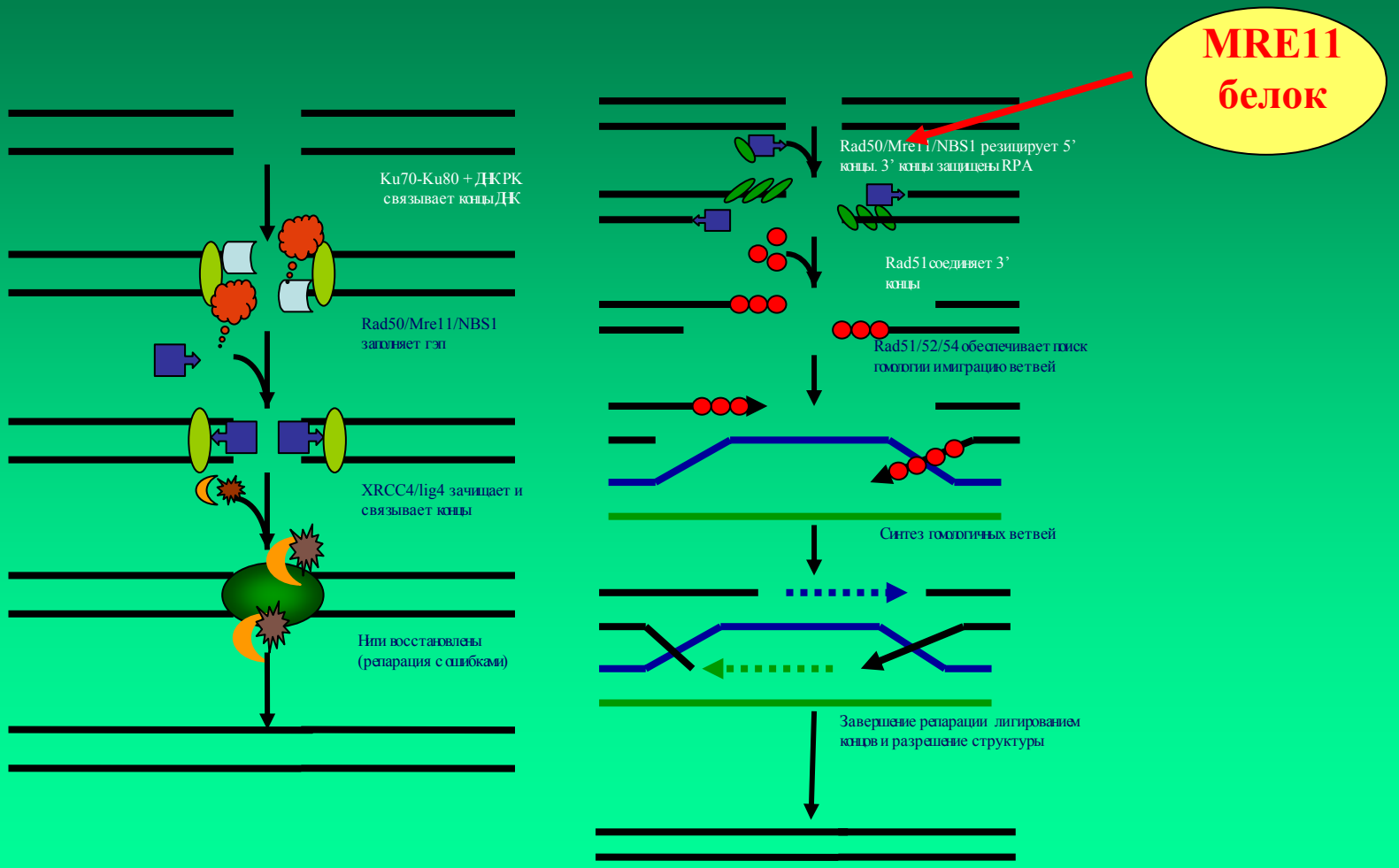
The mechanism of DSB DNA repair in human cells



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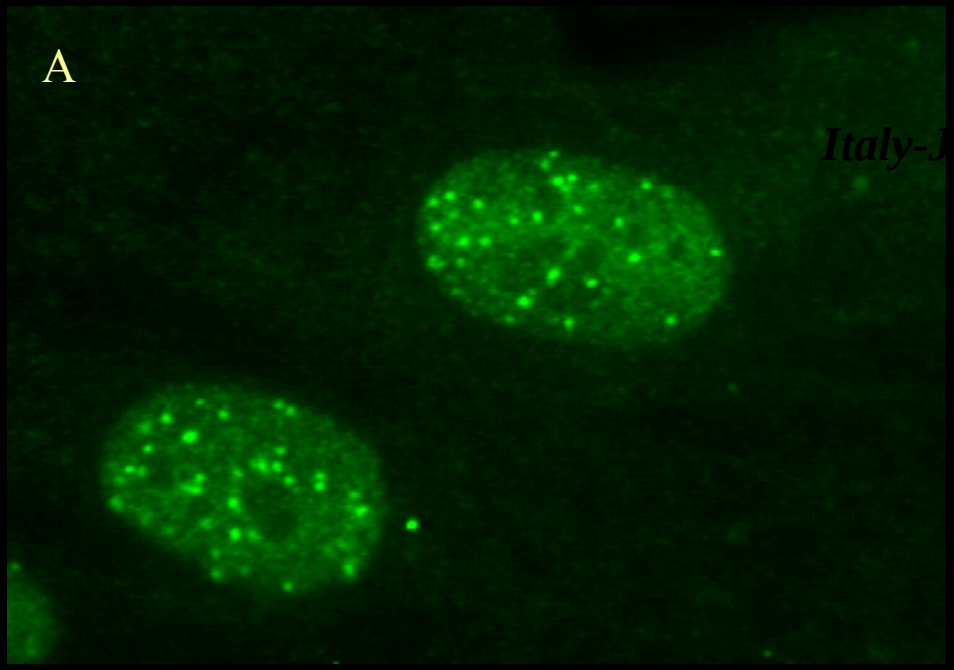
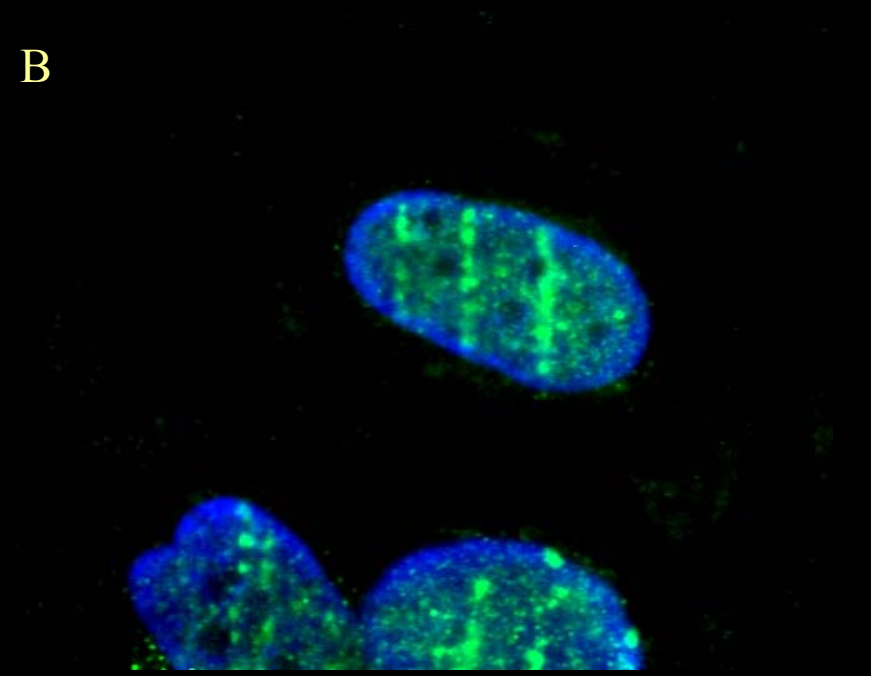
DSB (γ-H2AX) in human cells after X-ray (A) and heavy ion irradiation (B)





M.Vazquez., 2006

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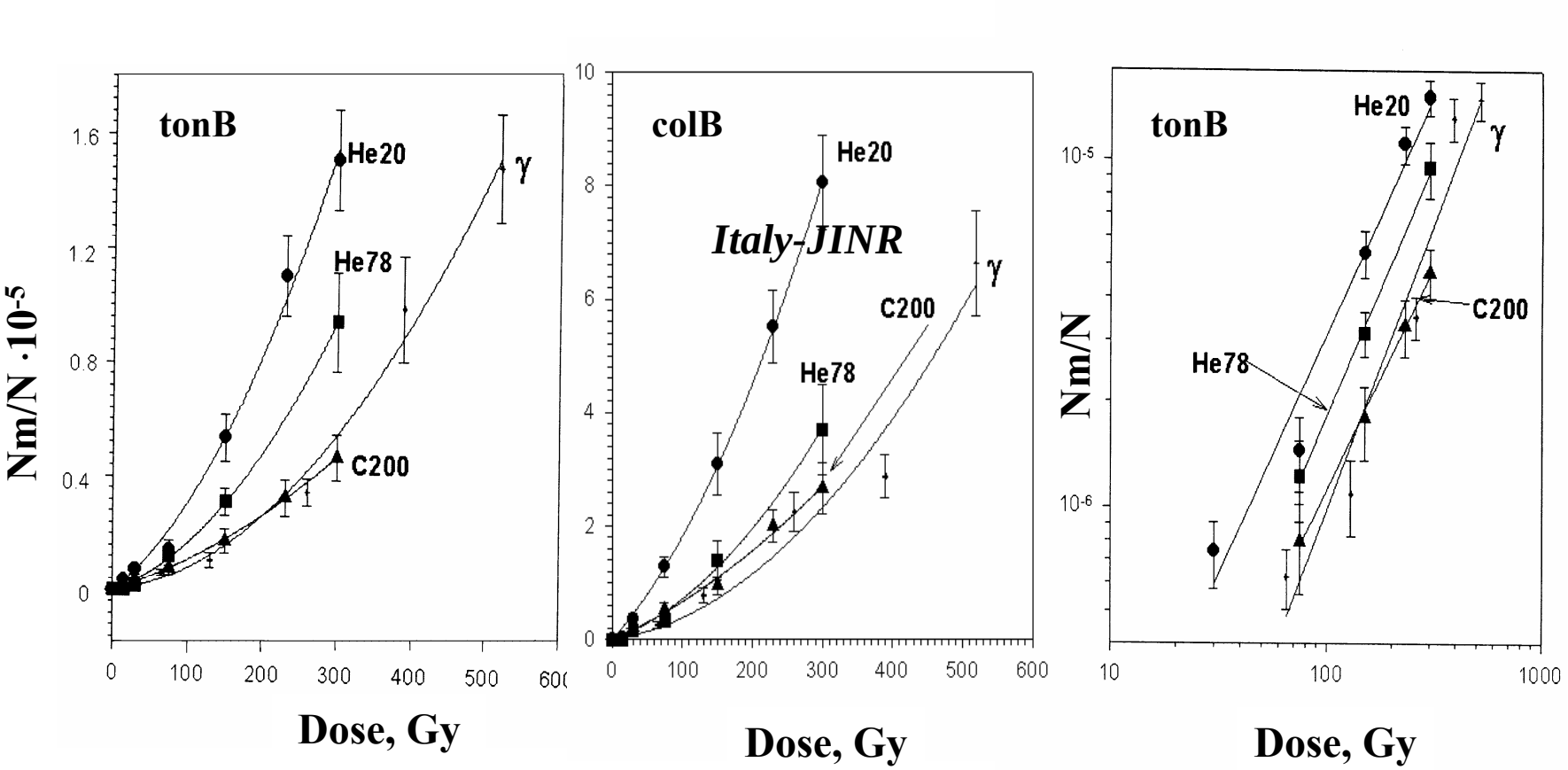
The frequency of tonB and colB mutation induction after γ-ray and heavy ion irradiation



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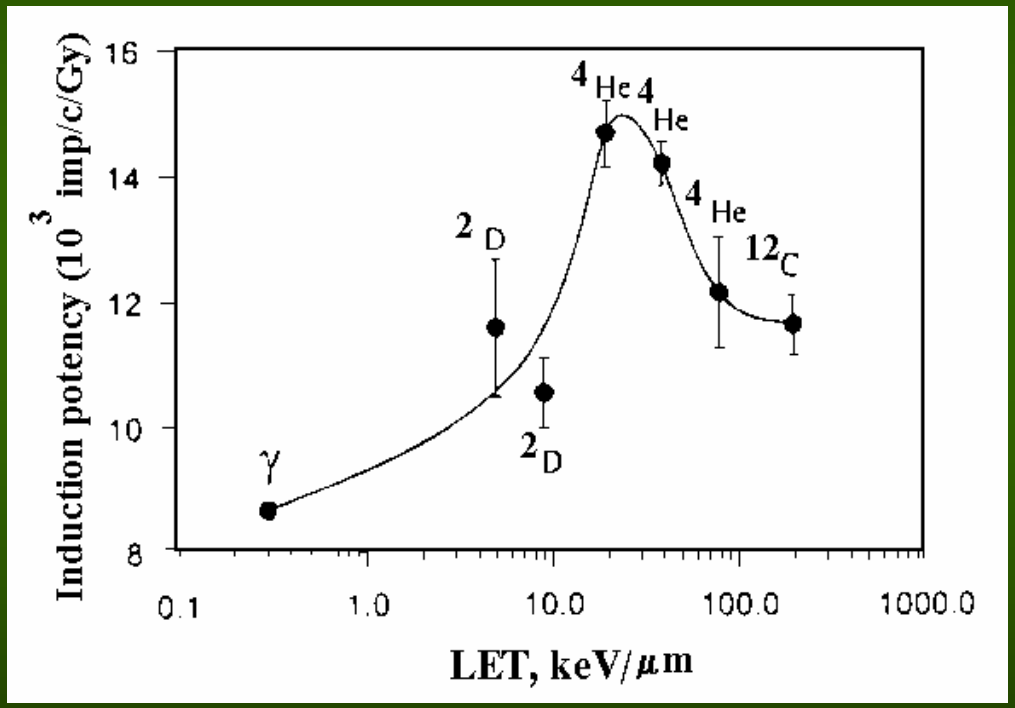
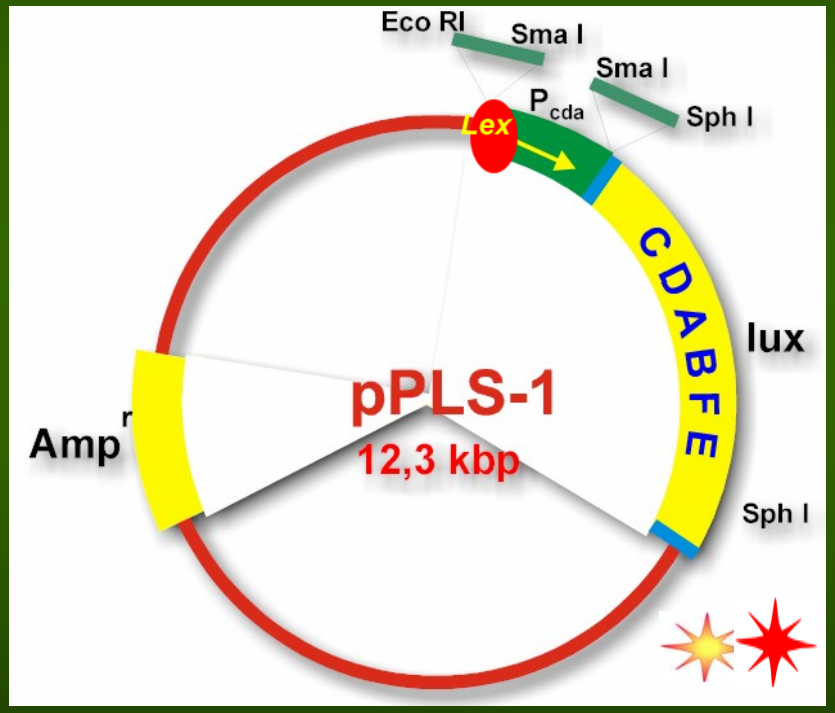
Induction of mutagenic DNA repair by heavy ions





luciferase

$FMNH_2 + RCHO + O_2 \rightarrow FMN + RCOOH + H_2O + h\nu$

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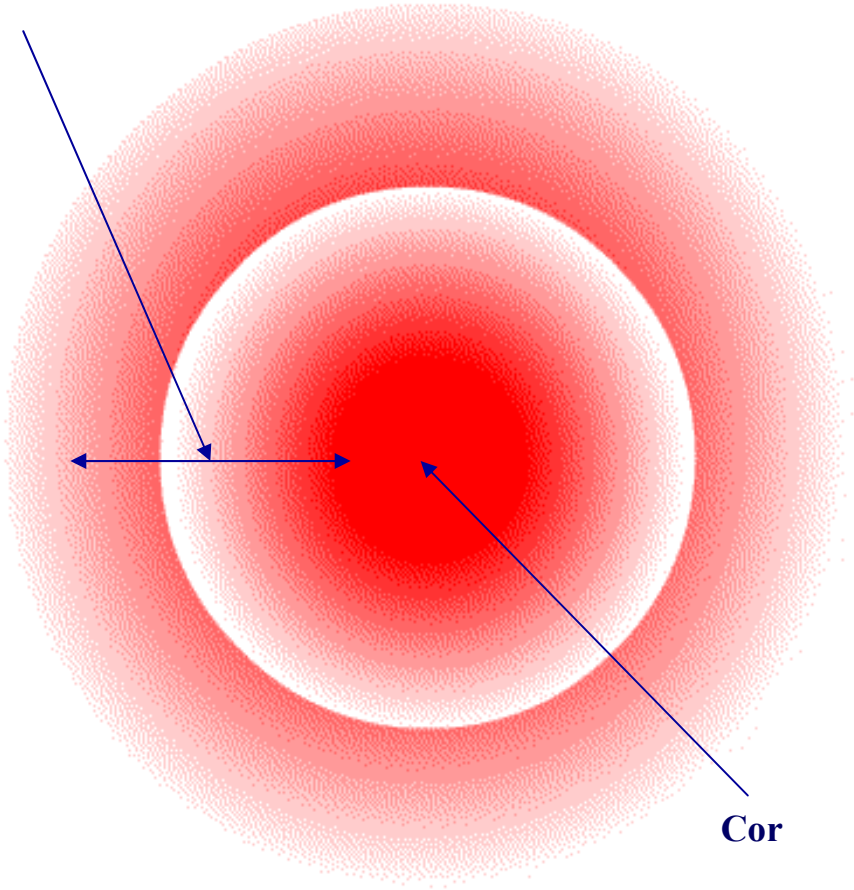
Mutagenic belt of heavy particle track



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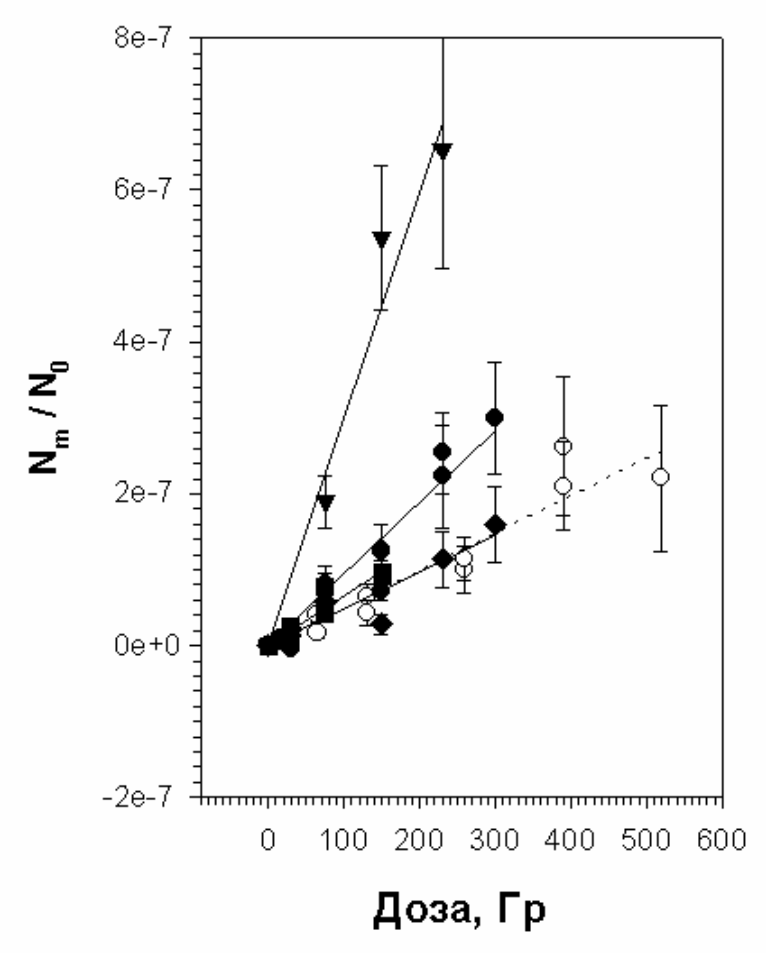
Induction of tonB⁻trp⁻ deletion mutations by heavy ions



○ - γ-rays;

● - ^{4}He (20 keV/μm);

▼ - ^{4}He (50 keV/μm);

■ - ^{4}He (78 keV/μm);

♦ - ^{12}C (200 keV/μm)

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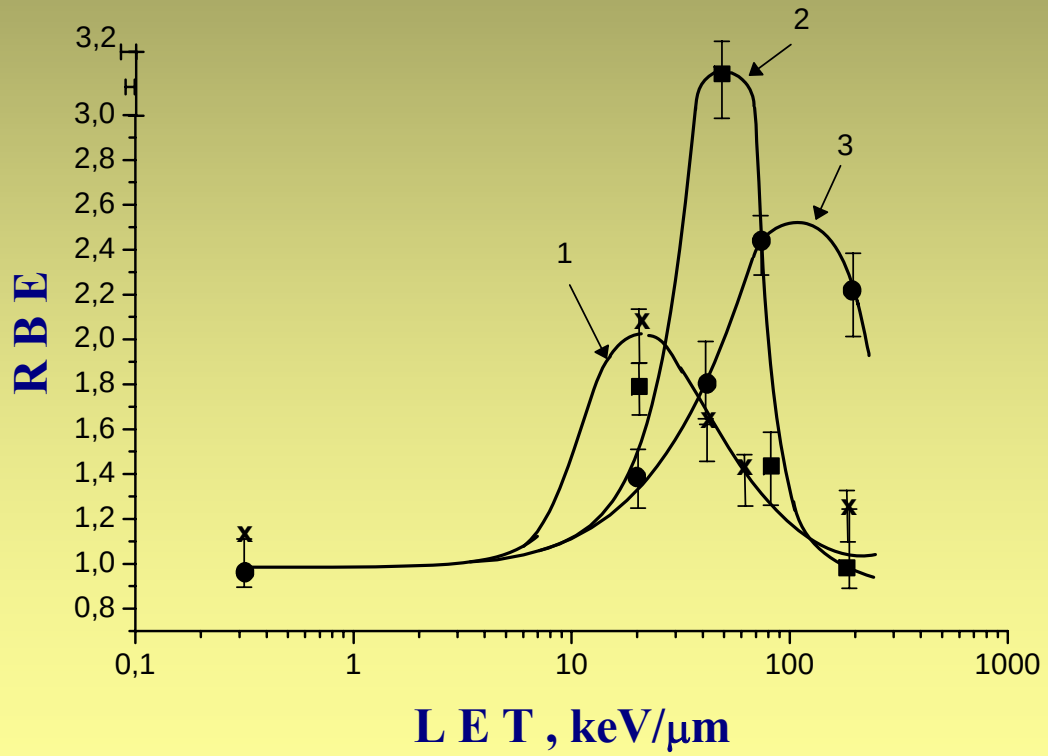
RBE on LET dependence



1 – tonB mutations

2 – tonBtrp^{-} deletions

3 – lethal effect

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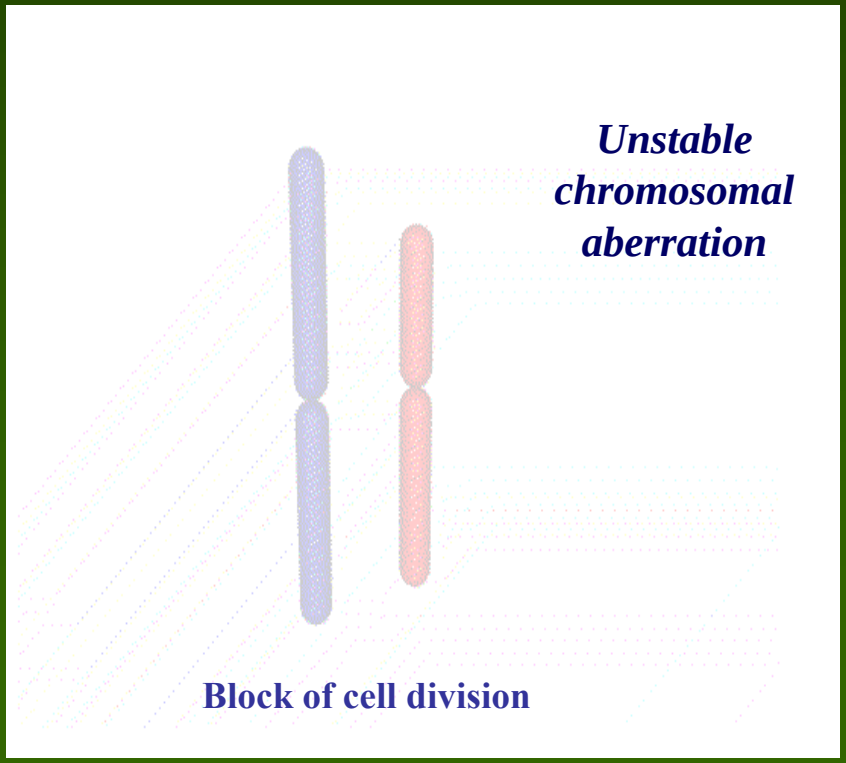
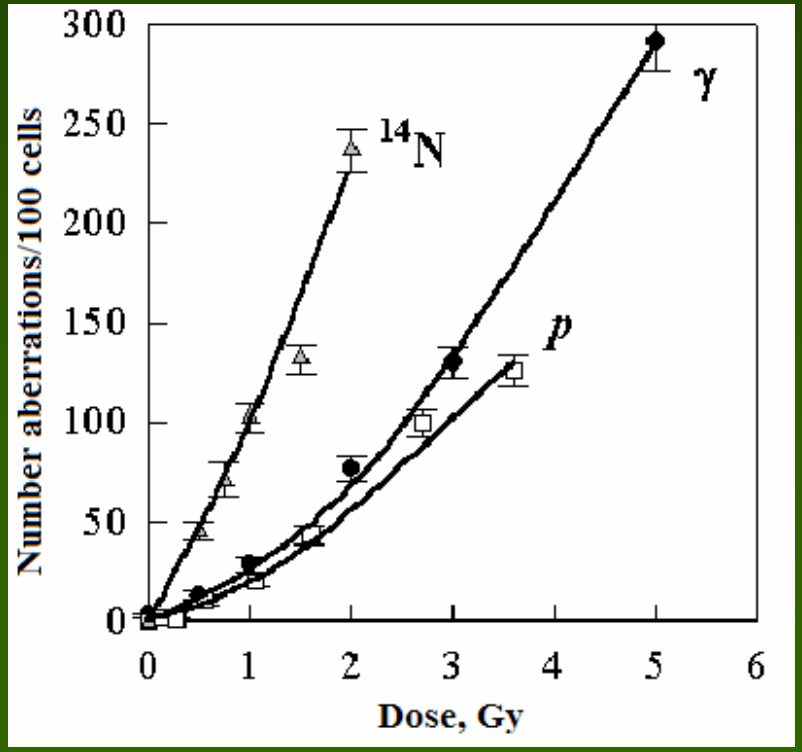
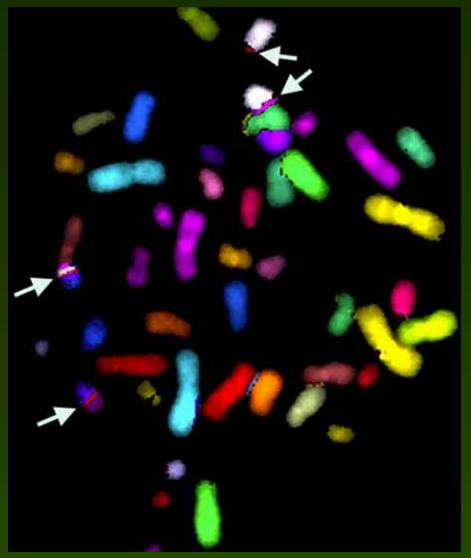
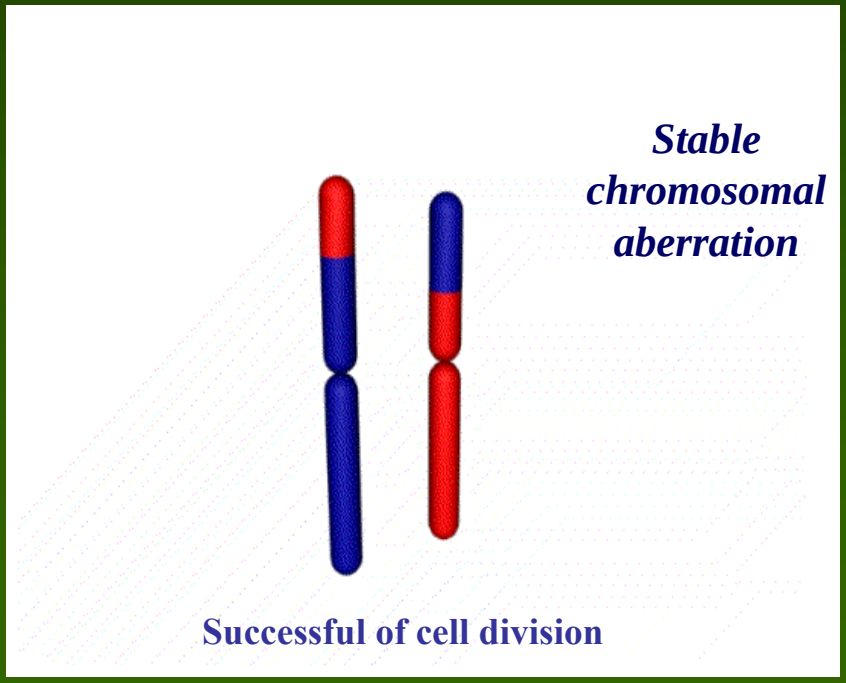
❖ *Formation of unstable chromosomal aberration after heavy ion irradiation of human cells*

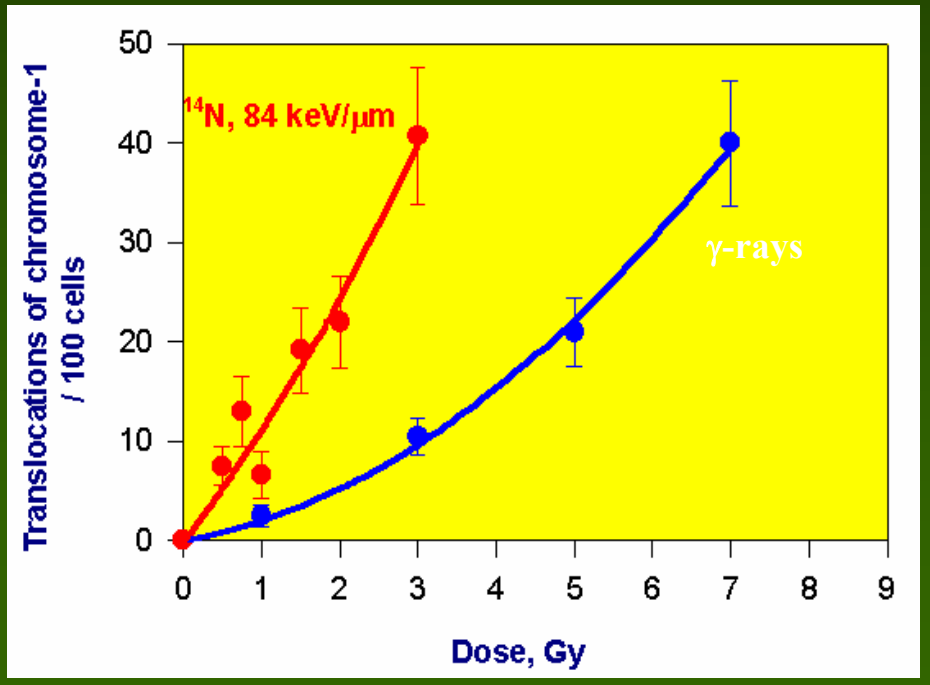




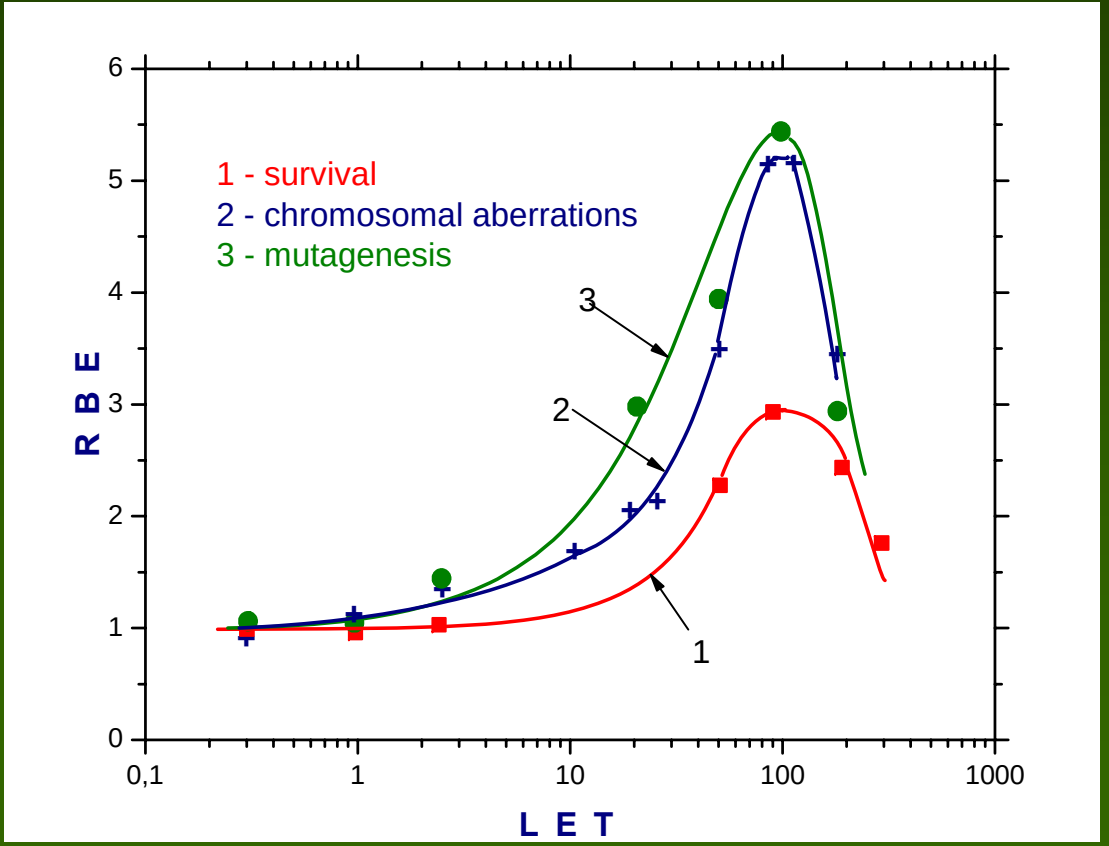
❖ *Formation of stable chromosomal aberration after heavy ion irradiation of human cells*







RBE as a function of LET on induction of mutations, chromosomal aberrations and cell inactivation



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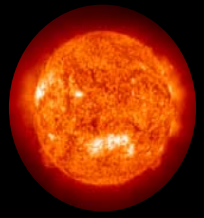
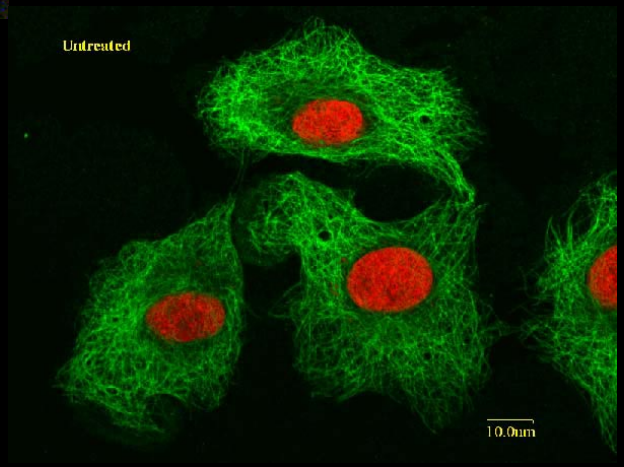
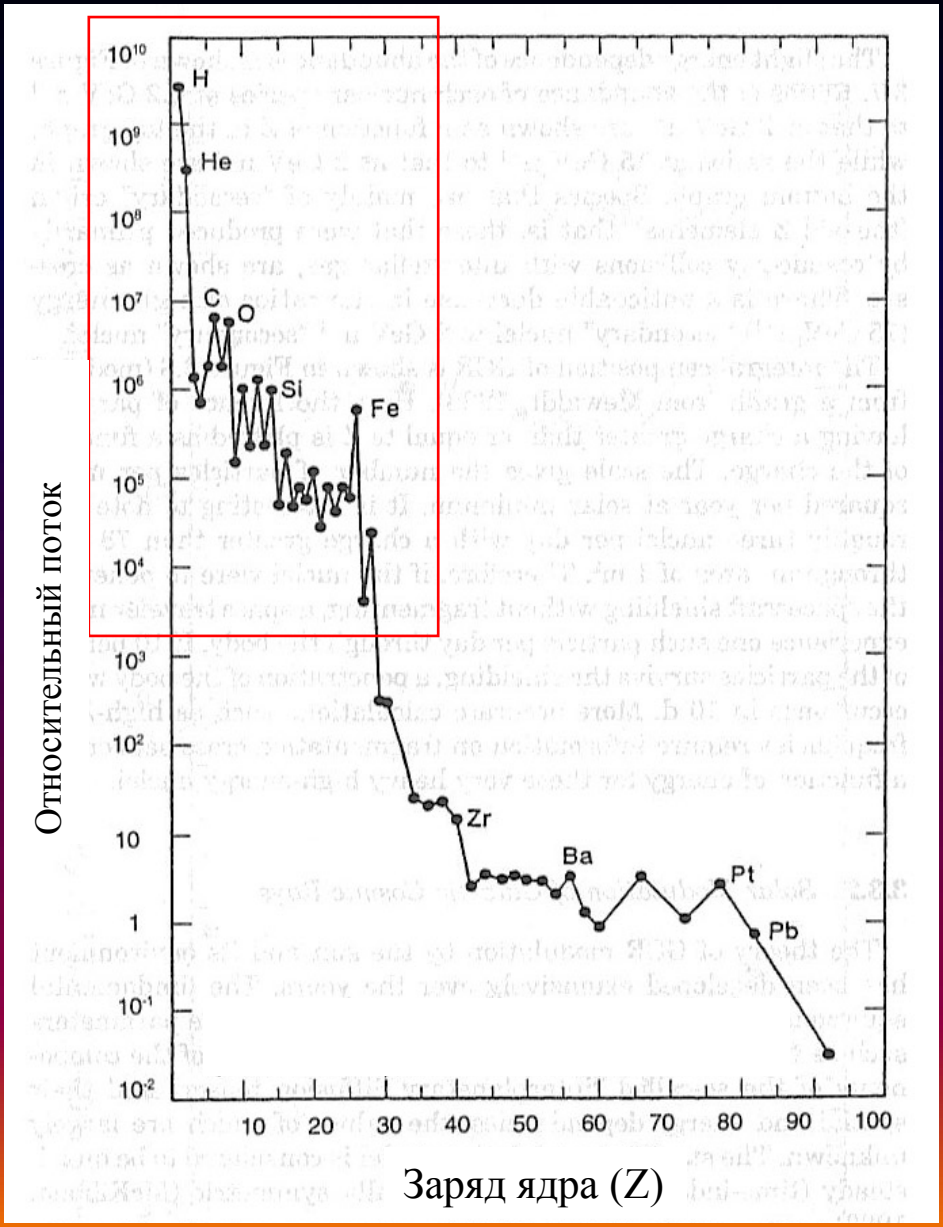
B.
Accelerated heavy ions is a tool for modeling of biological action of space radiation

The GCR flux

The integral flux of GCR particles of carbon and iron groups equals to 10^5 part cm-2 per year







The relative flux of GCR particles

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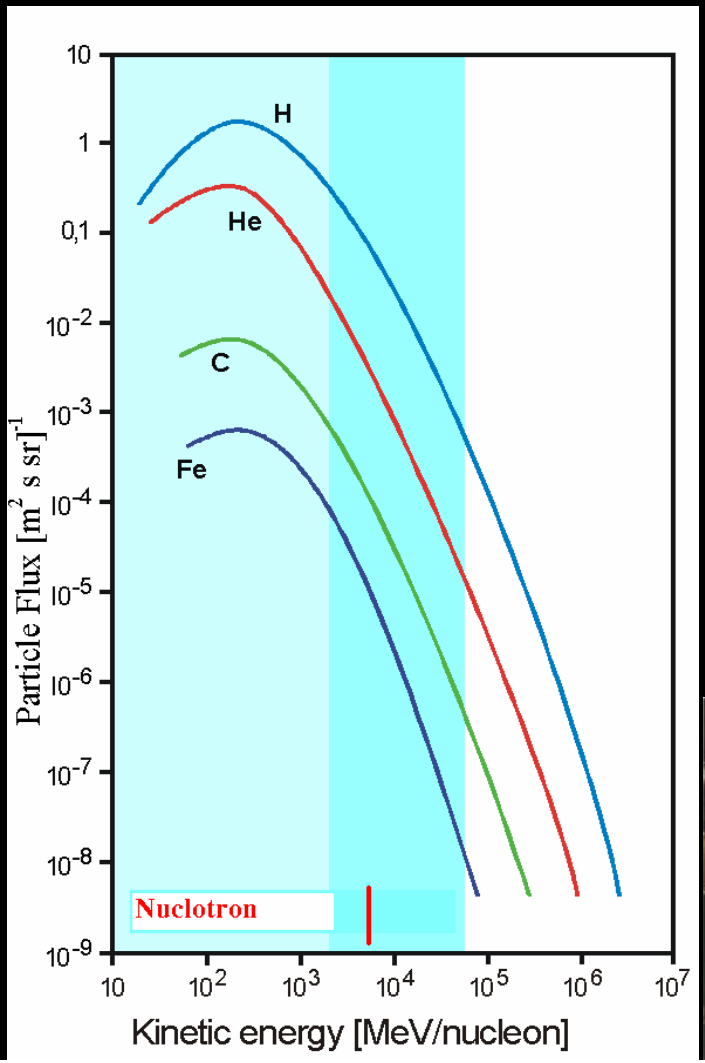
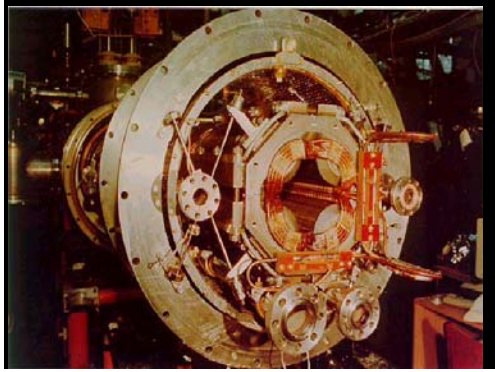
The energy spectrum of GCR and Nuclotron accelerator





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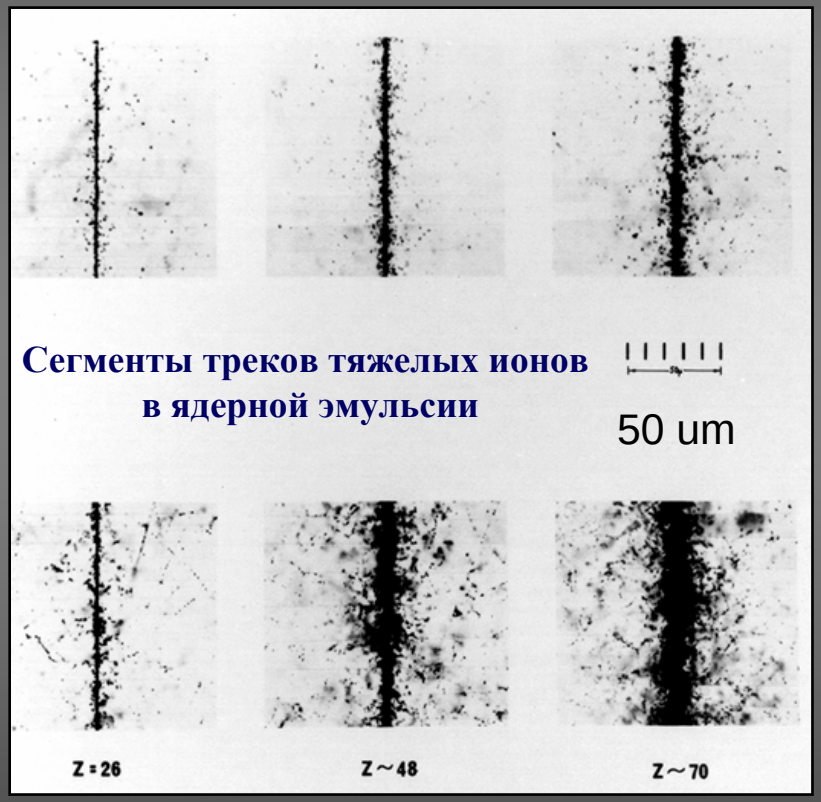
Tracks of heavy ions in nuclear emulsion



Fe

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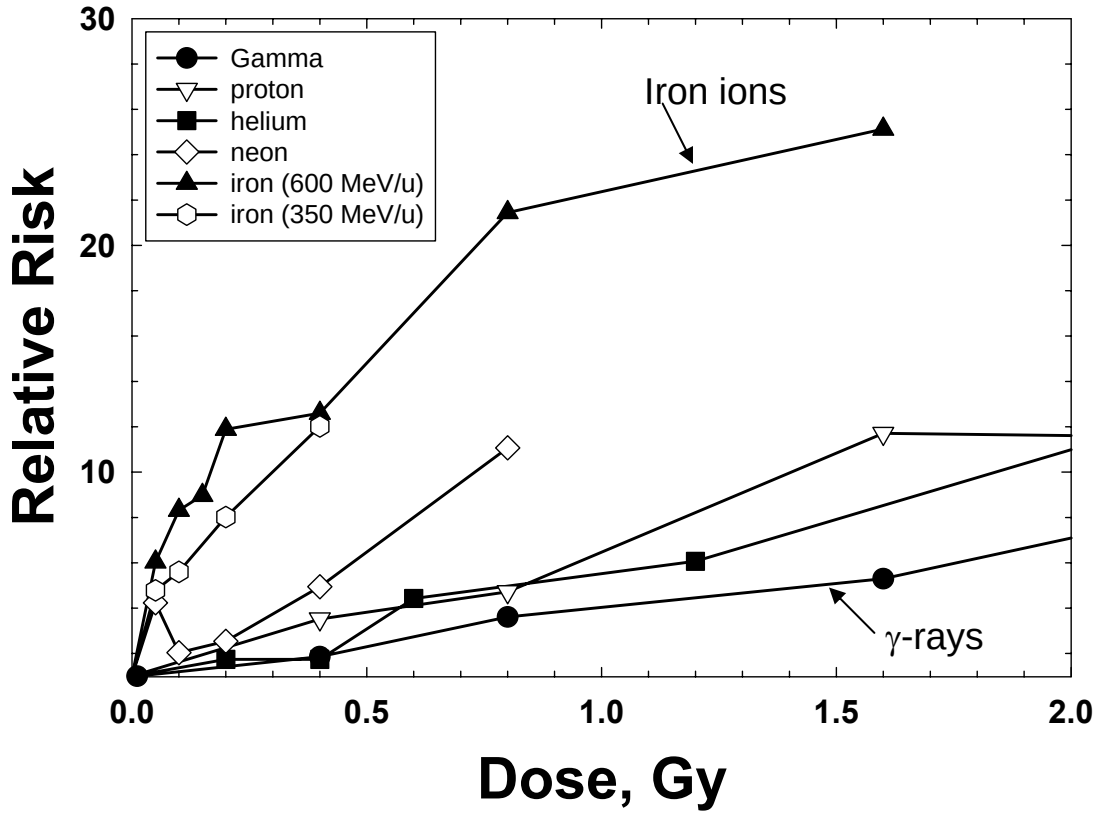
Consequences of action of Galactic heavy ions

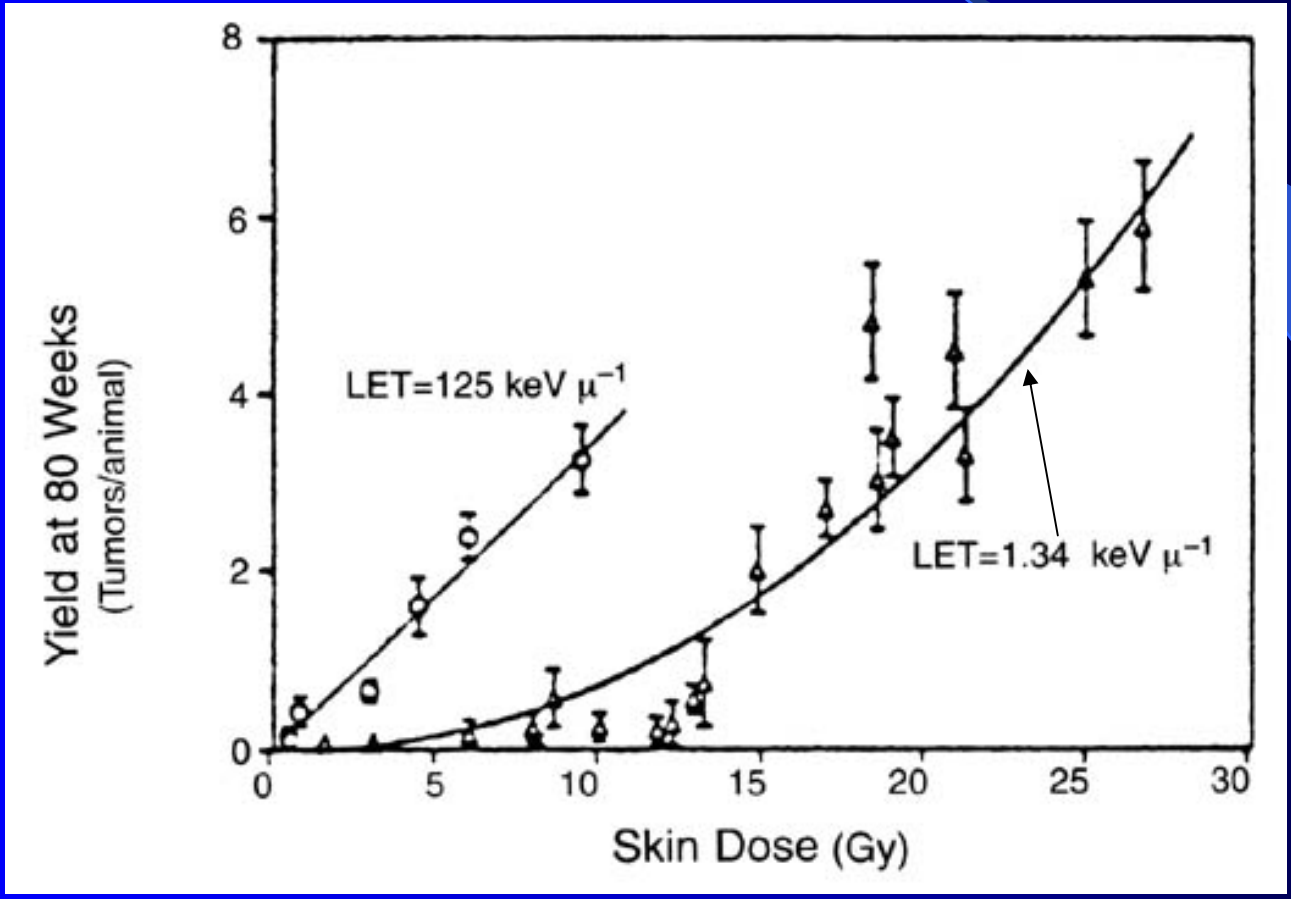
- **Induction of cancer;**
- **Formation of gene and structural mutations;**
- **Violation of visual functions:**
- **lesions of retina;**
- **cataract induction**
- **Violation of CNS functions**

Gardner tumors

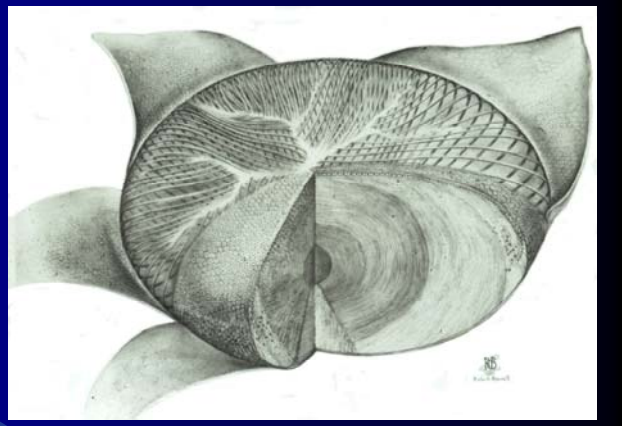


Nelson, 2006

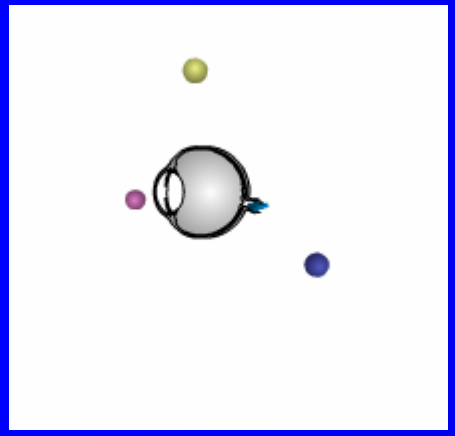
Skin cancer
(rats)



Burns, Albert, 1986



Cataract induction



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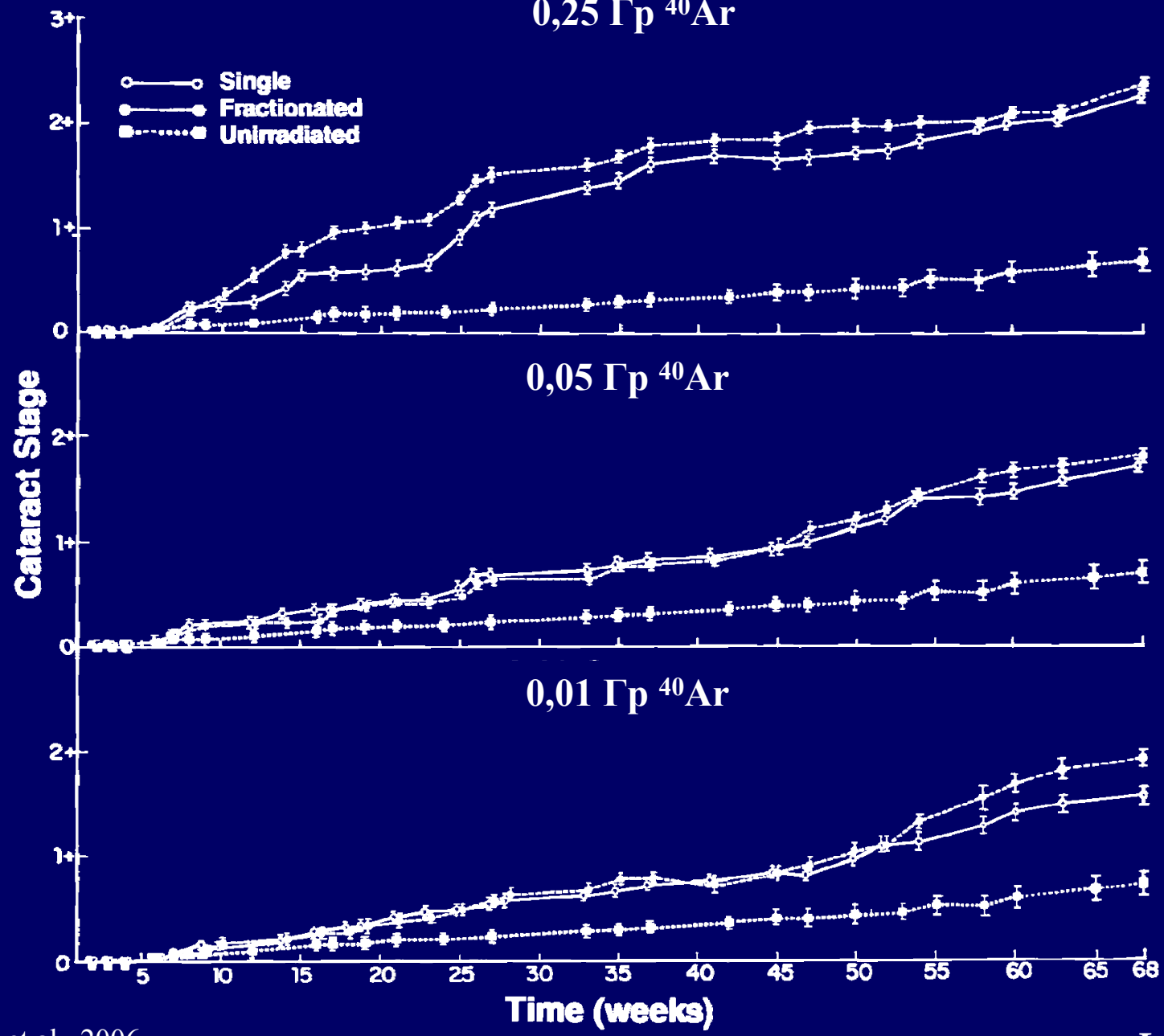

Worgul et al., 2006

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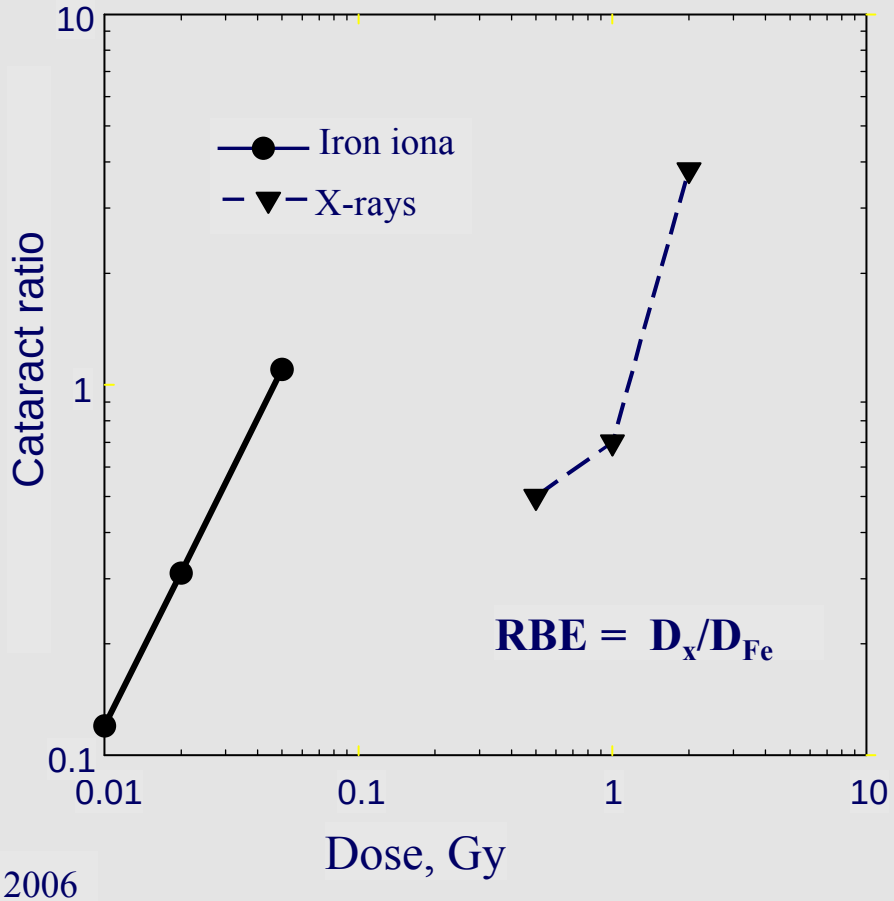
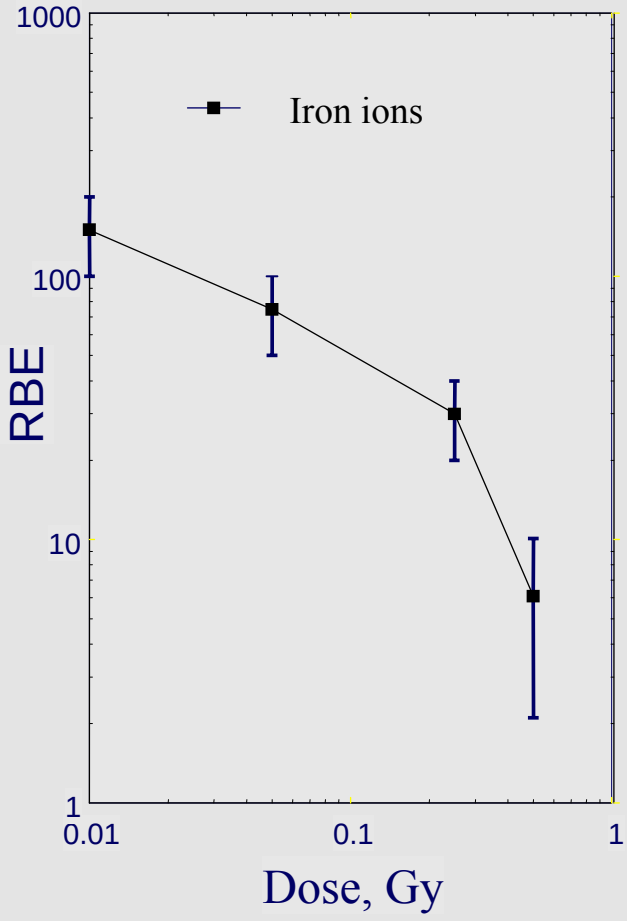
Cataract ratio after irradiation by iron ions and X-rays





Worgul et al., 2006

Accelerated heavy ions and CNS

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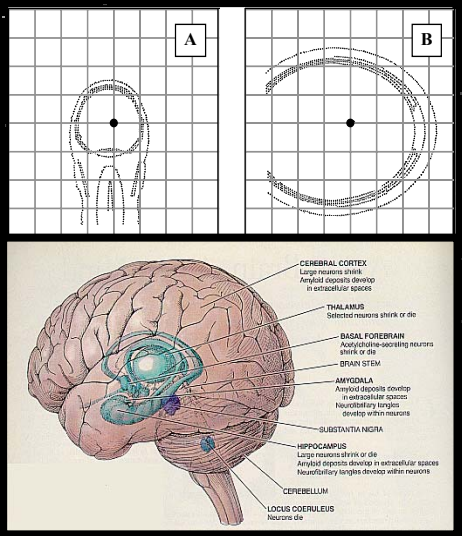
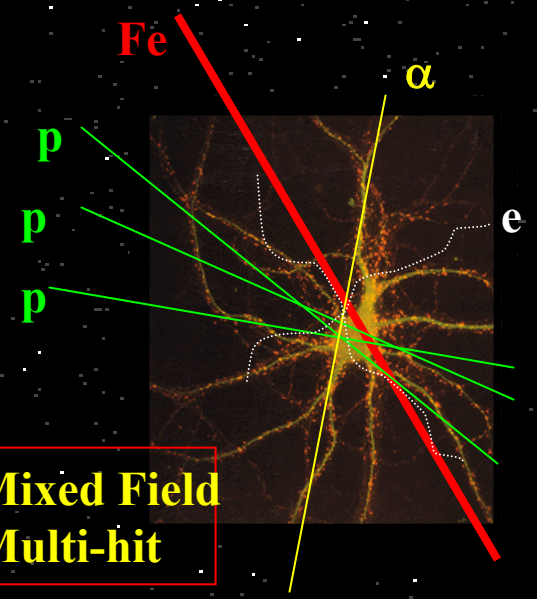
Cosmic ray hit frequencies in CNS critical areas



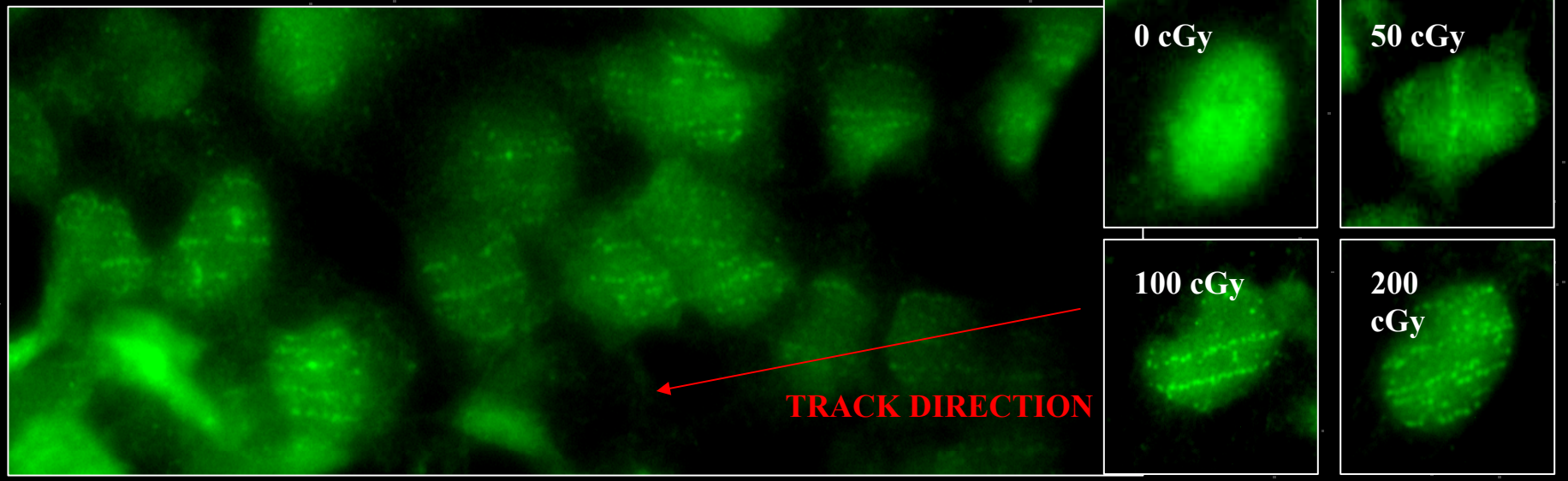
CNS in General

- 2 or 13% cells will be hit at least one Fe particle
- 8 or 46% would be hit by at least one particle with Z≥15
- Every nucleus will be traversed by a proton once every 3 days and a alpha particle once every 30 days.

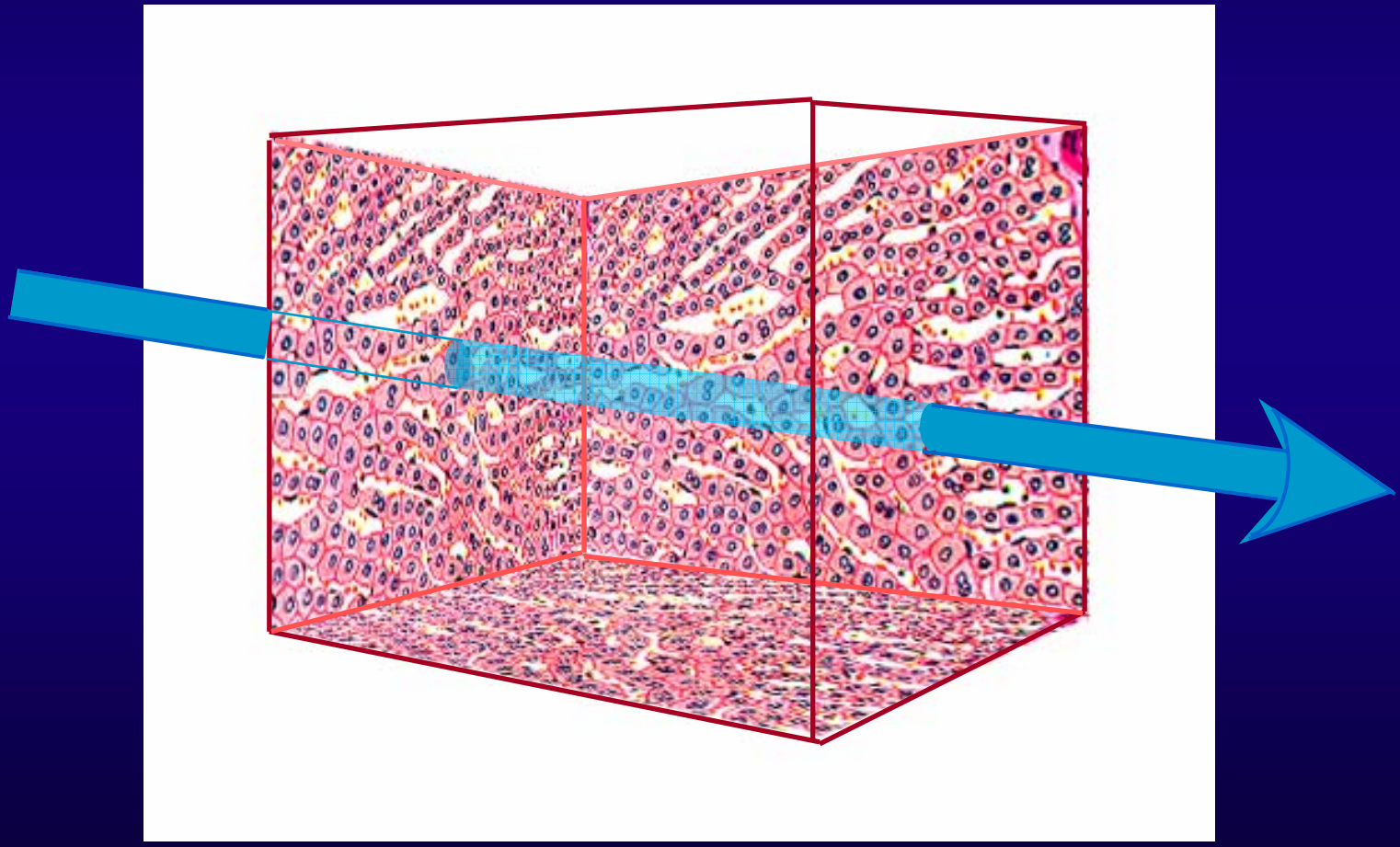


Mixed Field Multi-hit

FE ION TRACKS VISUALIZED BY MARKERS OF DNA DSBs (γH2AX)



Damages of large number cells in tissue by the single track of heavy ion



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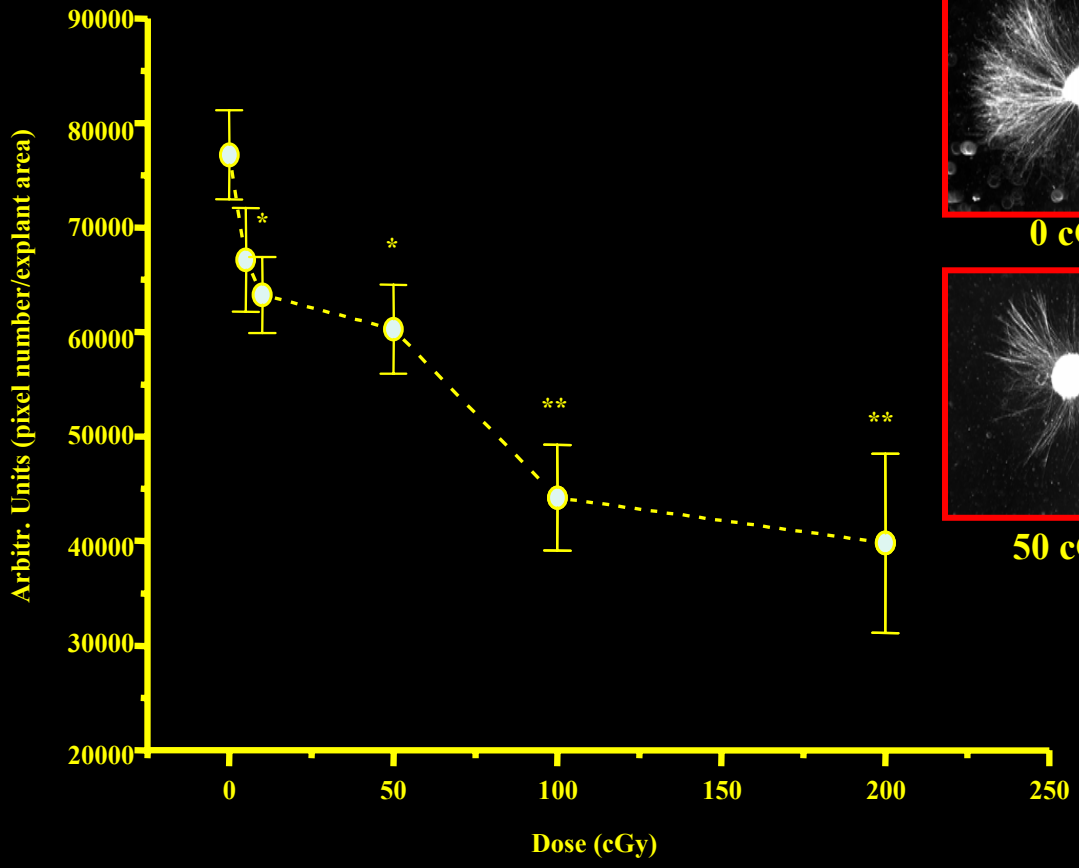
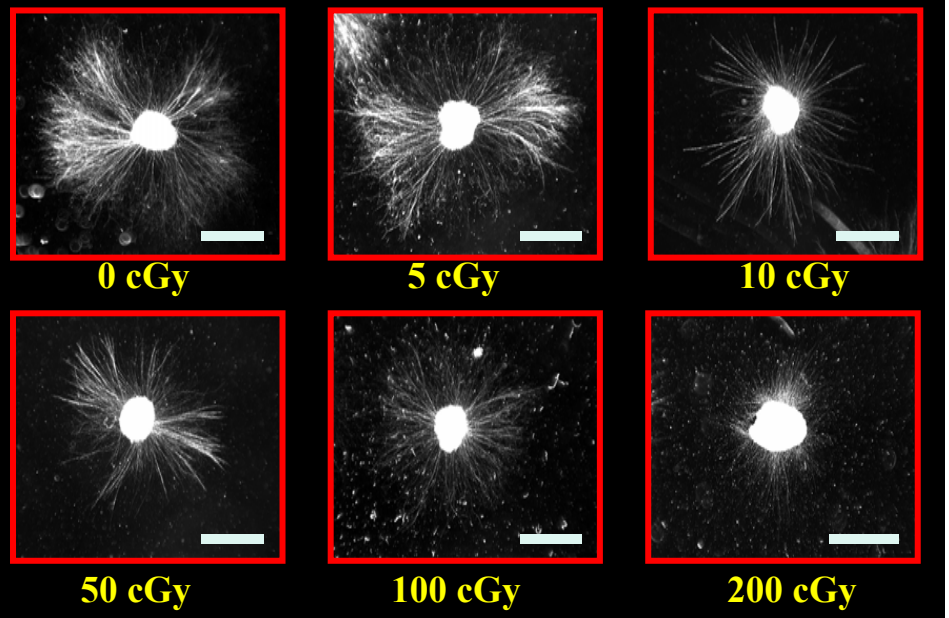
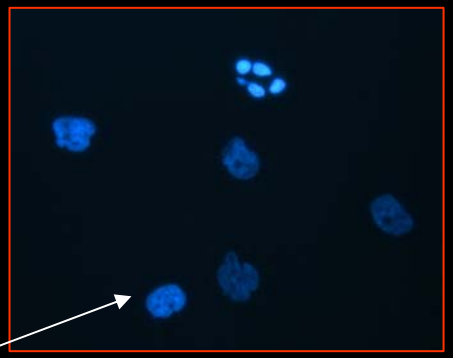
In Vitro Neurotoxic Effects of ^{56}Fe Ions on Retinal Explants

DOSE vs NEURITE GROWTH INDEX







apoptosis

Vazquez, 2006

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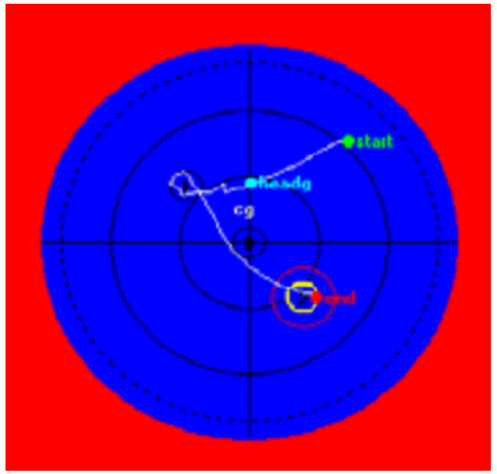
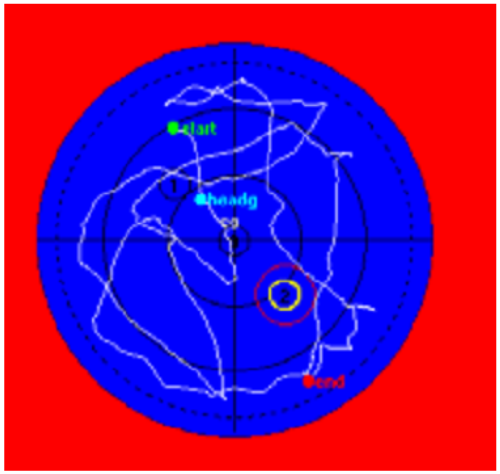
^{56}Fe ions, 1 GeV/amu

Control



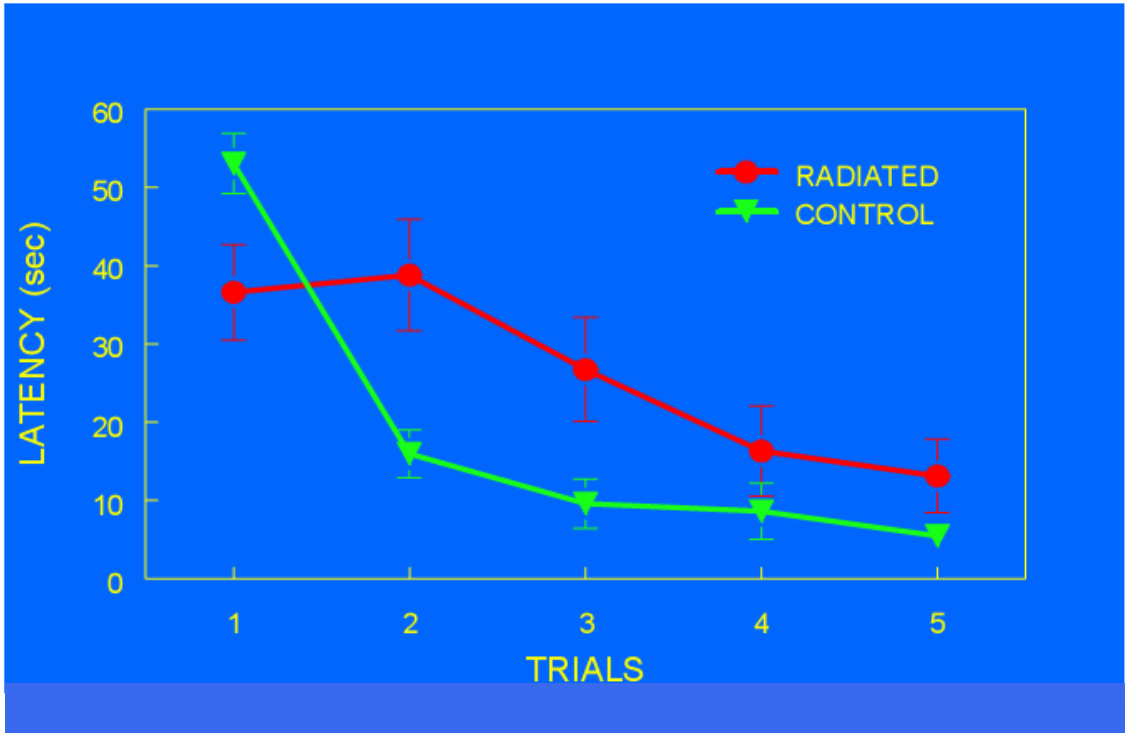
1.5 Gy



Cognitive tests

(Morris Water Maze: DAY 4, REVERSAL)

1 month after irradiation



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The energy deposition of heavy ions in genetic structures and tissues is characterized by high specifity. This determine the peculiarities of different radiation induced effects:

- Induction of clustered DNA damages;
- Repression or inactivation of DNA repair capacity;
- High values of RBE on different criterion;
- Repression or absence of modification effect of different radiomodificators (oxygen effect, radioprotectors, radiosensitizers).

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Thank you for the
attention!