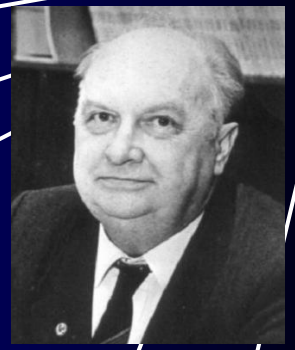
Baldin Seminar 20



Radiobiological Effects of Accelerated Heavy Ions

Laboratory of Radiation Biology

On Earth - **accelerators of heavy charged particles**

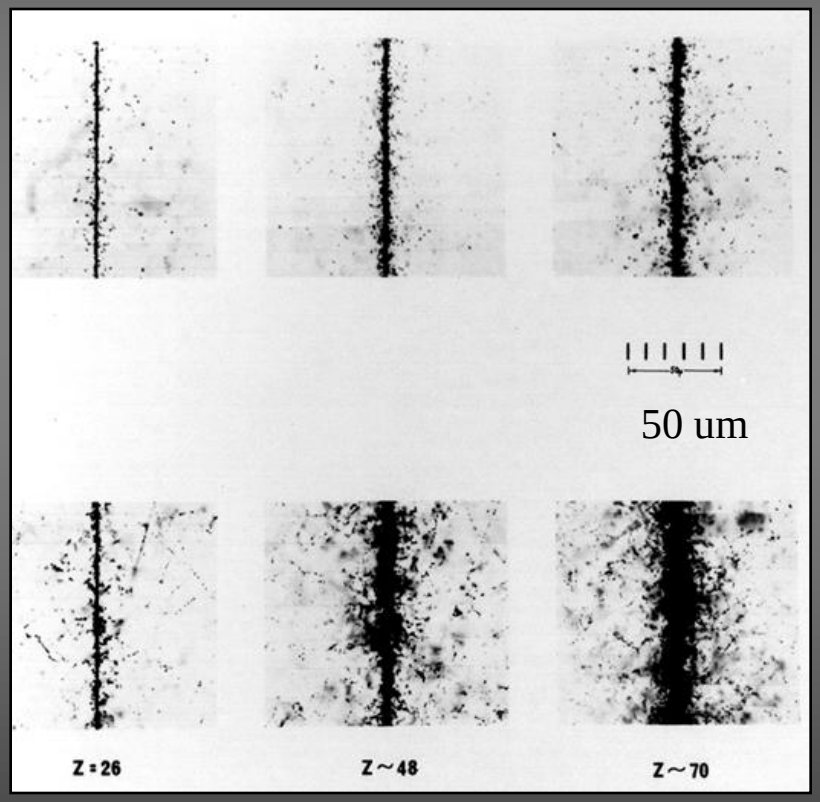
The sources of heavy ions of high energies

In space – **cosmic rays from Galaxy**

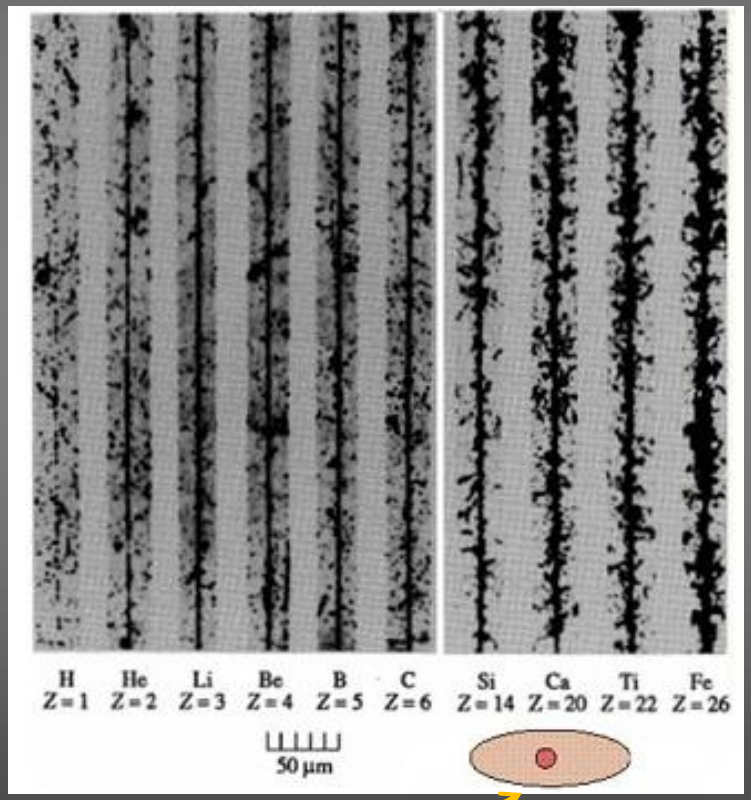
The JINR accelerators

Accelerator	Particles	Energy (up to)	Lab
Phasotron	Protons	660MeV	LNP
U-200, U-300	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	3 GeV/amu	LPHE

Tracks of heavy ions in nuclear emulsion



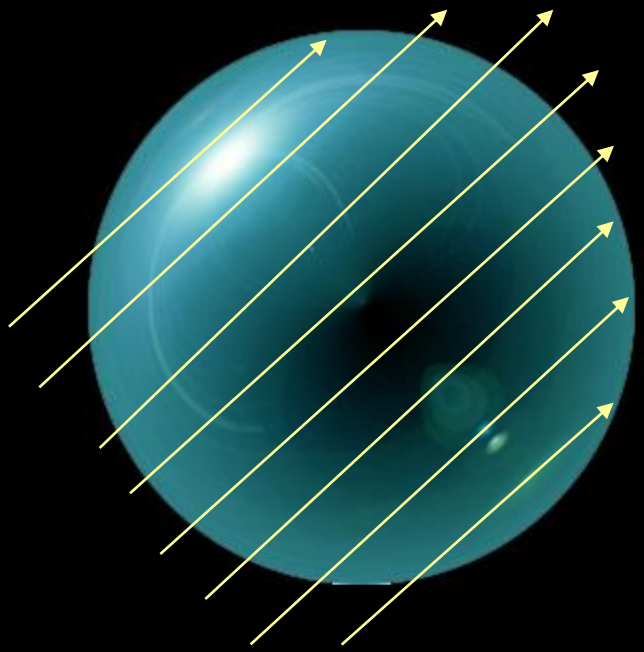
Fe



Mammalian cell

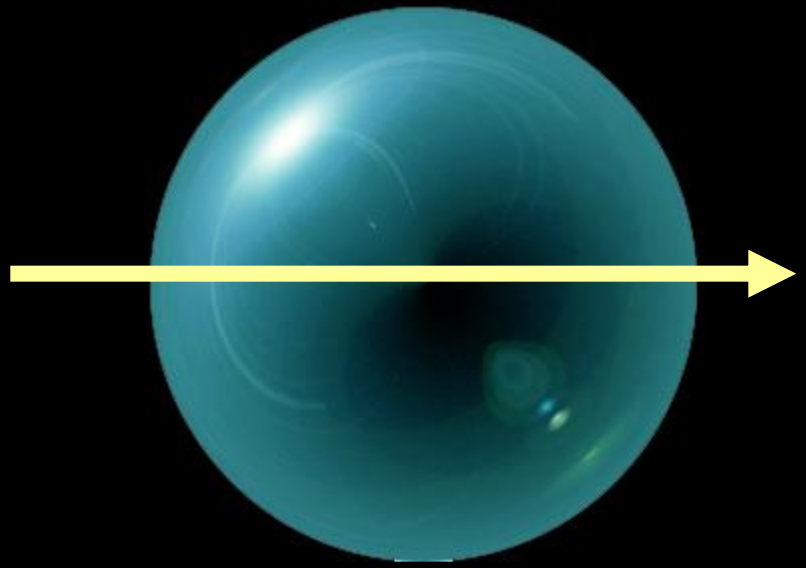
The dose distribution of radiation in matter

1 unit of the dose

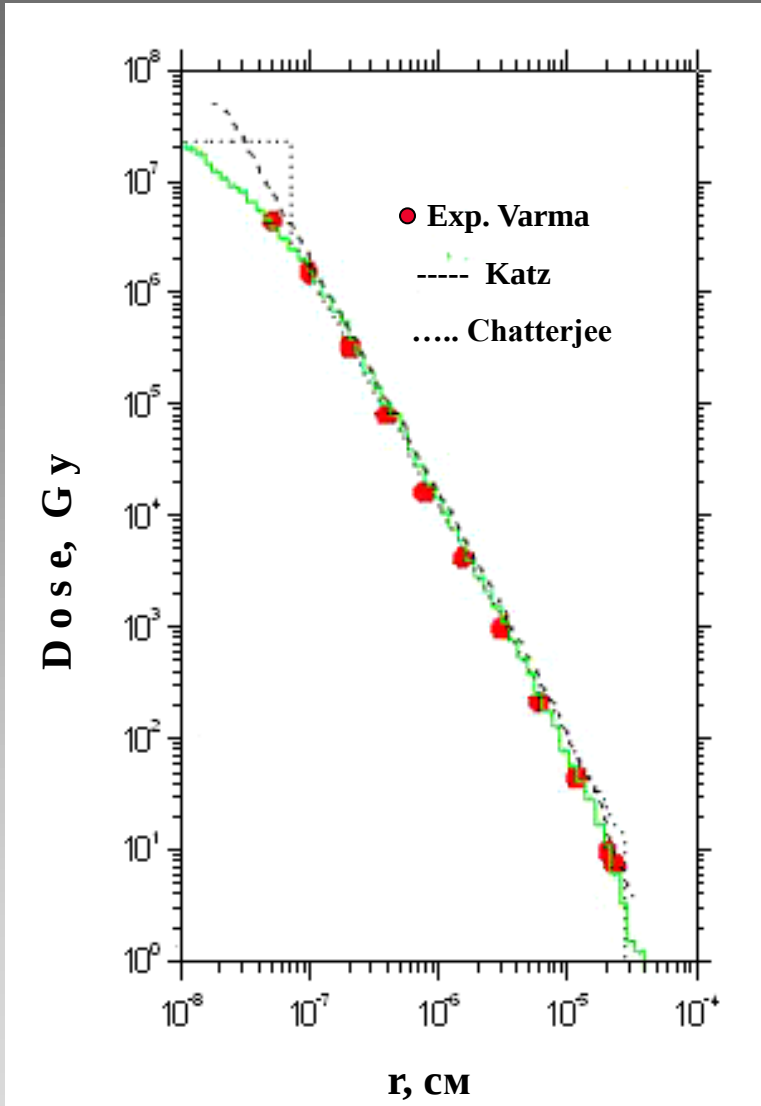


X-rays

1 unit of the dose



Fe ion

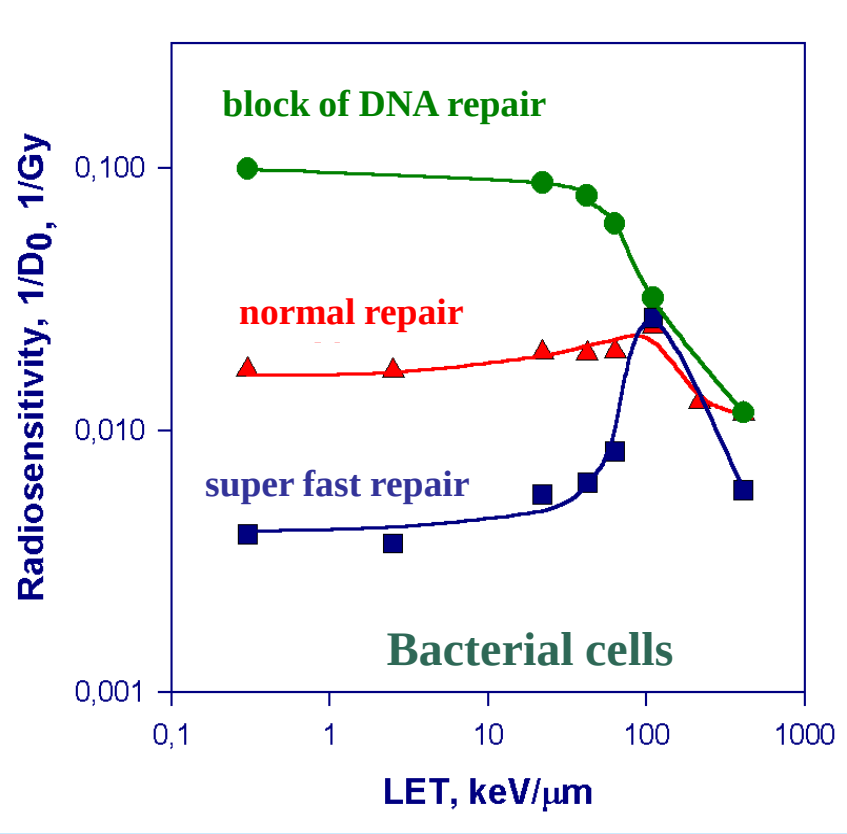


Radial dose distribution in track of heavy ion (^{12}C, 2,57 MeV/u)

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

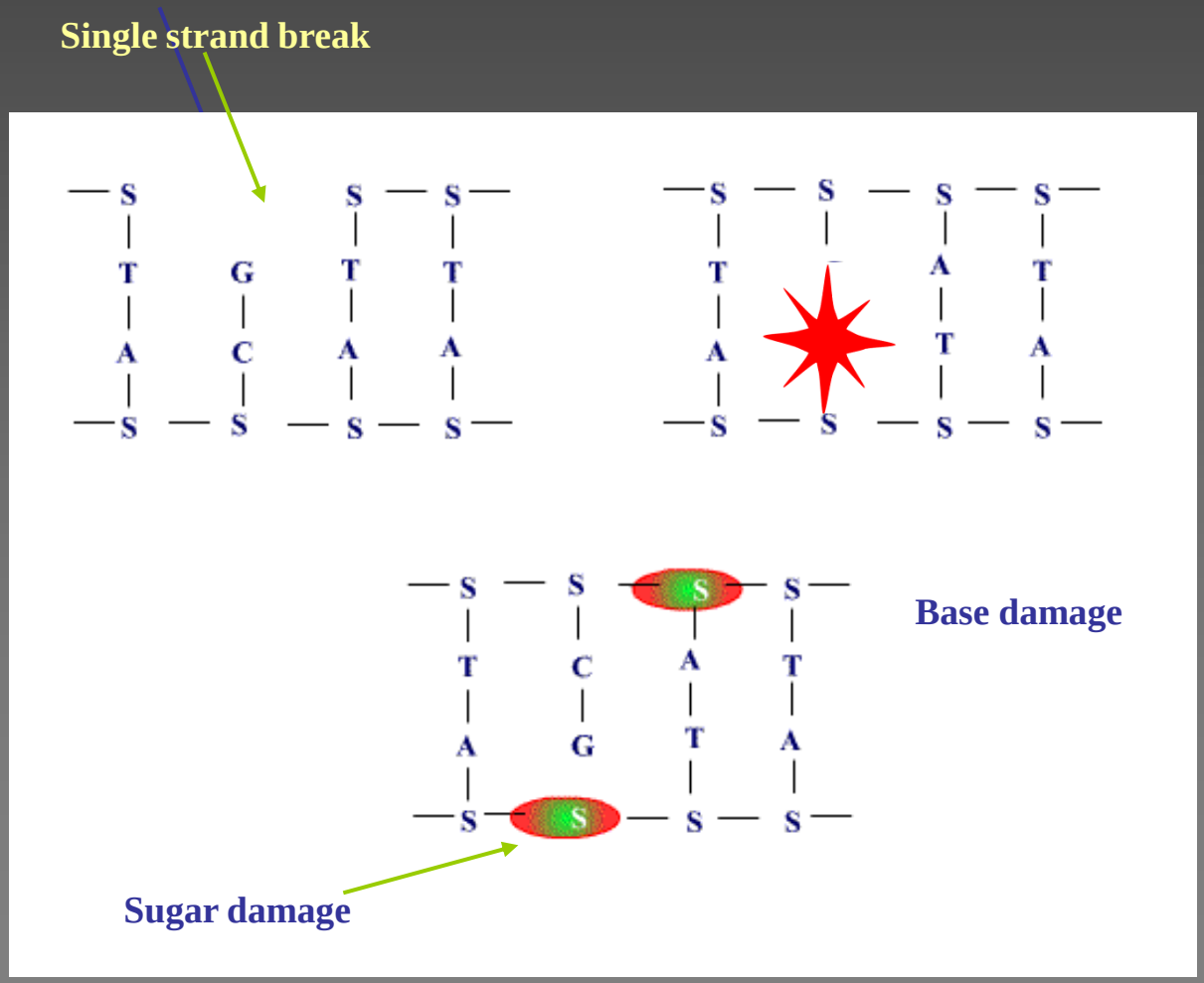
A.
Heavy ions is a powerful tool for the solve of fundamental problems of radiation genetics

The RBE problem was solved at the Flerov Lab accelerators



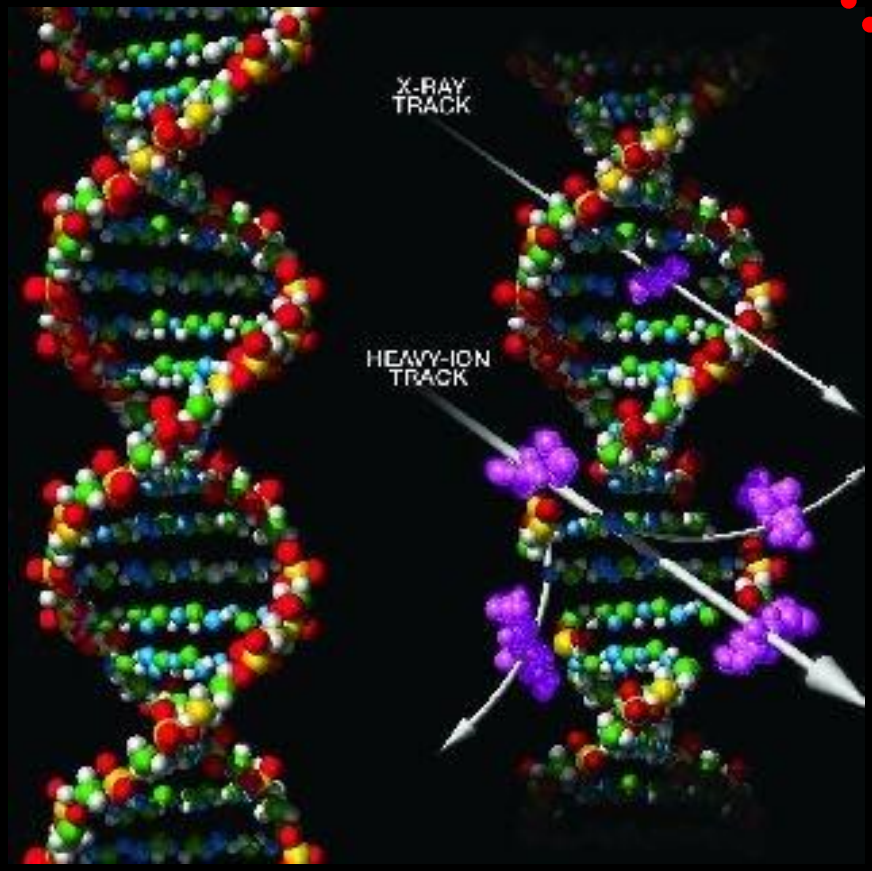
DNA repair capacity **of the living cells determines the type of RBE on LET dependence**

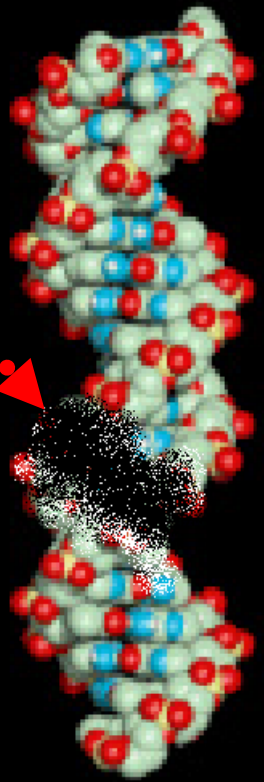
Single DNA damages



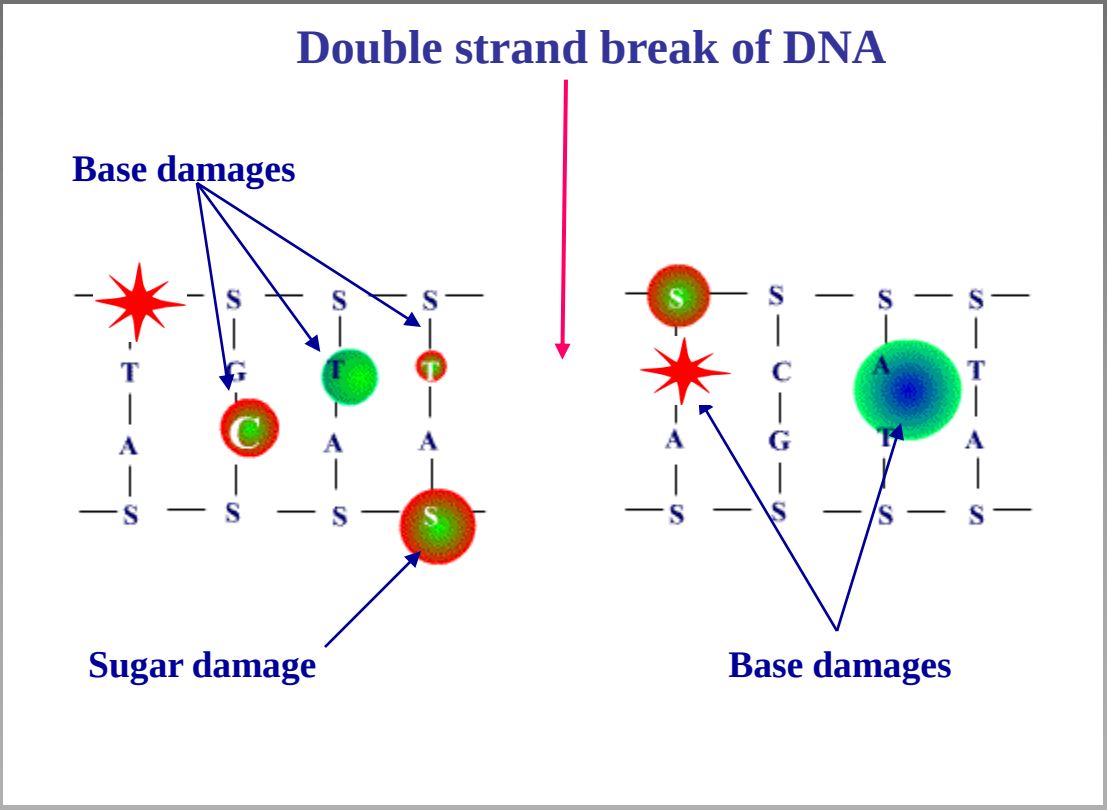
Clustered DNA damages

Fragment of DNA

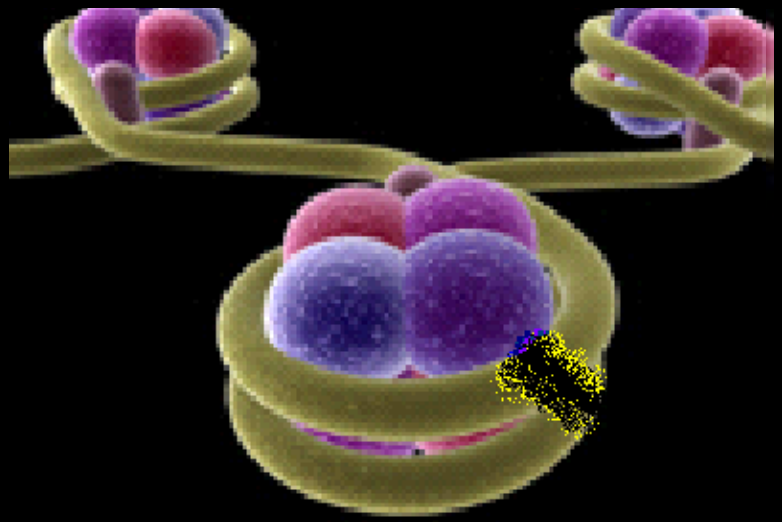




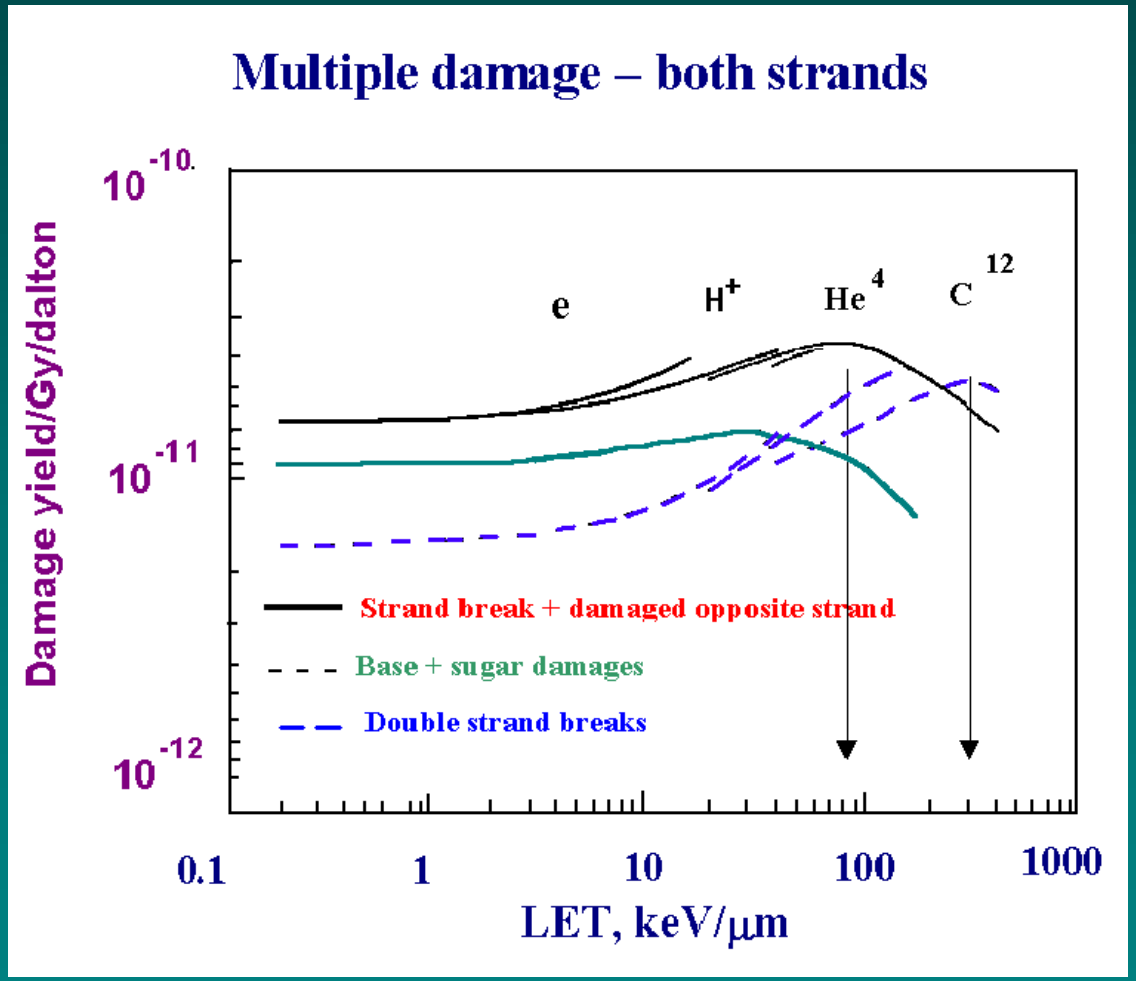
Clustered DNA damages



Clustered DNA damages in nucleosome

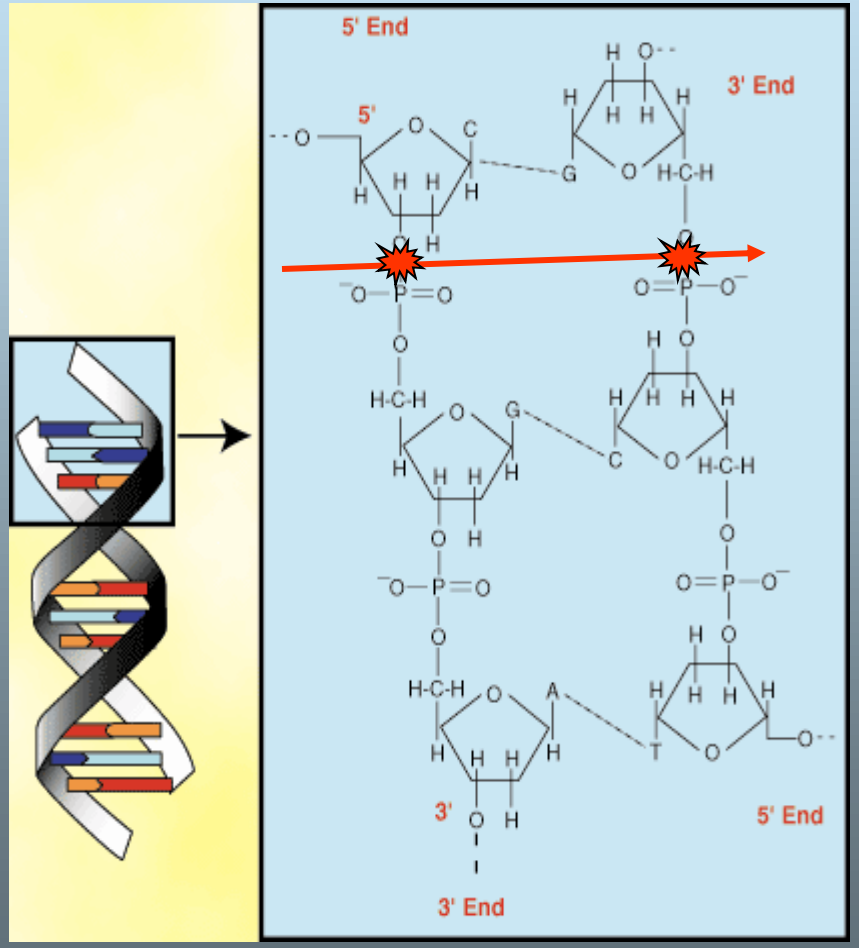


Yield of clustered damages on both DNA strands versus LET

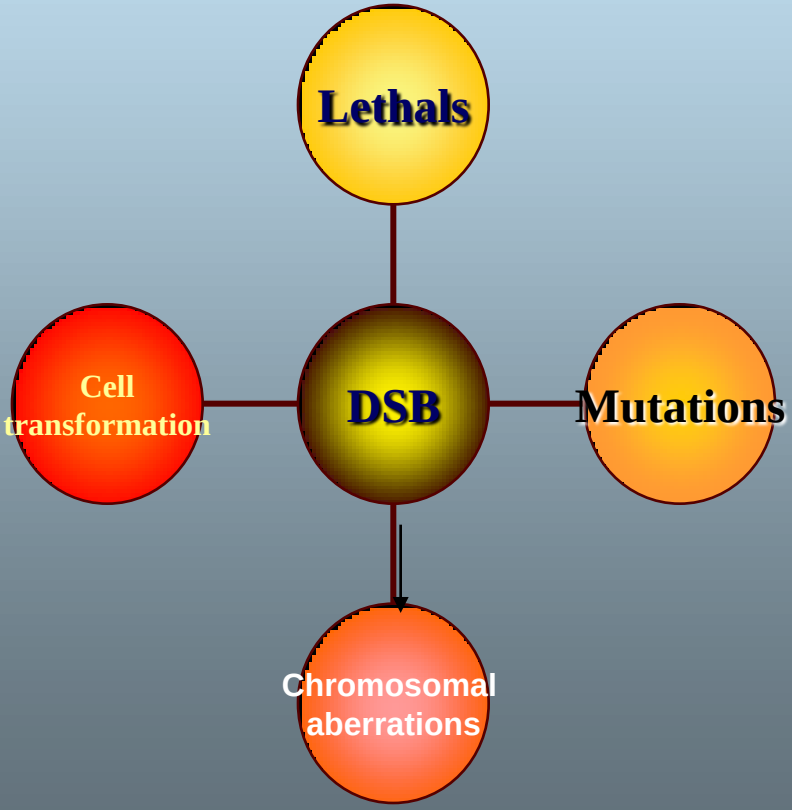


LABORATORY OF RADIATION BIOLOGY

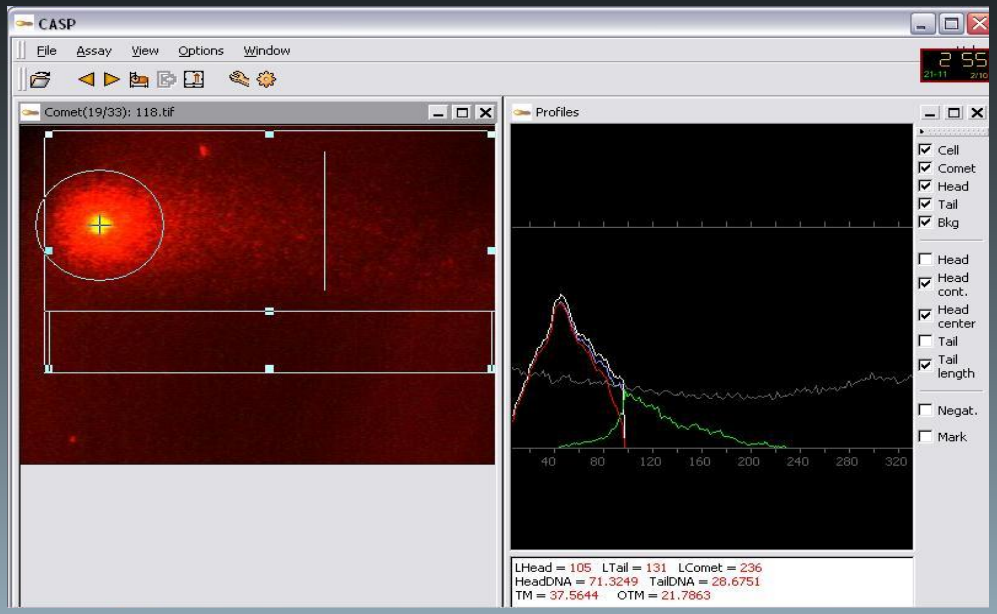
Double strand break of DNA

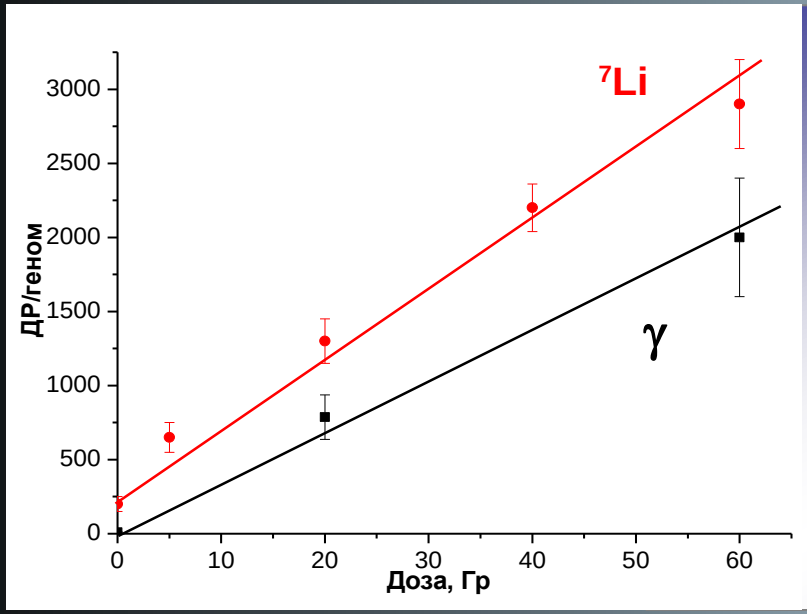


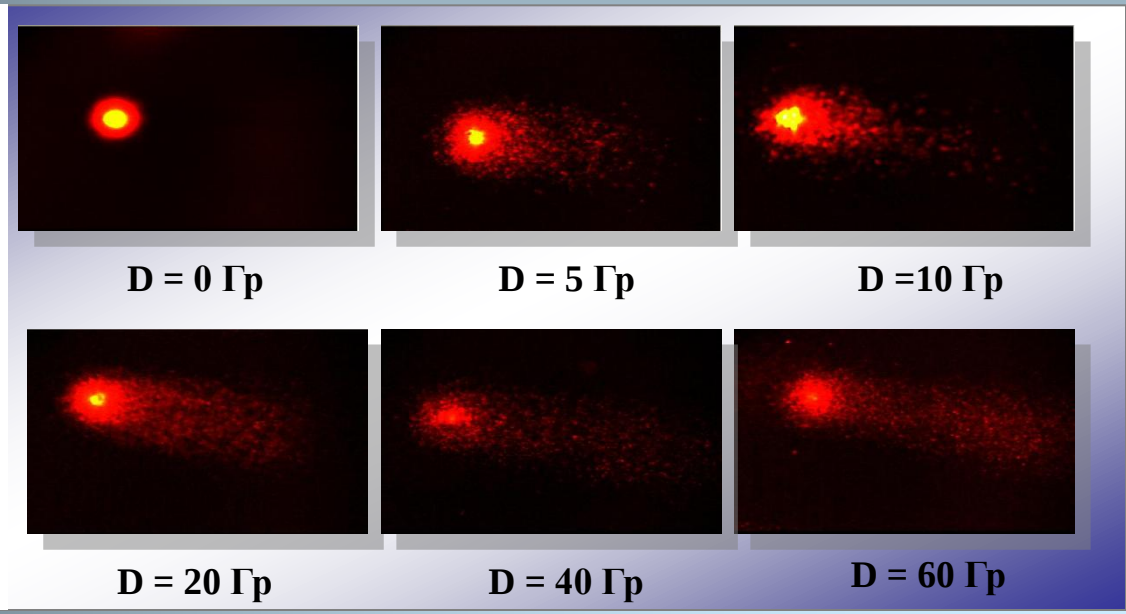
Consequences of DSB induction in cell genome



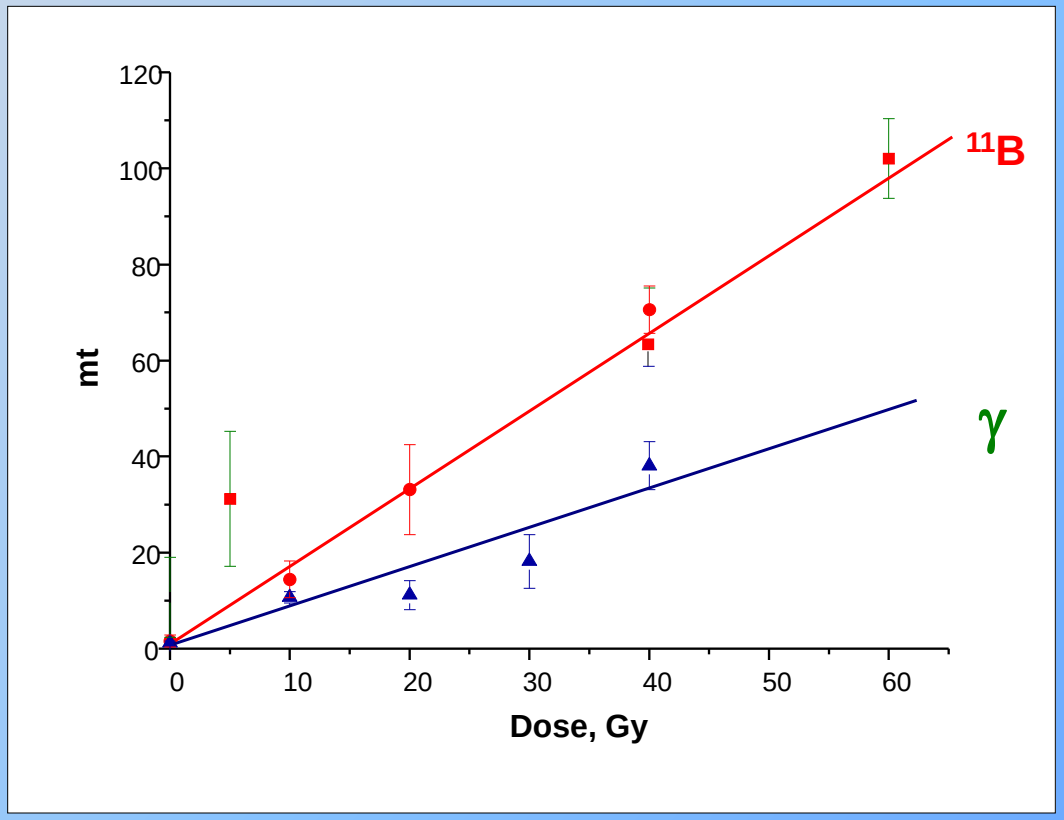
“Comet assay” for detection of DNA lesions







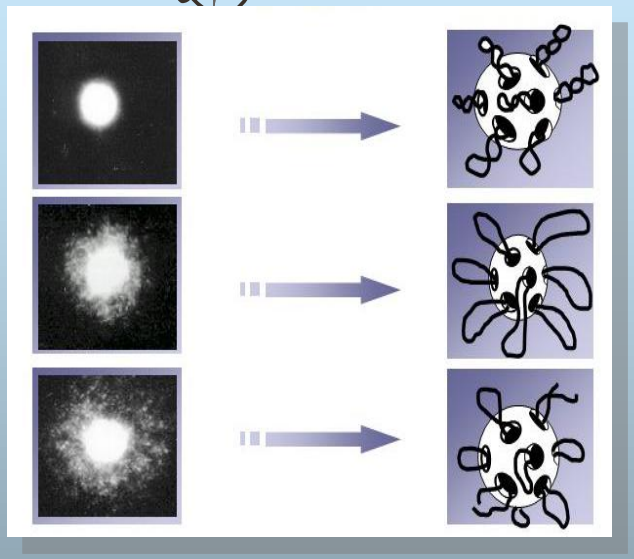
DSB induction in human lymphocytes by γ-rays and accelerated ^{11}B (40 keV/μm) ions

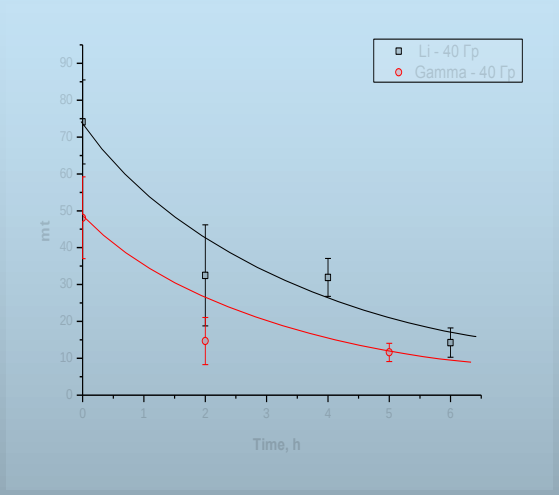


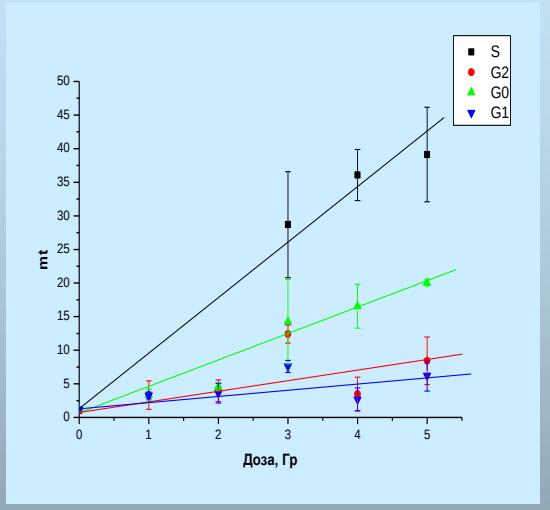
LRB

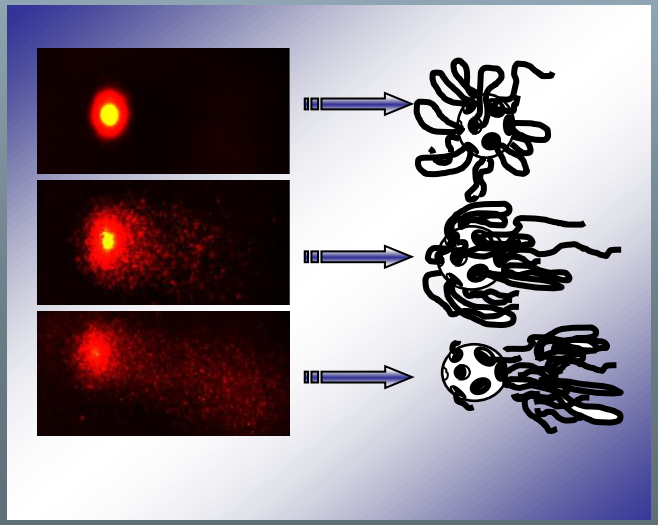
LABORATORY OF RADIATION BIOLOGY

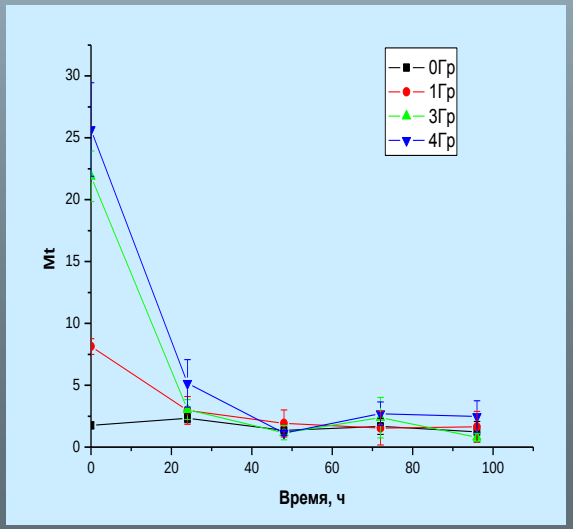
Kinetics of DNA repair

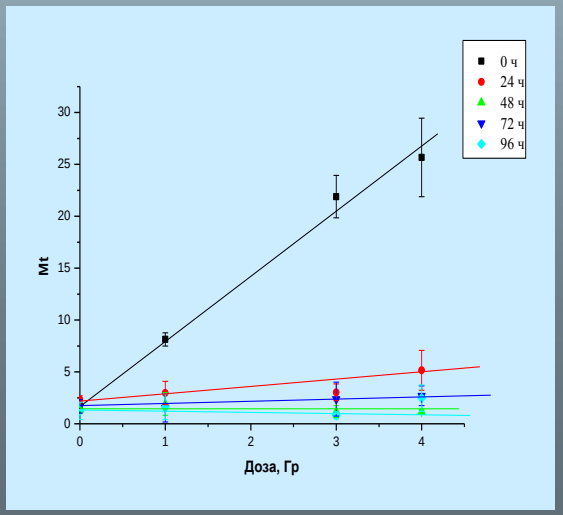




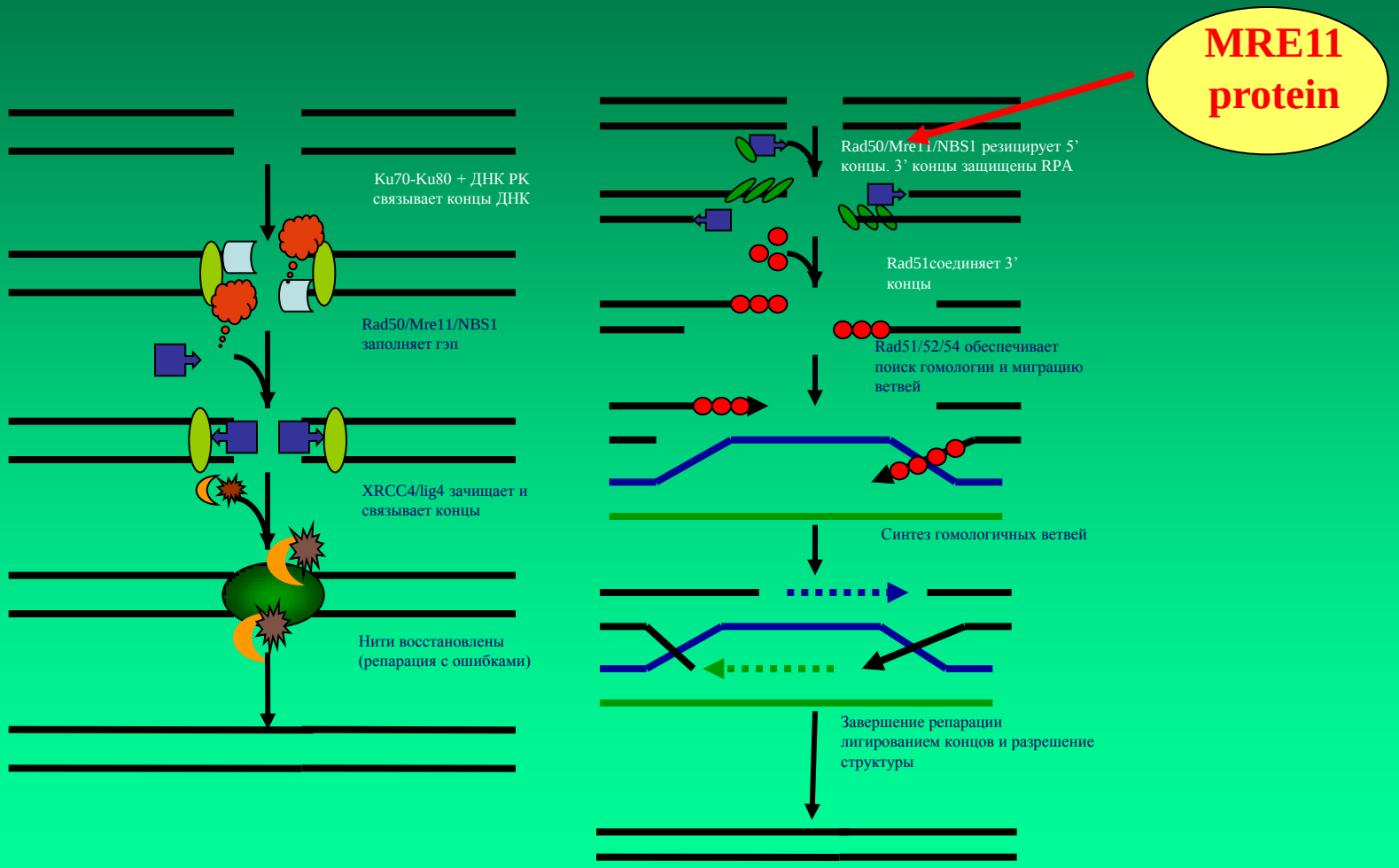




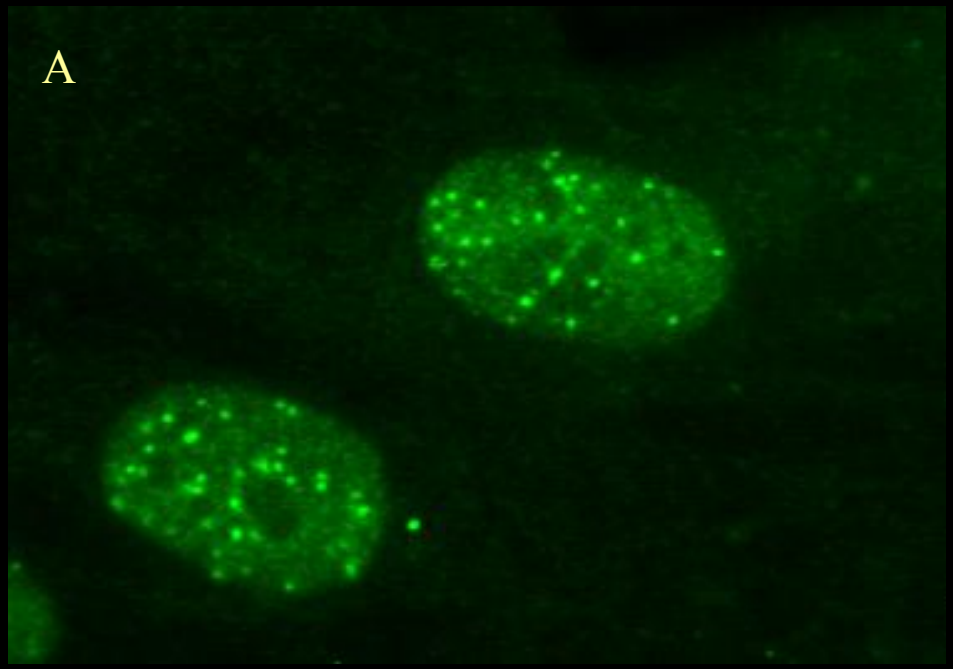


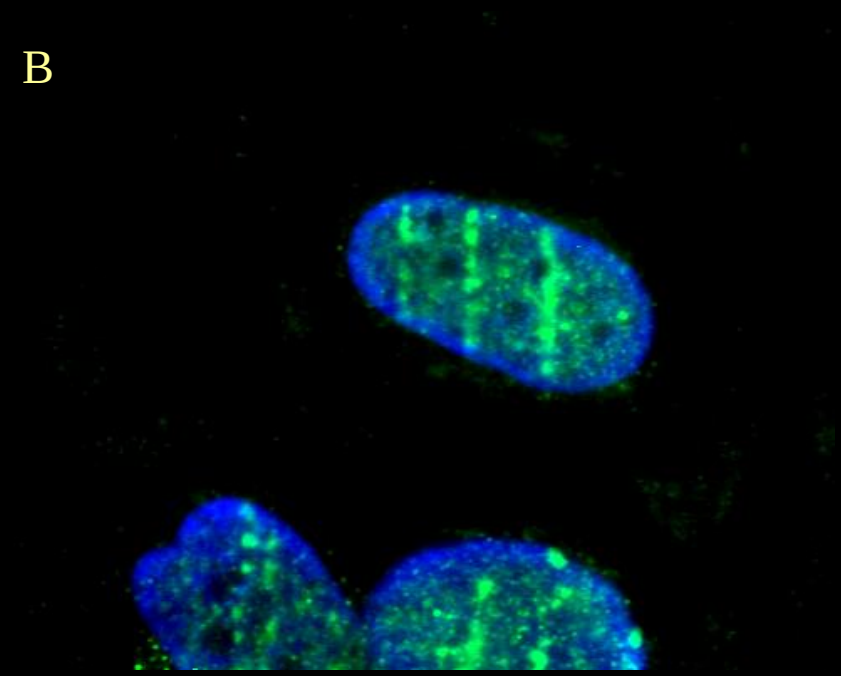


The mechanism of DSB DNA repair in human cells



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

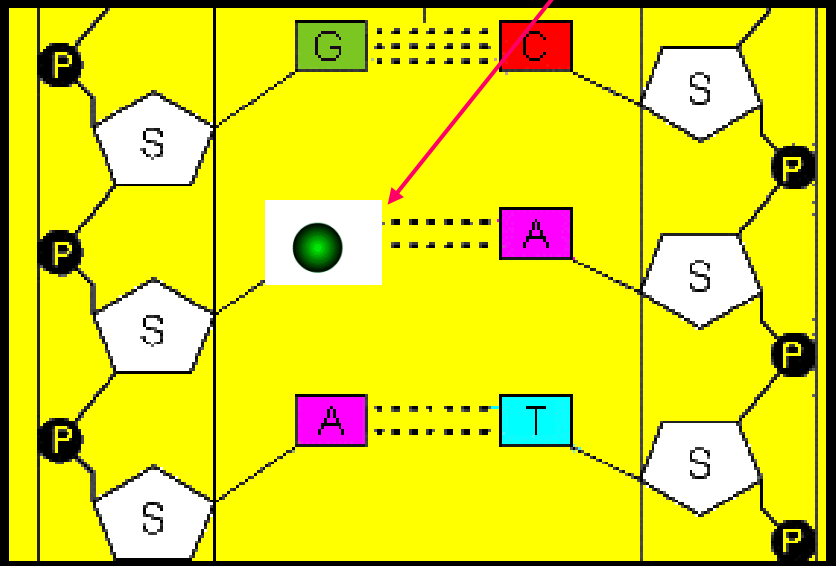




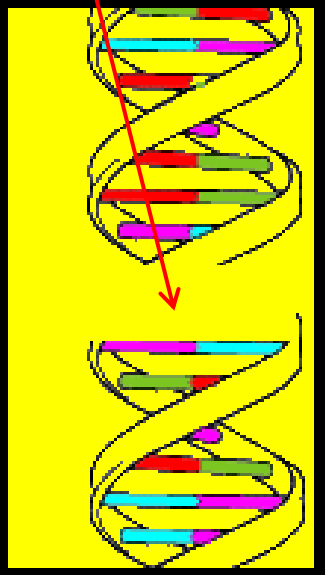
Radiation induced mutagenesis

Gene mutation

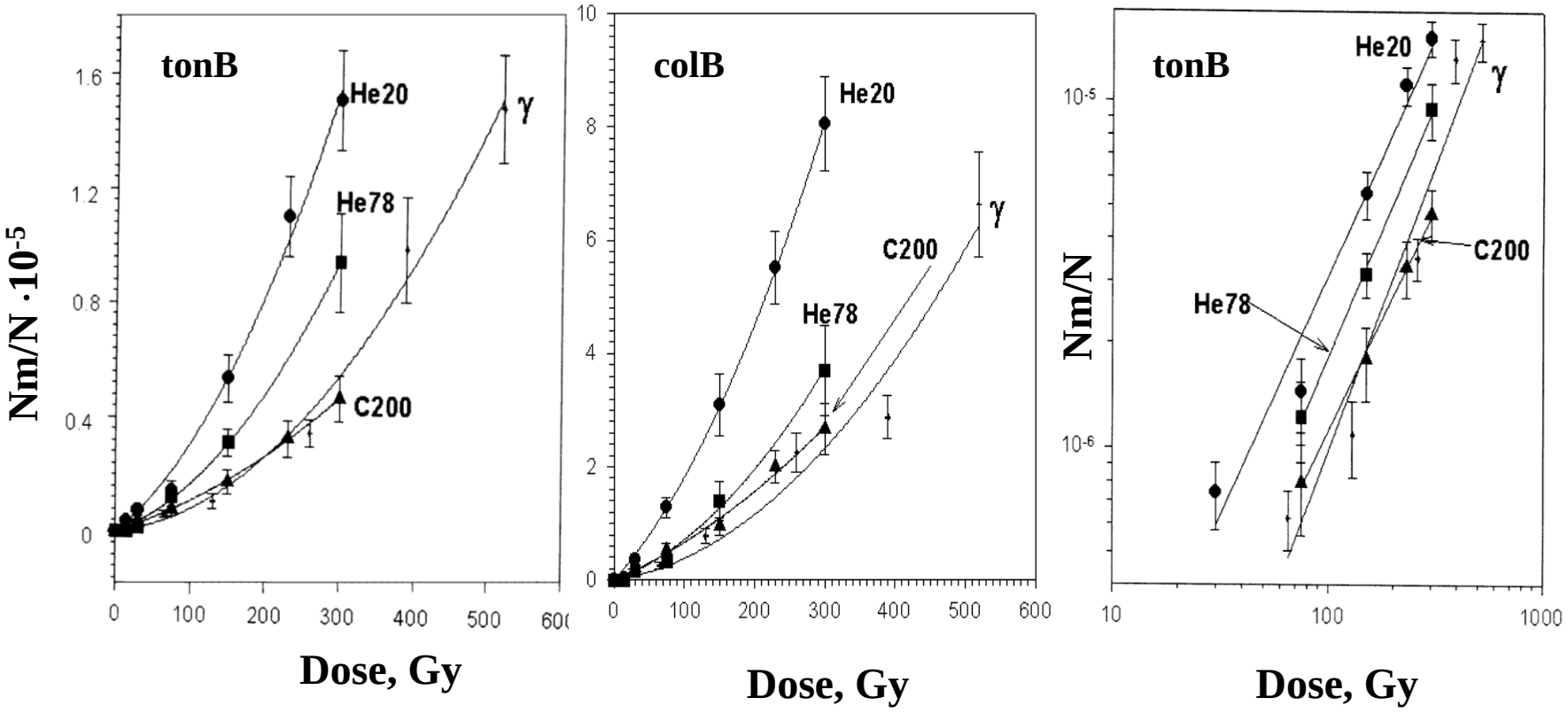
Guanine



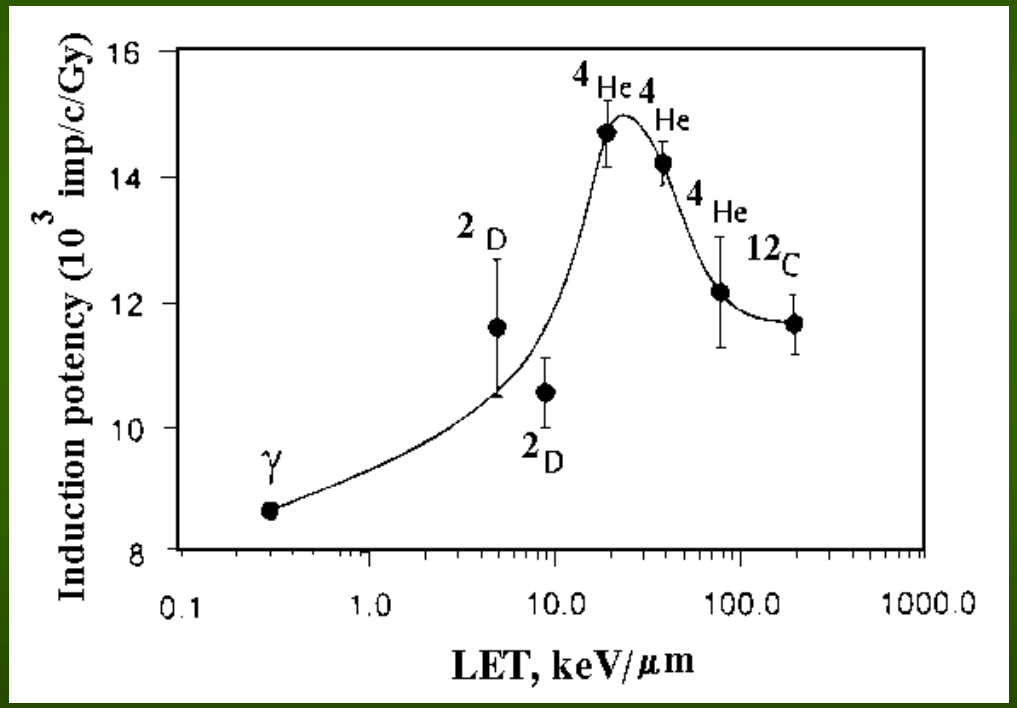
Structural mutation

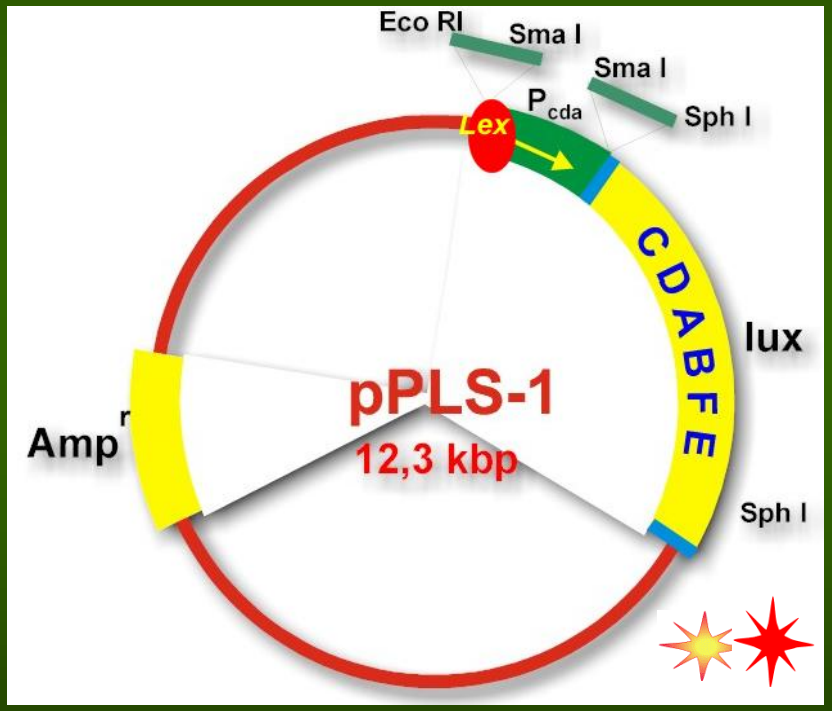


The frequency of tonB and colB mutation induction after γ-ray and heavy ion irradiation



Induction of mutagenic DNA repair by heavy ions

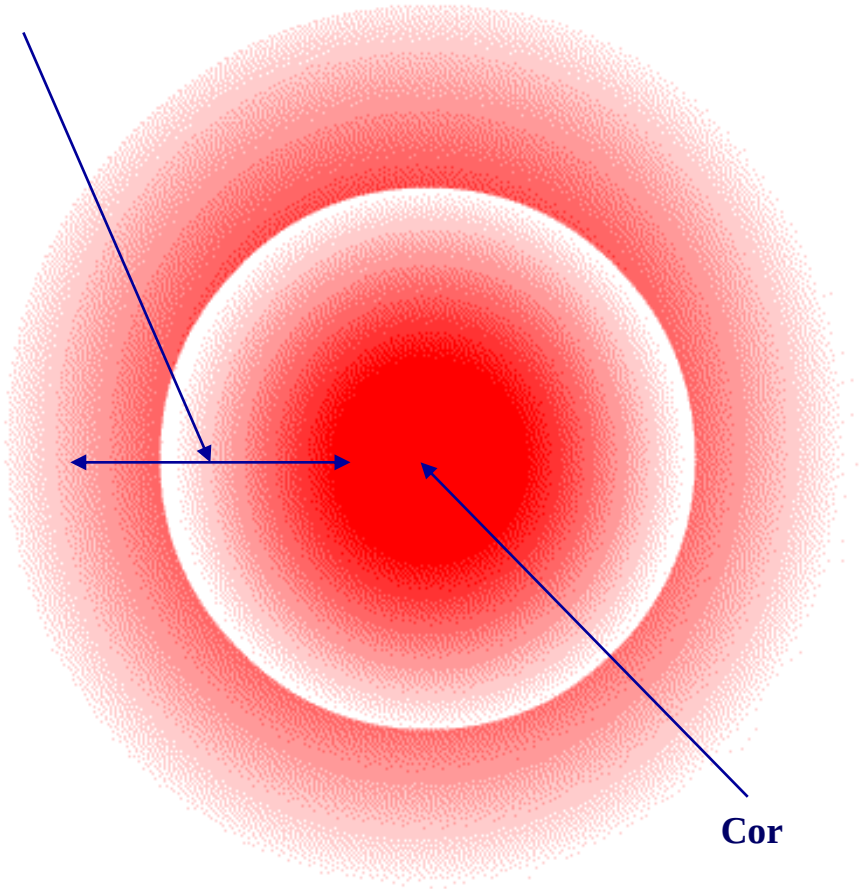




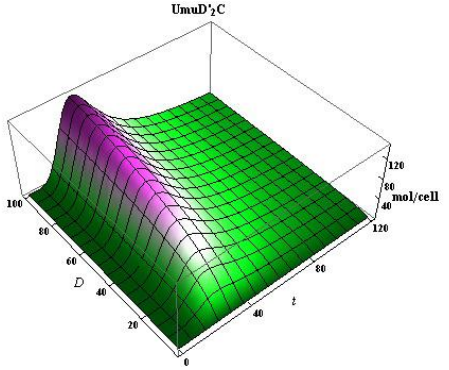
luciferase

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

Mutagenic belt of heavy particle track



The genetic net for induction of gene mutations by ionizing radiations in E.coli bacteria



γ

ПДР

ЭДР

polA

ДНК

polA зависимые П

Л

КП

ПМП

Pol III

Pol V

M

recA-lexA

SOS сигнал

RecA*

UmuD

UmuD'

LexA

recA

lexA

umuD

SSB

UmuC

umuC

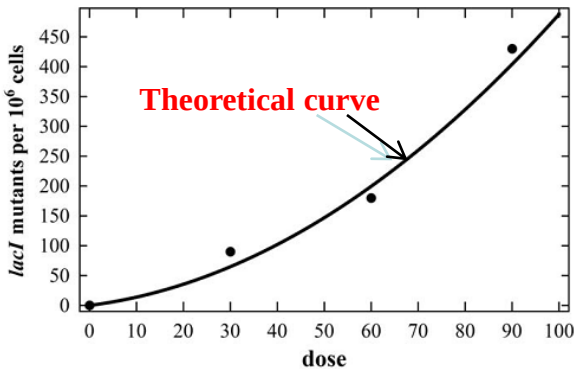
UmuD2C

UmuD'D

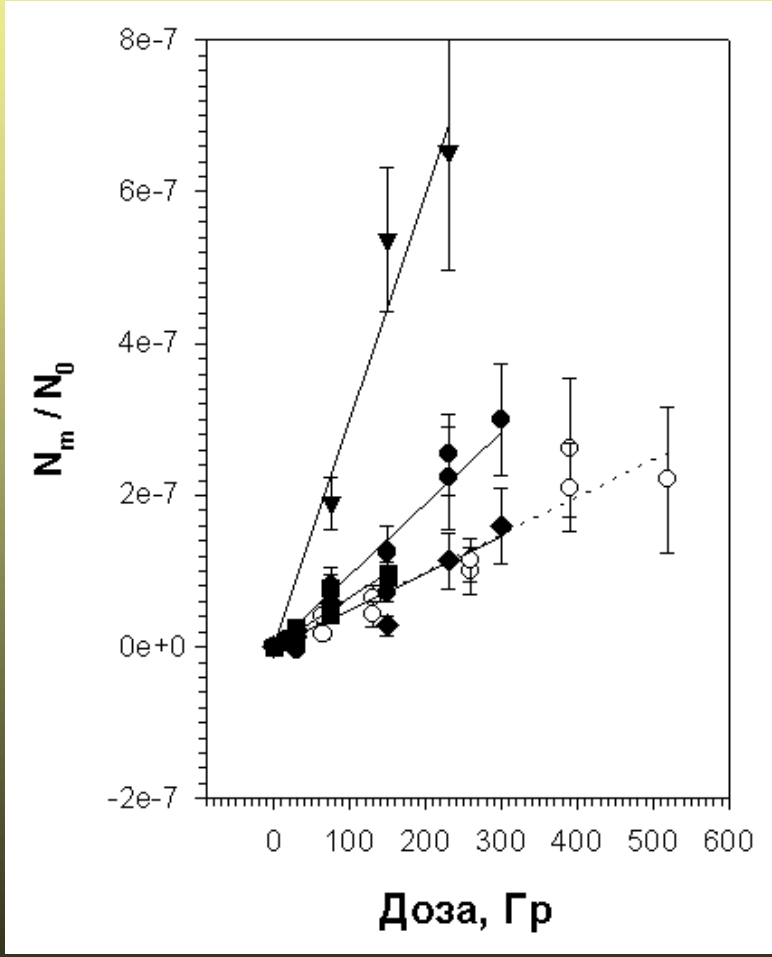
UmuD'2C

Регуляция клет. цикла

SOS мутагенез



Induction of tonB⁻trp⁻ deletion mutations by heavy ions



○ - γ-rays;

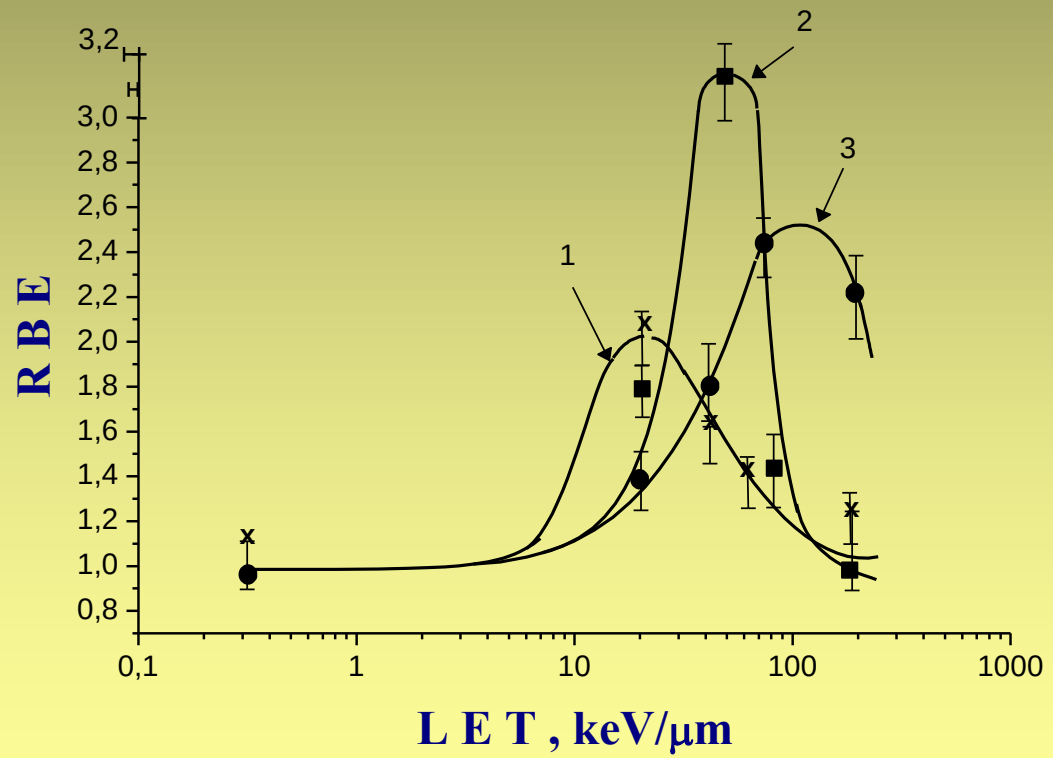
● - ^{4}He (20 keV/μm);

▼ - ^{4}He (50 keV/μm);

■ - ^{4}He (78 keV/μm);

♦ - ^{12}C (200 keV/μm)

RBE on LET dependence

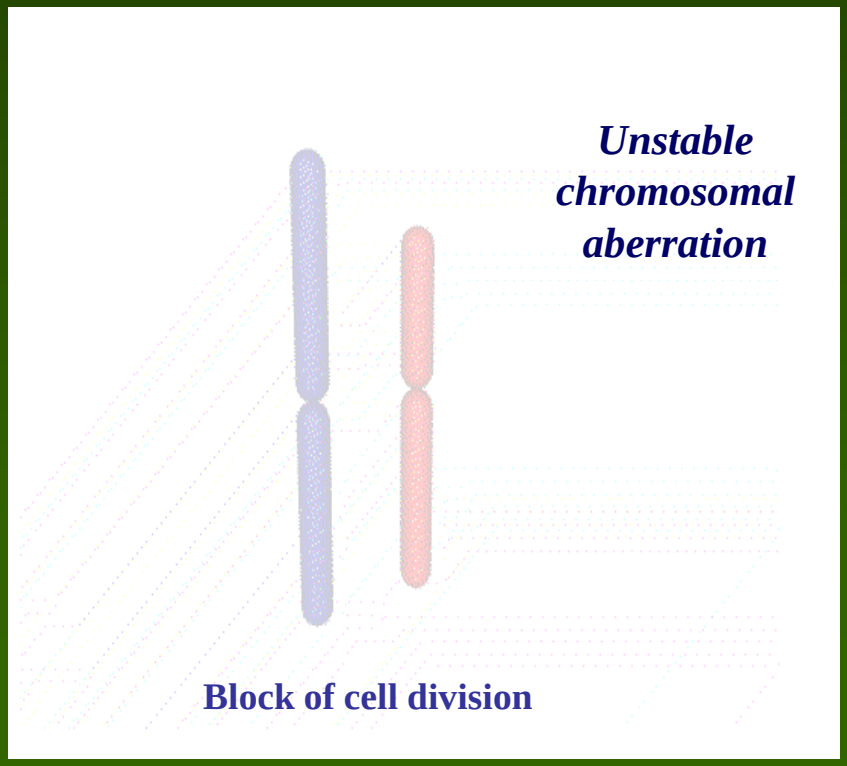


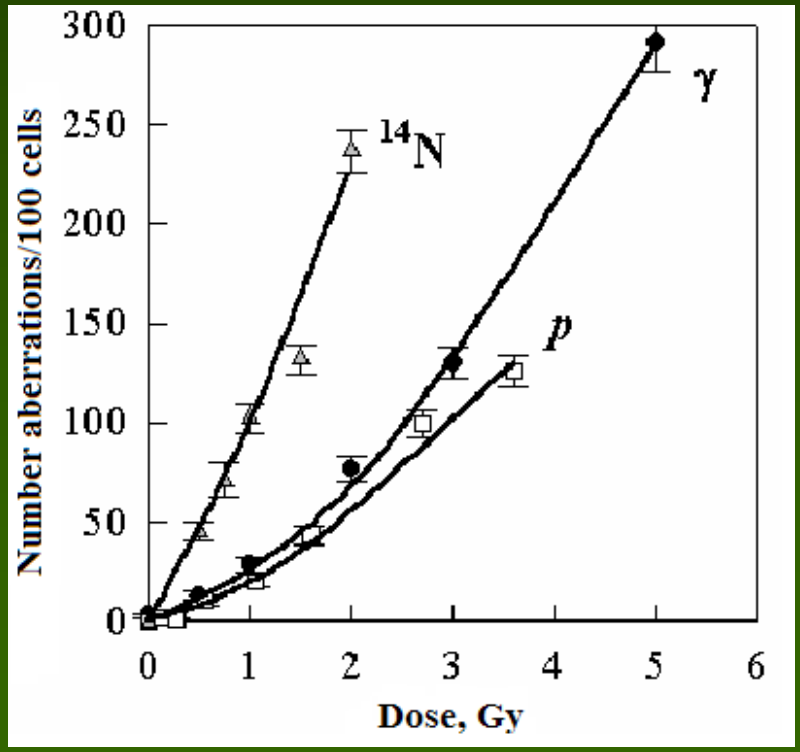
1 – tonB mutations

2 – tonBtrp^{-} deletions

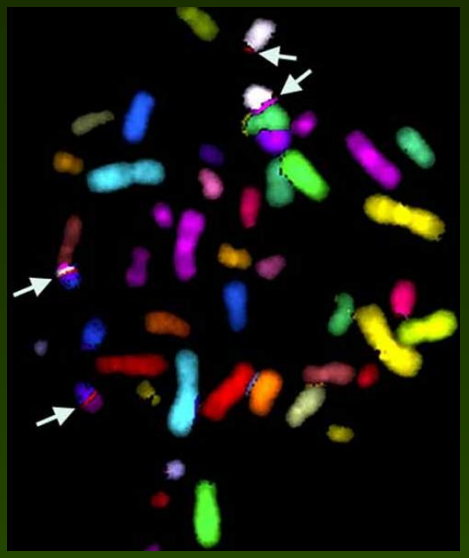
3 – lethal effect

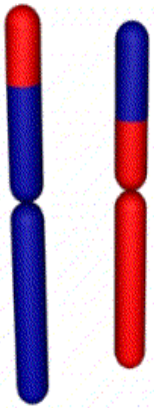
❖ *Formation of unstable chromosomal aberration after heavy ion irradiation of human cells*





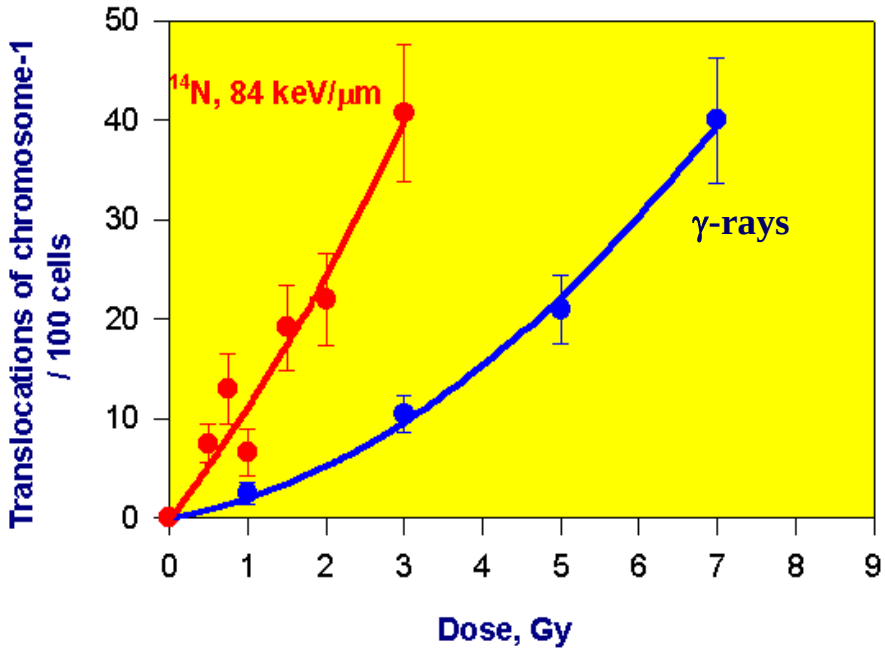
❖ *Formation of stable chromosomal aberration after heavy ion irradiation of human cells*



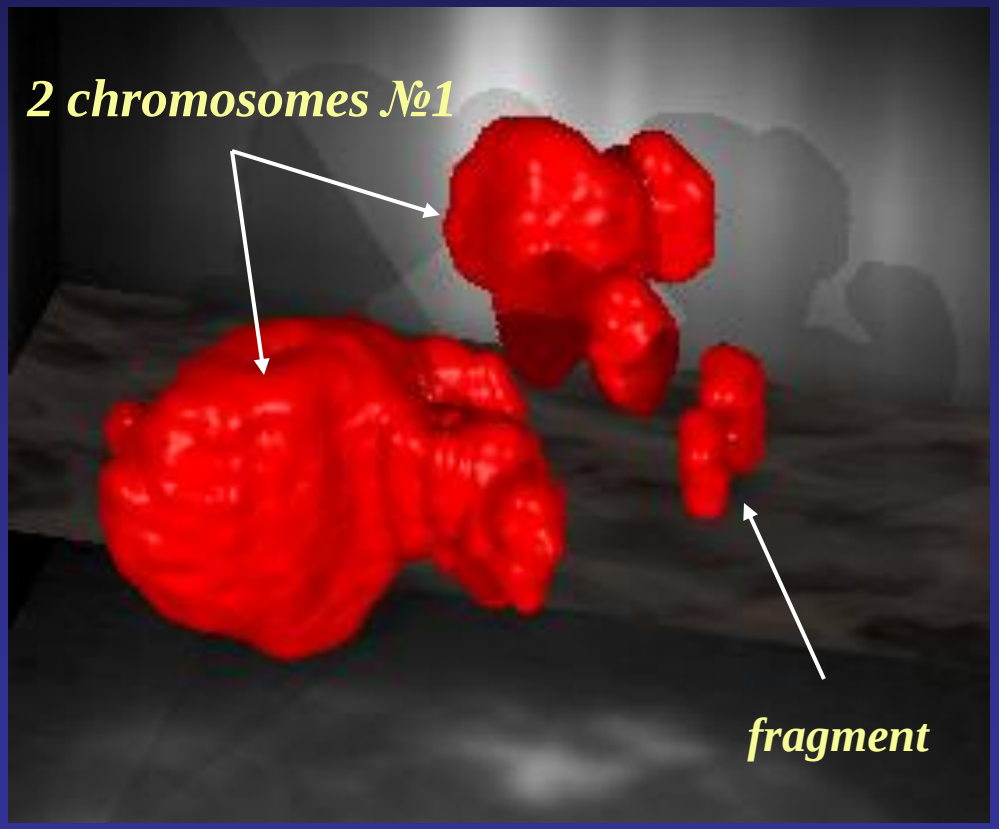


Stable chromosomal aberration

Successful of cell division

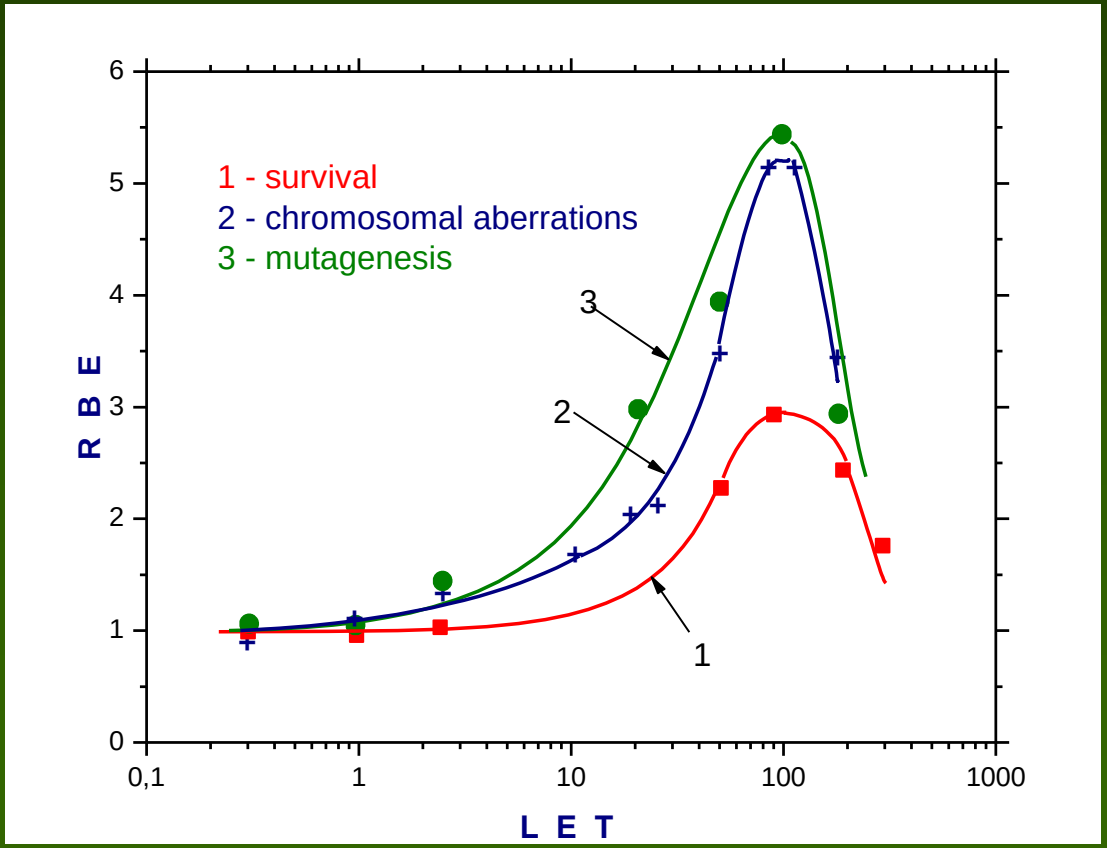


3 D dimension of human chromosome

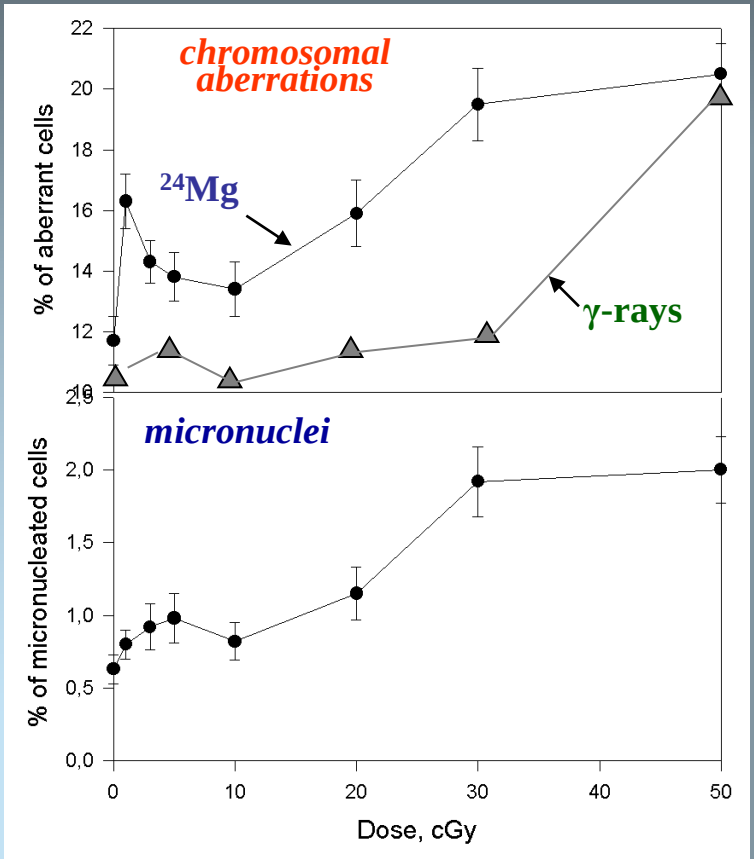


Chromosome 1 of human lymphocyte nucleus in interphase with fragment after irradiation 1 GeV protons at synchrophasotron. The 3 D dimension picture was obtained by using FISH technique and confocal microscopy.

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



Cytogenetical effect of low doses of accelerated ^{24}Mg *ions*



The frequency of cells with chromosome aberrations. **Chinese hamster cells exposed to ^{24}Mg ions with energy 500 MeV/nucleon**

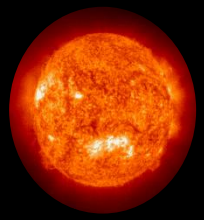
B.

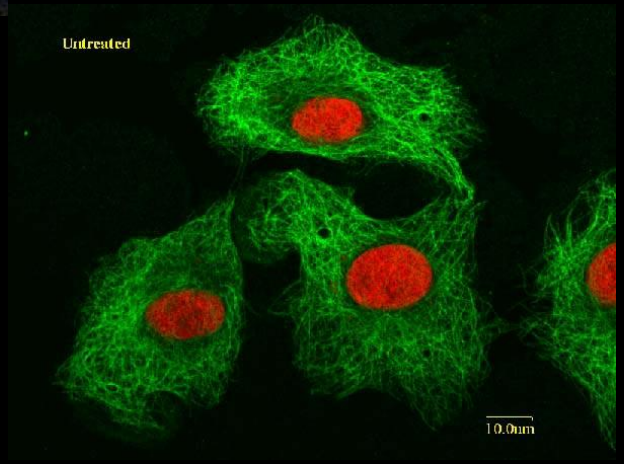
Accelerated heavy ions is a tool for modeling of biological action of space radiation

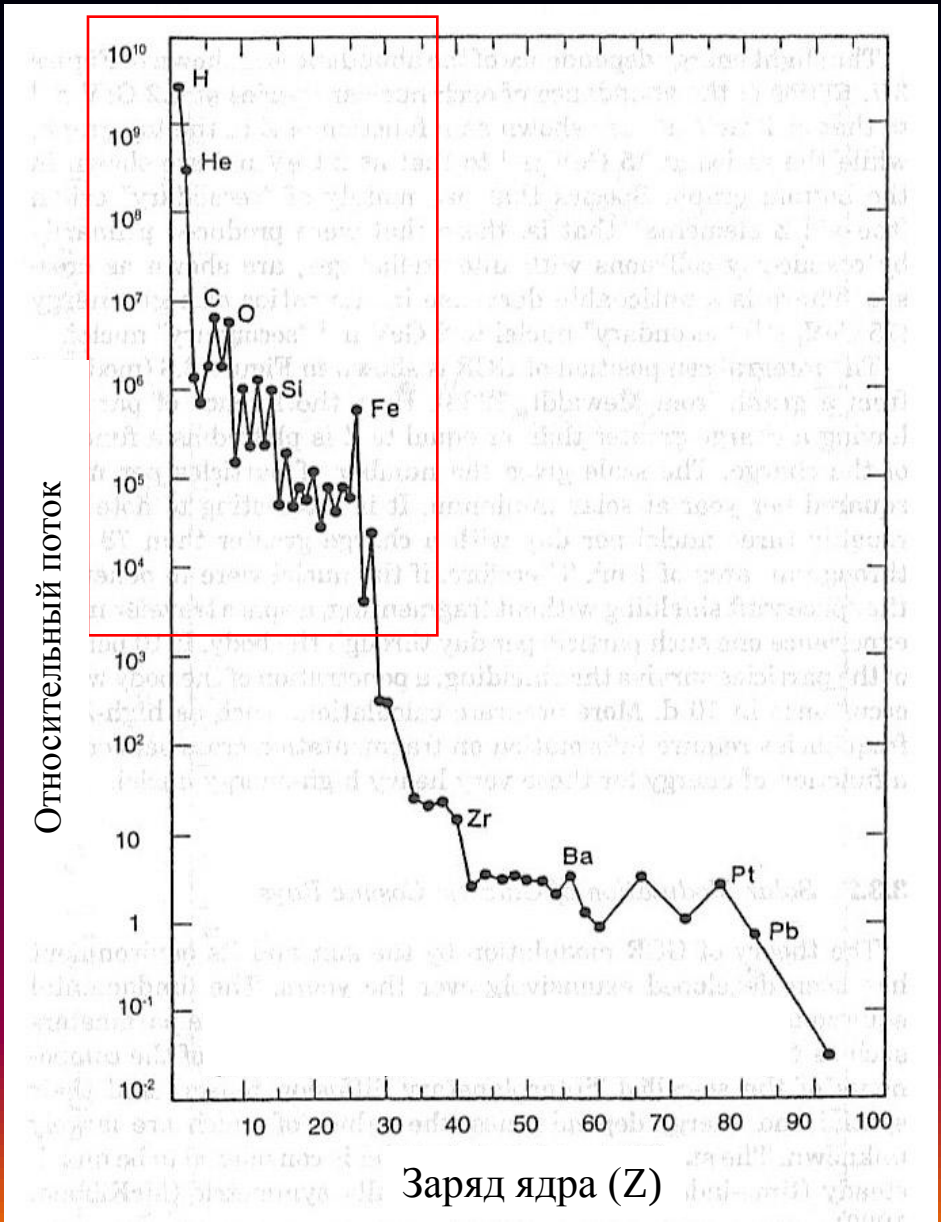
Heavy charged particles from Galaxy are the most dangerous type of cosmic radiation

The GCR flux

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

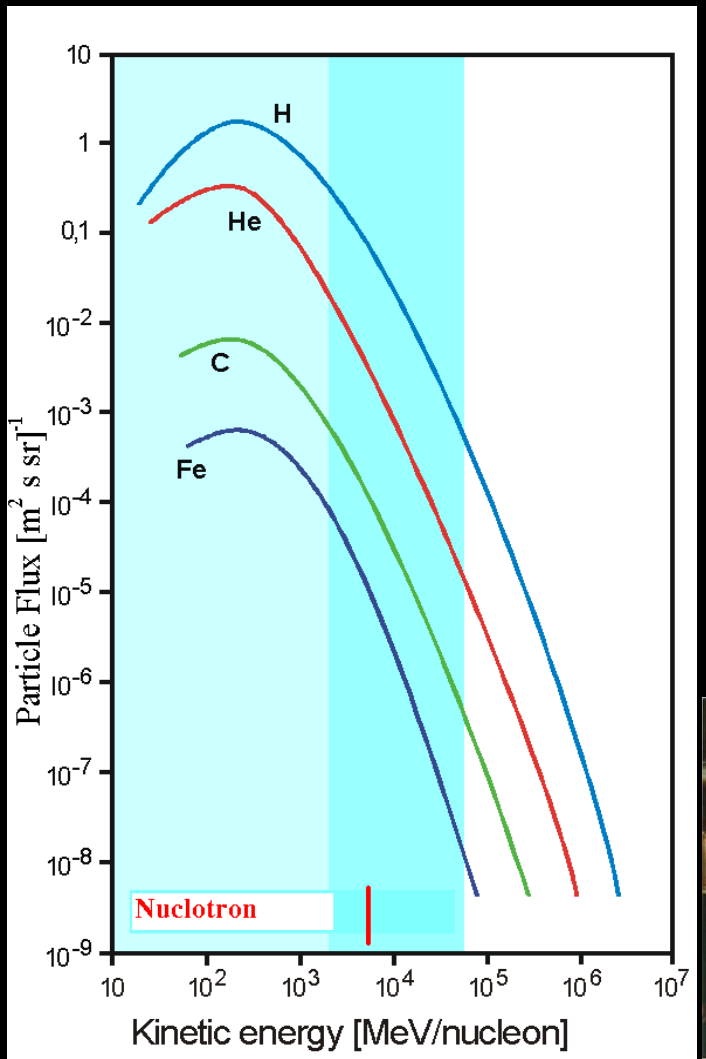


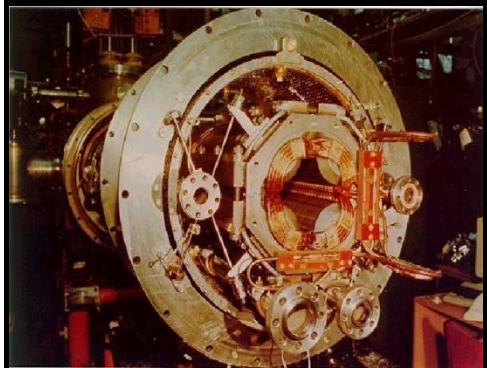




The relative flux of GCR particles

The energy spectrum of GCR and Nuclotron accelerator

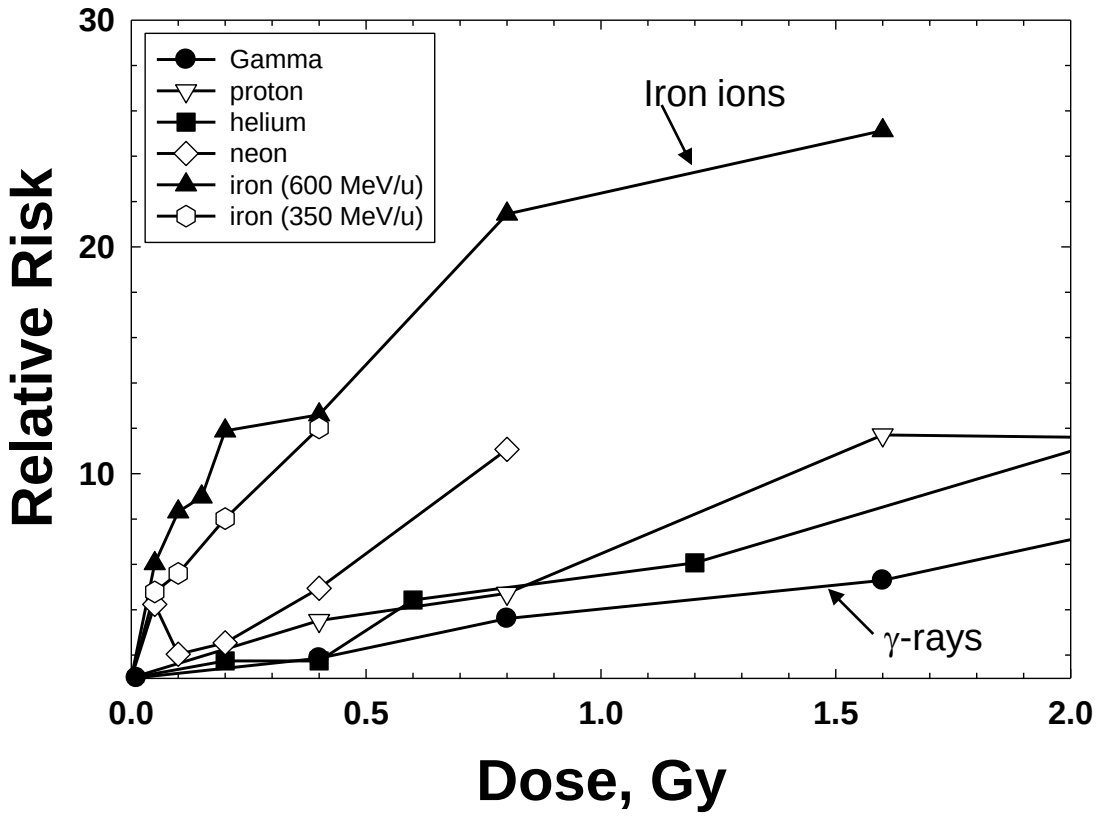




Consequences of action of Galactic heavy ions

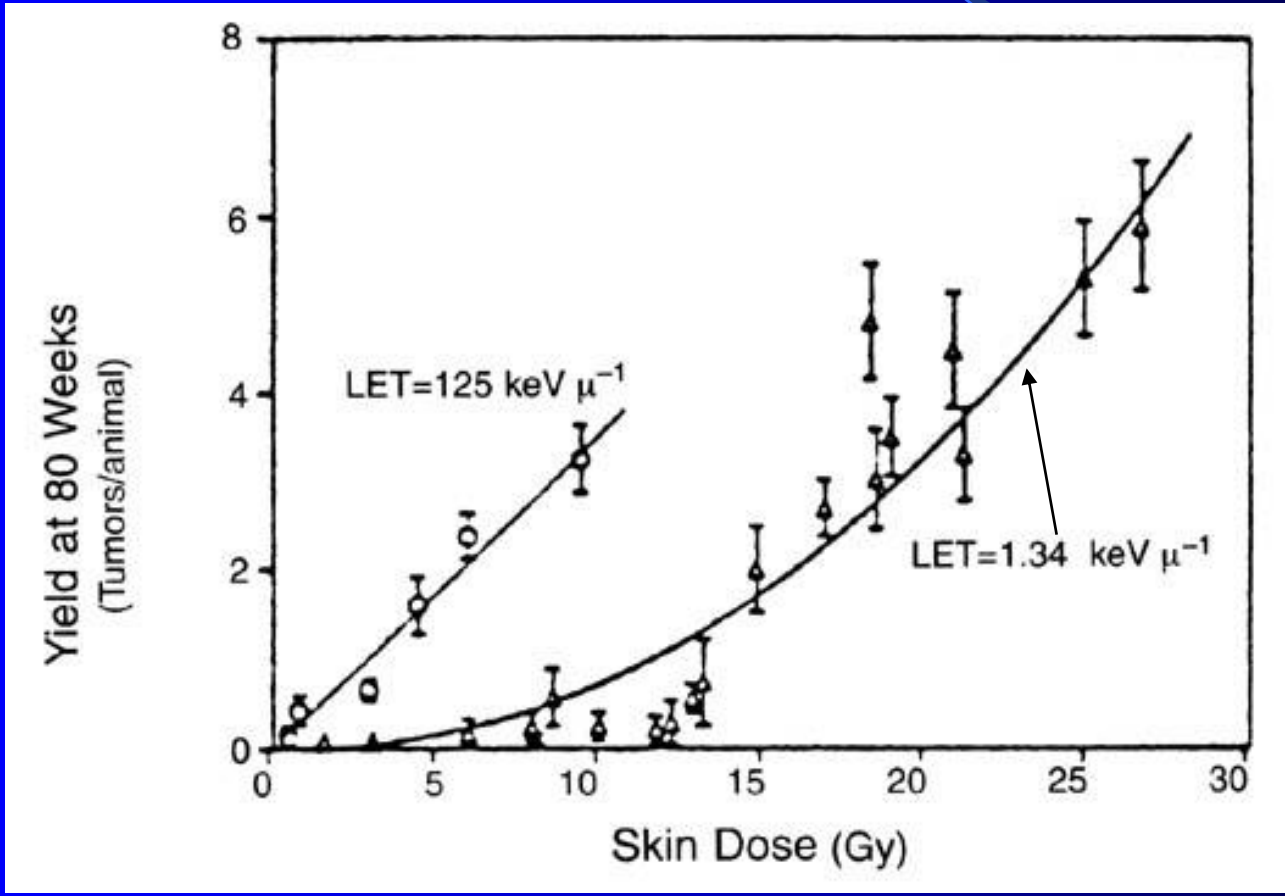
- **Induction of cancer;**
- **Formation of gene and structural mutations;**
- **Violation of visual functions:**
- **lesions of retina;**
- **cataract induction;**
- **CNS violation**

Gardner tumors

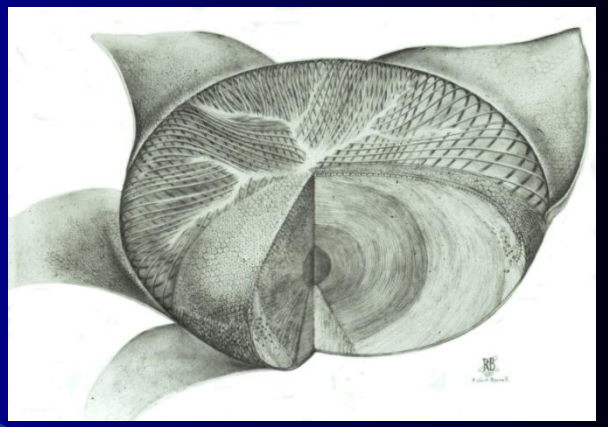


Nelson, 2006

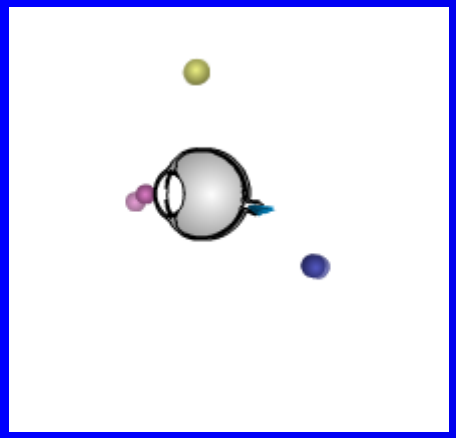
Skin cancer
(rats)

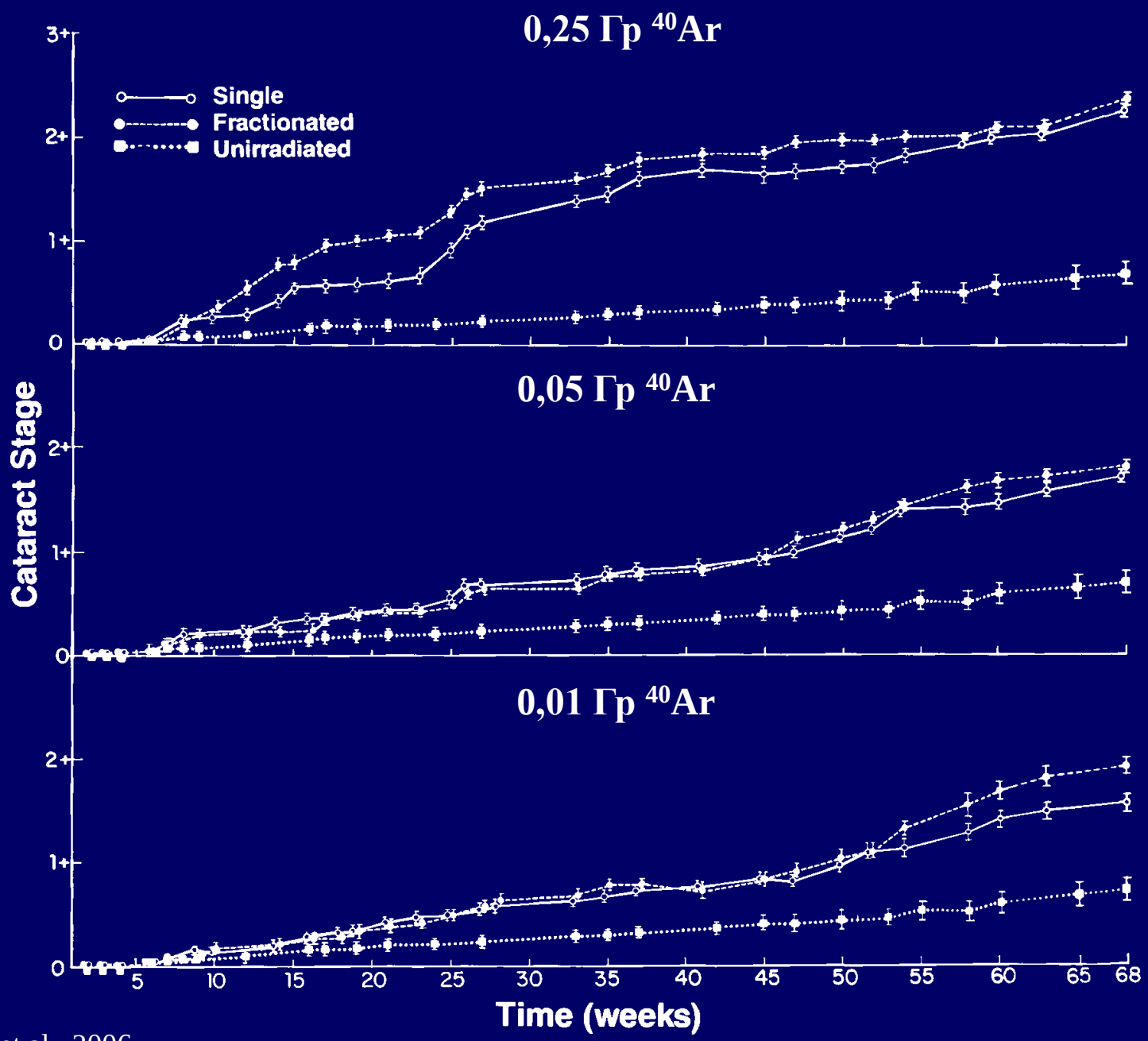


Burns, Albert, 1986



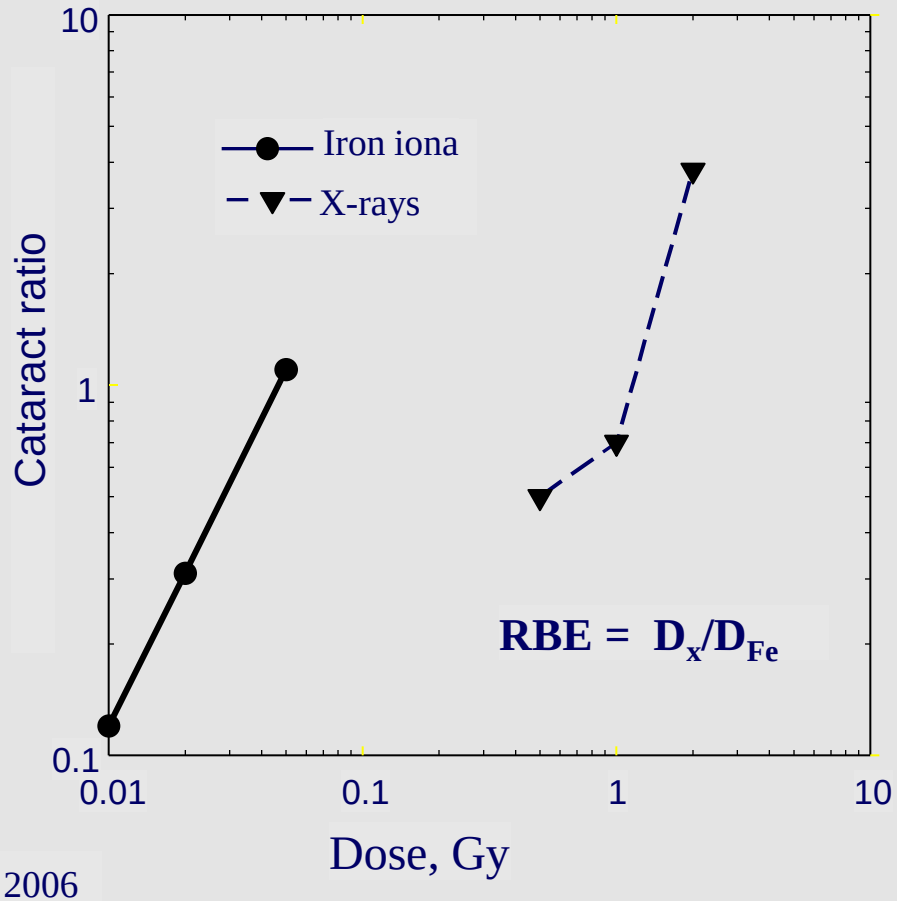
Cataract induction

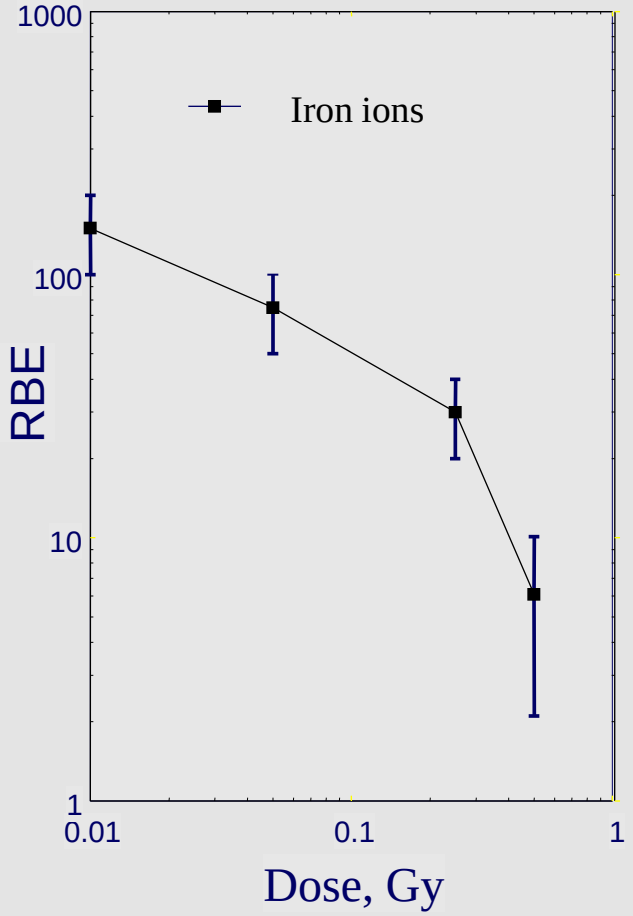




Worgul et al., 2006

Cataract ratio after irradiation by iron ions and X-rays

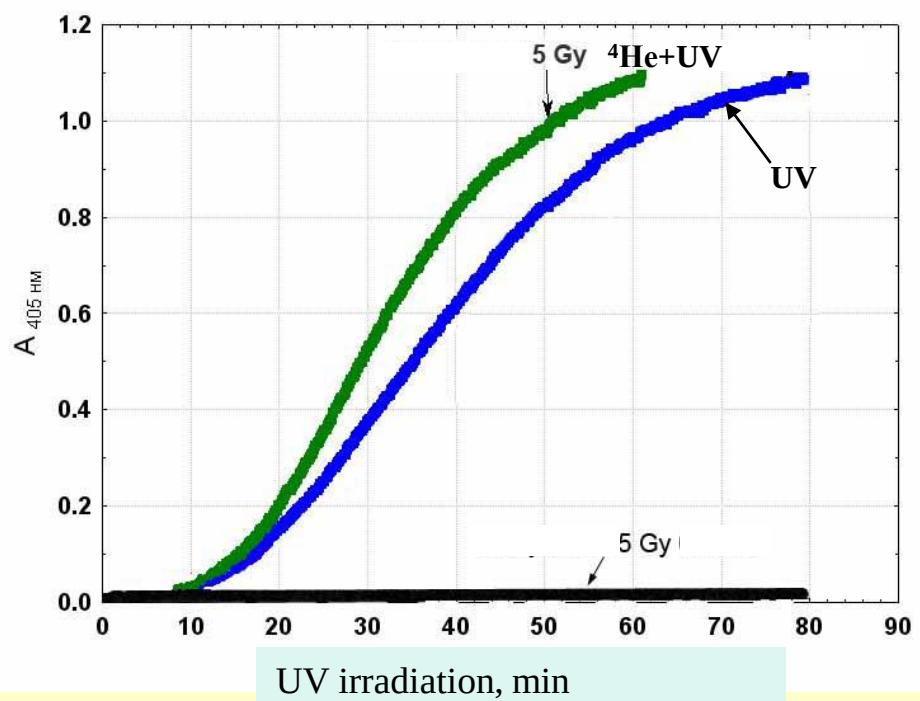




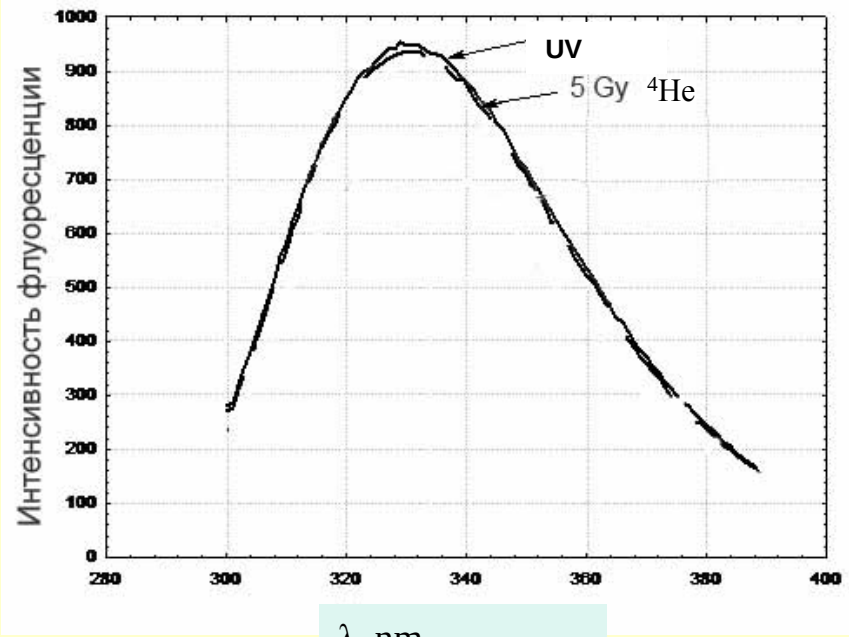
Worgul et al., 2006

Latent damages of β_L-crystalline after irradiation by He ions and UV irradiation

UV aggregation of β_L-crystalline after irradiation by He ions (30 MeV)

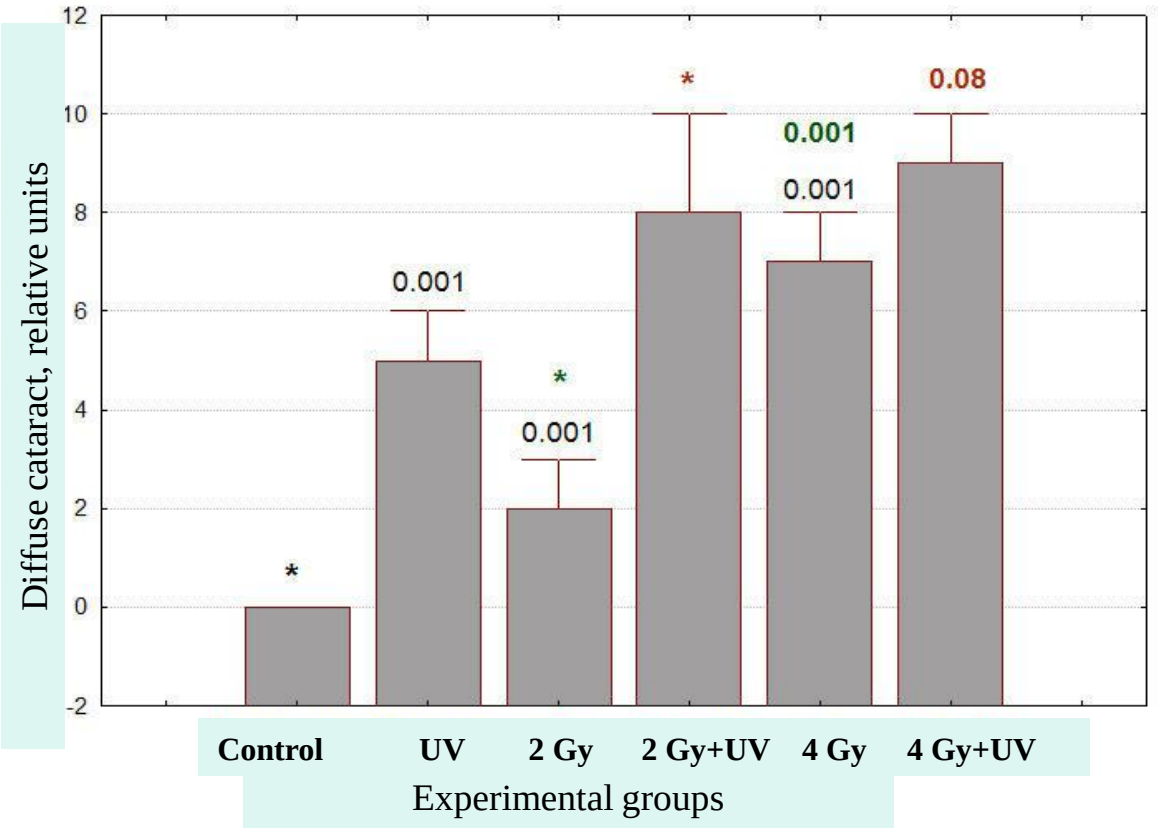


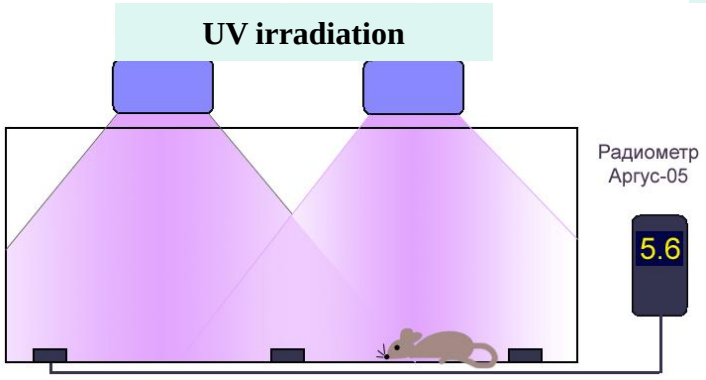
Spectrum of β_L-crystalline fluorescence after irradiation by He ions (30 MeV)



Diffuse opacification of lens in mice

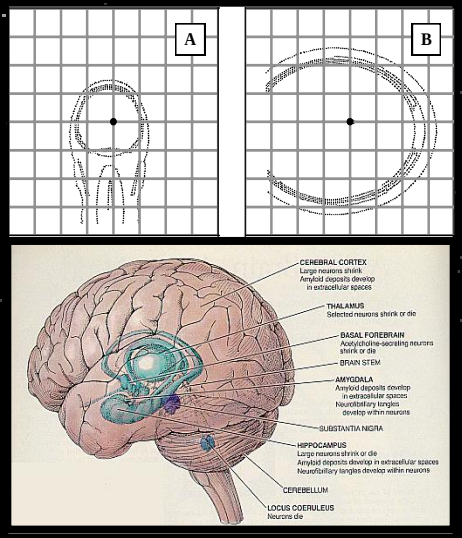
in vivo





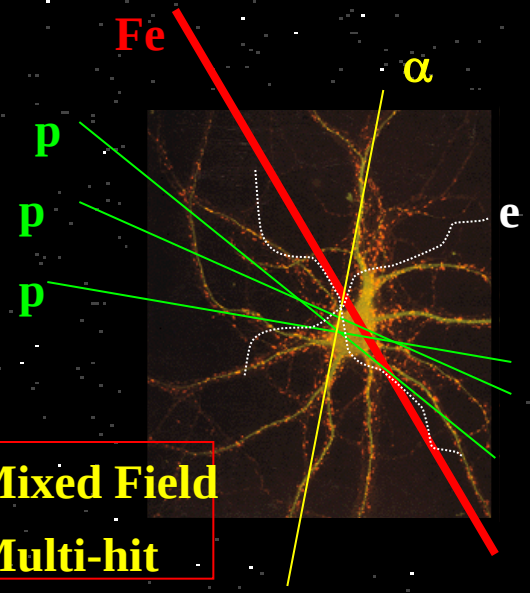
Accelerated heavy ions and CNS

Cosmic ray hit frequencies in CNS critical areas



CNS in General

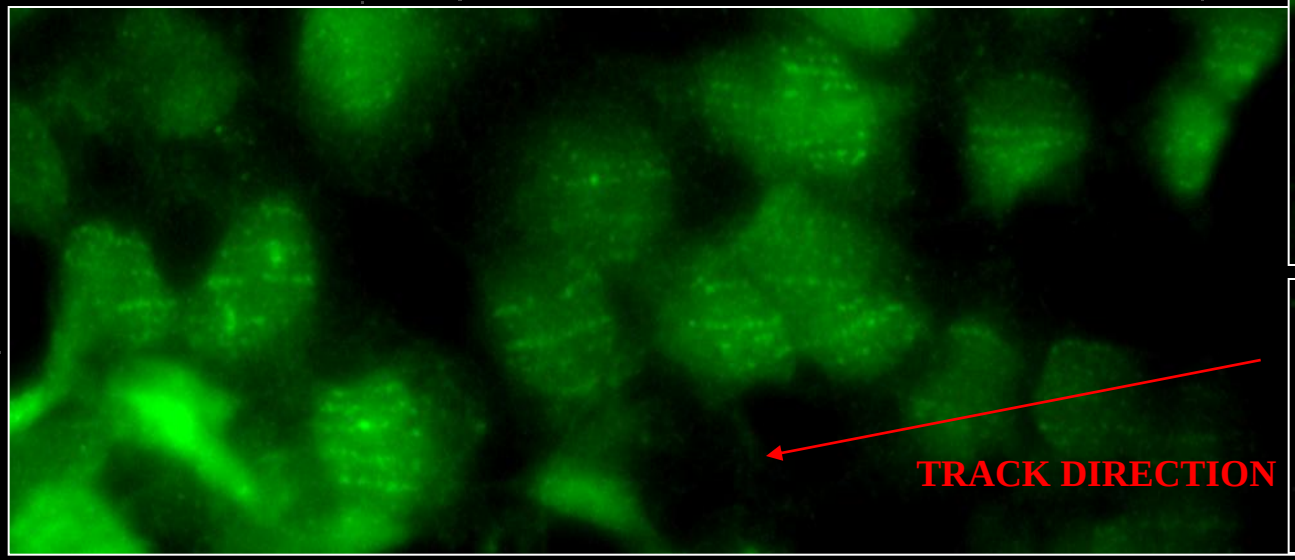
- 2 or 13% cells will be hit at least one Fe particle
- 8 or 46% would be hit by at least one particle with Z≥15
- Every nucleus will be traversed by a proton once every 3 days and a alpha particle once every 30 days.

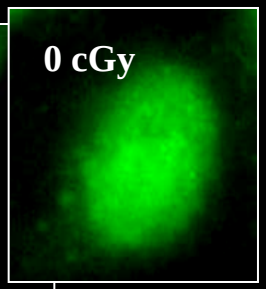


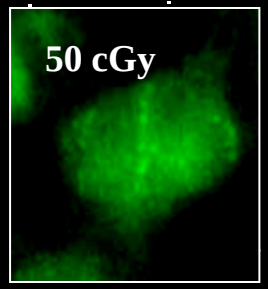
Mixed Field

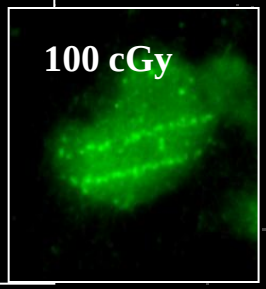
Multi-hit

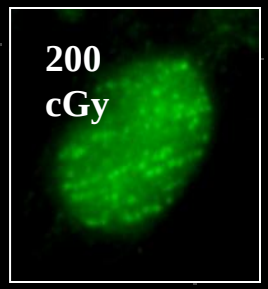
FE ION TRACKS VISUALIZED BY MARKERS OF DNA DSBs (γH2AX)



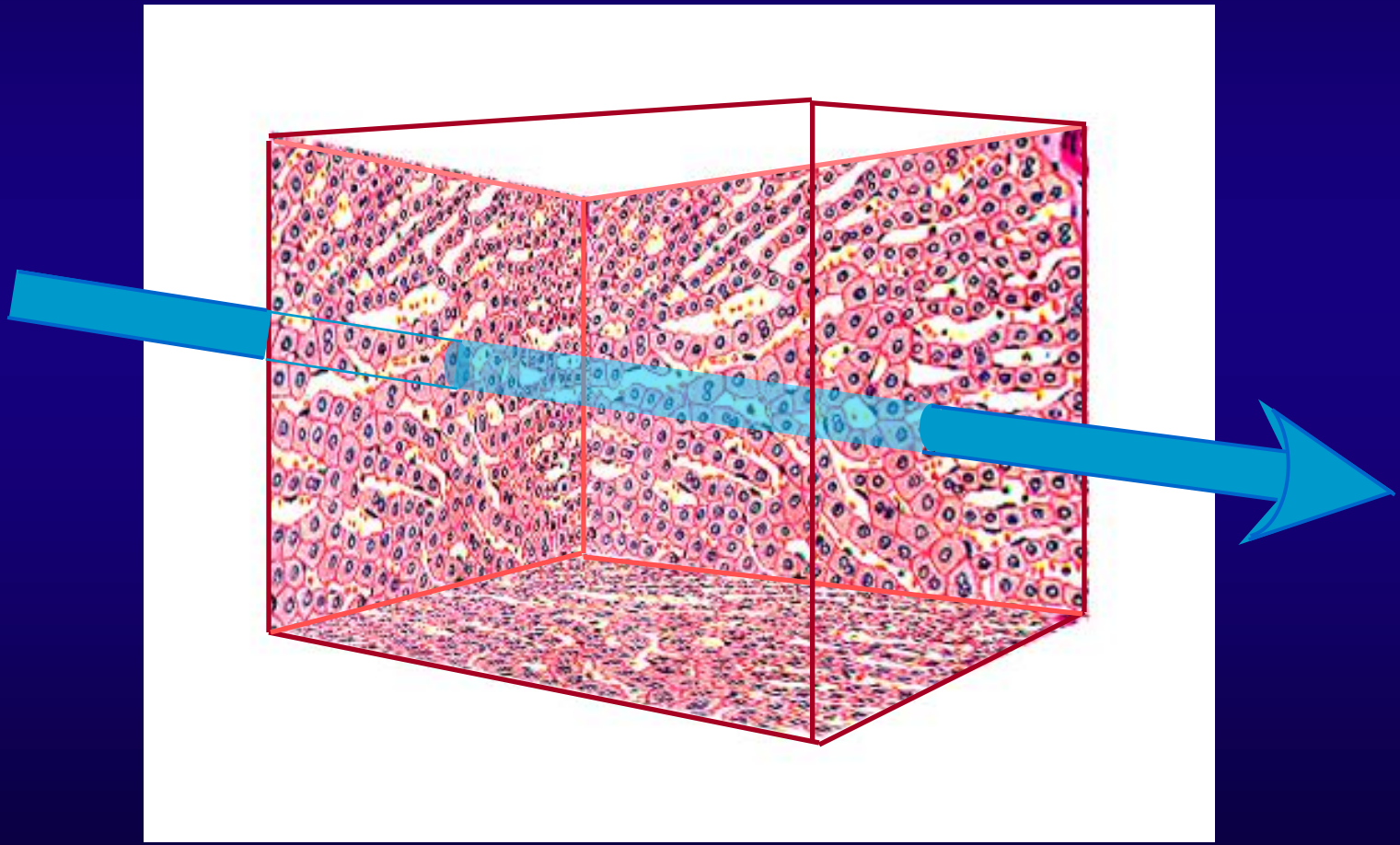




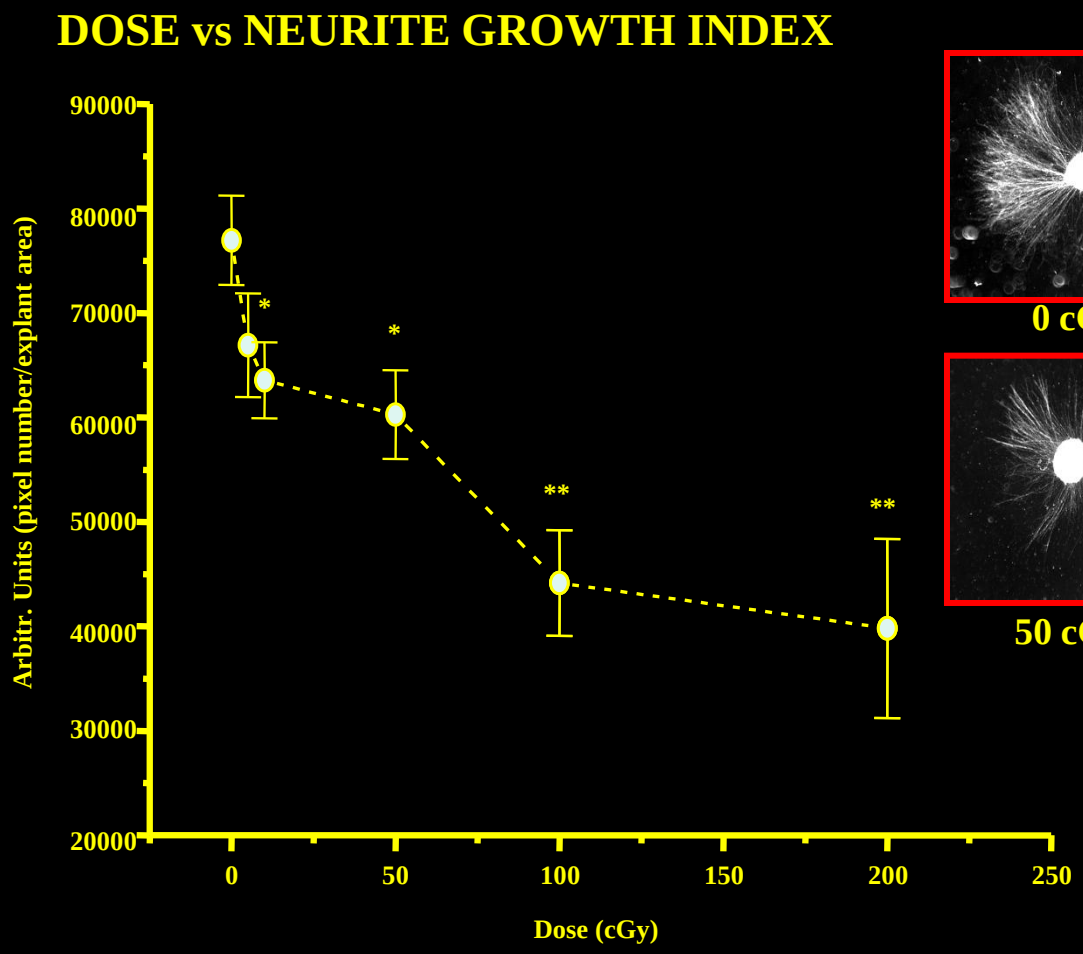


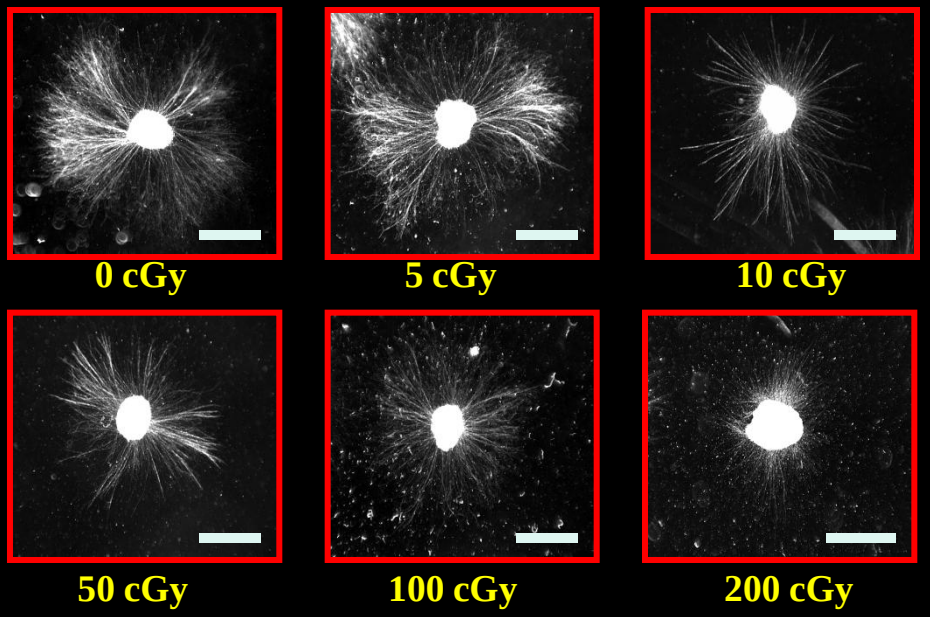


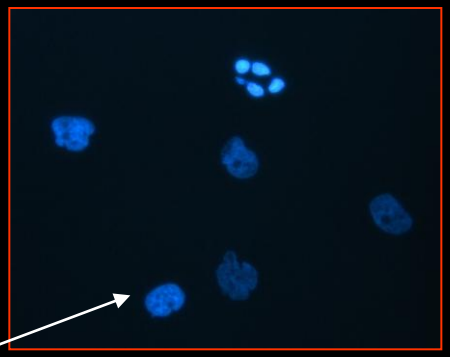
Damages of large number cells in tissue by the single track of heavy ion



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

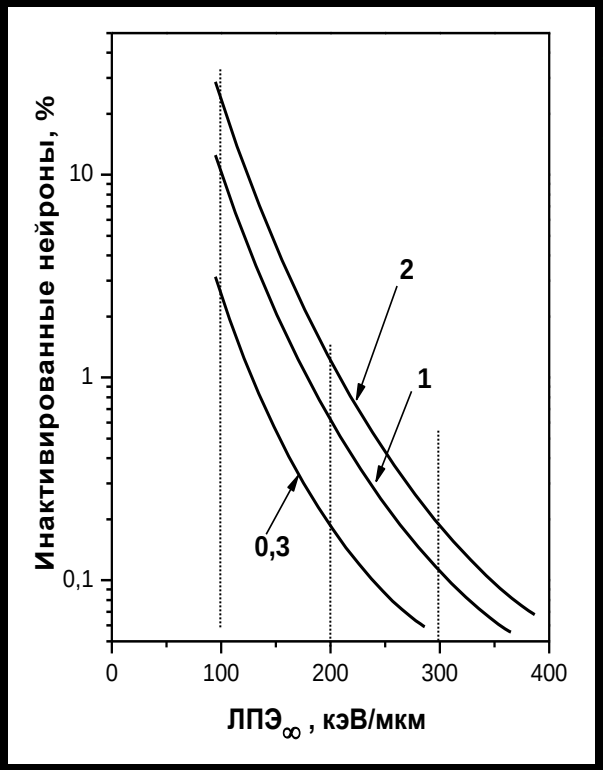




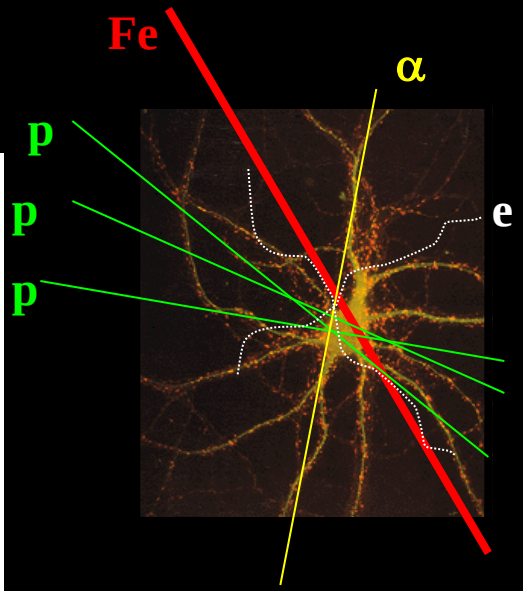


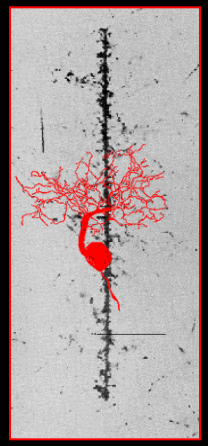
apoptosis

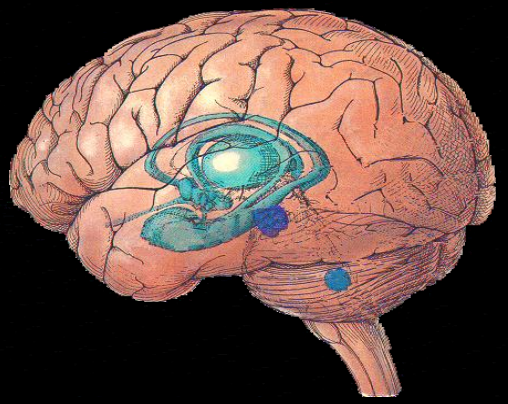
Vazquez, 2006

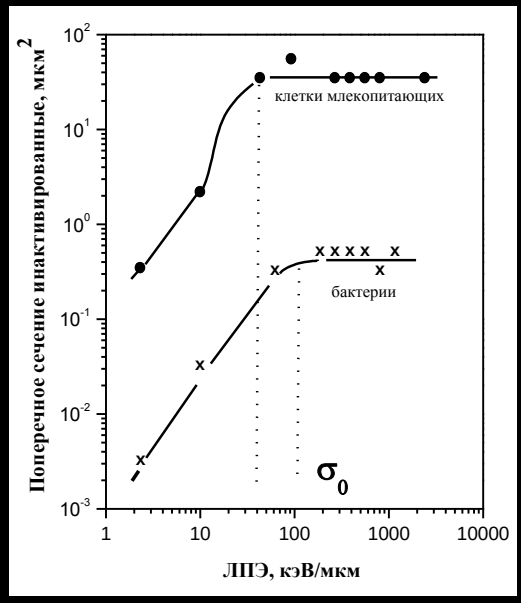


Количество инактивированных нейронов с r = 10 мкм в зависимости от пороговых значений ЛПЭ частиц при различной продолжительности полёта (0,3; 1 и 2 года)

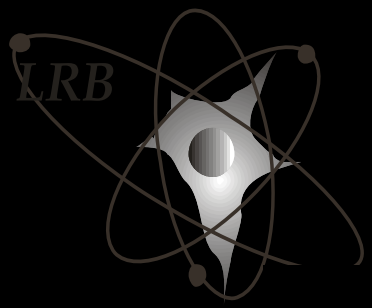








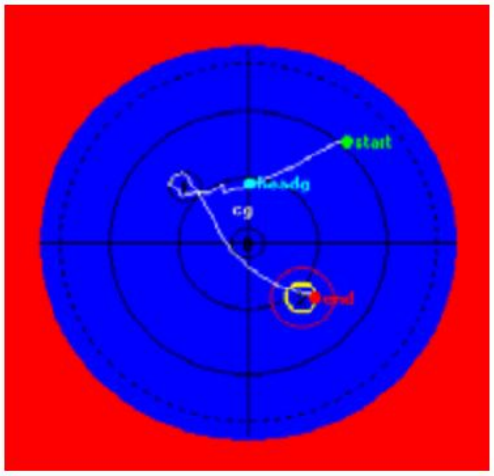
Зависимость поперечного сечения инактивации клеток млекопитающих и бактерий E.coli от ЛПЭ ускоренных тяжелых ионов



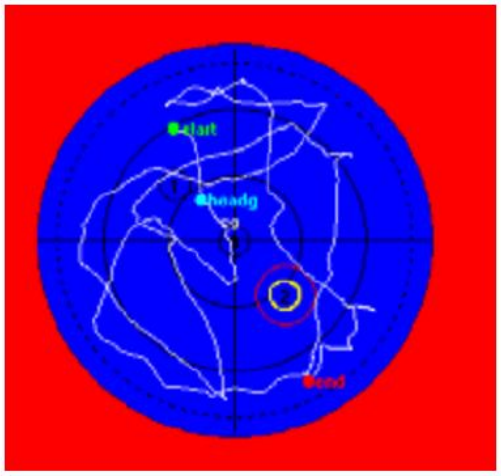
LABORATORY OF RADIATION BIOLOGY

^{56}Fe ions, 1 GeV/amu

Control



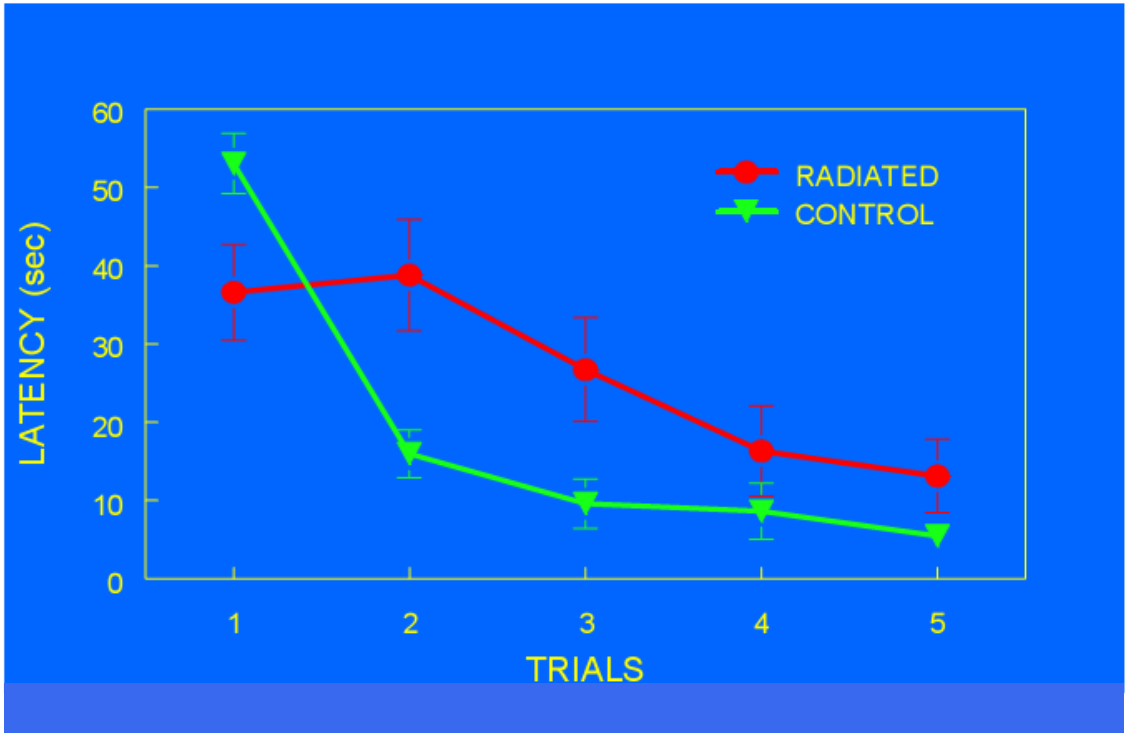
1.5 Gy



Cognitive tests

(Morris Water Maze: DAY 4, REVERSAL)

1 month after irradiation



Thank you for the attention!