Radiation Damage in Yeast *Saccharomyces cerevisiae* Physiological Environment

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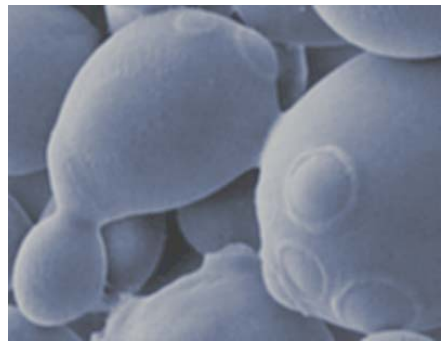
Yeast - unicellular model microorganism:

- high growth and reproduction rates
- many similarities with higher eukaryotic cells
- simple and well characterized genome
- easy to manipulate

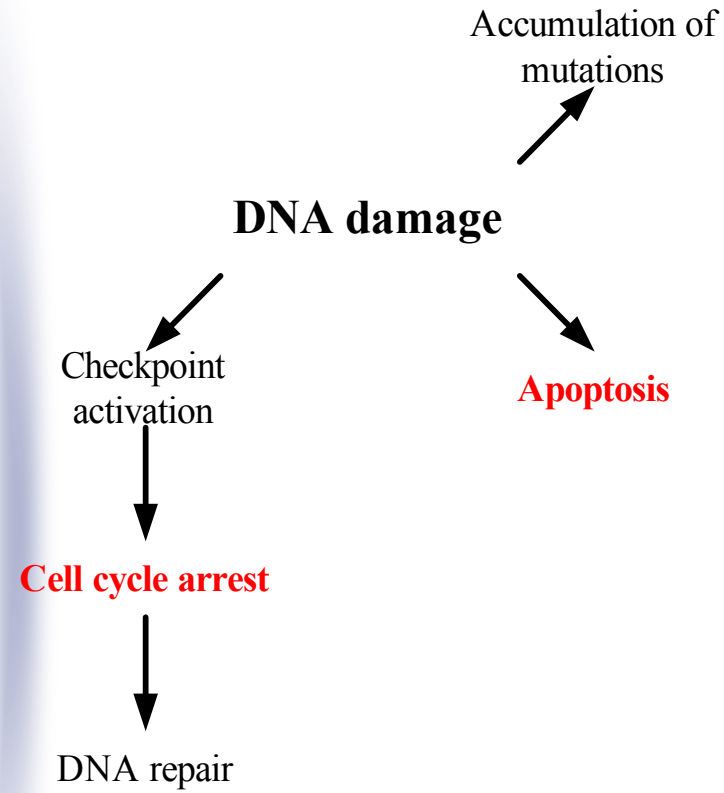


Sensitivity to radiation:

Low dose effects at 0.1 - 2Gy.

High dose – up to 800Gy.

Processes after the DNA damage



- **Apoptosis** – programmed cell death
- Propagation and accumulation of **mutations**
- DNA repair mechanisms through the **checkpoint pathways activation**

Level of resistance to various stresses correlates with the RAS/cAMP pathway activity.

Adaptive response could be caused by the misfolded proteins – prions: yeast strains growth on acid media showed apoptosis, while induction of prions prevent apoptosis.

Objectives of investigations

Modelling:

✓ Irradiation source optimization and received dose estimation.

✓ Modeling of final yeast response according to the damage and repair mechanisms.

Experiments:

✓ Determination of the cell cycle stages responsive to DNA repair checkpoint activation and cell cycle arrest.

✓ Determination of the cell cycle stages at witch radiation triggers apoptosis.

✓ Investigation of the prion-proteins influence on radiation induced apoptosis in the cell.

EXPERIMENTS:
Exposing to ionizing radiation (γ, X-ray and UV).

Stages of experiment:

- Irradiation of the cells at appropriate points of the cell cycle.
- Yeast cell population synchronization at particular stages of the cell cycle (sensitive for radiation).
- Determination of the cell cycle progression by Flow Cytometry method.

Available radiation sources:

Electron accelerator (E = 21 MeV)

γ ^{60}Co (E = 1.173MeV, 1.332MeV, A = 1.9×10^{14}Bq)

γ ^{137}Cs (E = 661keV, A = 2.6×10^{12}Bq)

γ ^{57}Co (E = 0.661keV, 122keV, A = 3.7×10^{7}Bq)

X-ray (10 - 120 keV)

UV irradiation (290-100nm range) 253.7nm (performed experiments)

First experiment (previewed) - irradiation of synchronized yeast cells by ^{137}Cs γ rays.

SIMULATION MODEL: Radiation - yeast cell response

MCNPX code:

- Monte Carlo N particle transport code.
- Exact irradiation geometry description - exact estimation of deposited ionizing radiation dose.

$$D\ [MeV/g] \times 1.602 \times 10^{-10} = D\ [Gy]$$

- Radiation source optimization for specific yeast cell part (surface or nucleus) in case of α particles.
- *Convertation of irradiation energy (and type) using different (W, Ta, Cu or Pb) plates.*

Virtual Cell (VC) Radiobiology Software (by R.D. Stewart, PNNL-13579. Version 1.10J):

- Monte Carlo methods are used for nucleotide excision repair of DNA (SSB, DSB) damage.
- Simulations are based on survival data as a function of dose.
- Evaluation of dose - yeast response effects.
- Comparison of simulation results with experimental results.

Main instruments and facilities that might compliment COST Action P9 RADAM and WG3:

- UV irradiation facility (Vilnius University)
- Irradiation by ^{60}Co γ rays (Oncology center in Lithuania)
- Linear electron accelerator (Oncology center)
- ^{57}Co γ source for low dose irradiation (Institute of Physics)
- X-ray tube (Vilnius University)
- Laboratory of yeast controlling parameters investigation (alterations in cell division, cell growth and evolution, Vilnius University).
- DNA analysis by flow cytometer (Immunology Institute)
- Gas Isotope Ratio Mass Spectrometer with chromatograph (Institute of Physics, expected on second half of 2004)

Thank YOU !