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Exploiting Cancer Vulnerability by Targeting the  
DNA Damage Response  
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cancers MDPI

# Gamma Radiation Induces Apoptosis by Over Expression of PERP Effector of p53-dependent Cell Death in HeLa Cells.

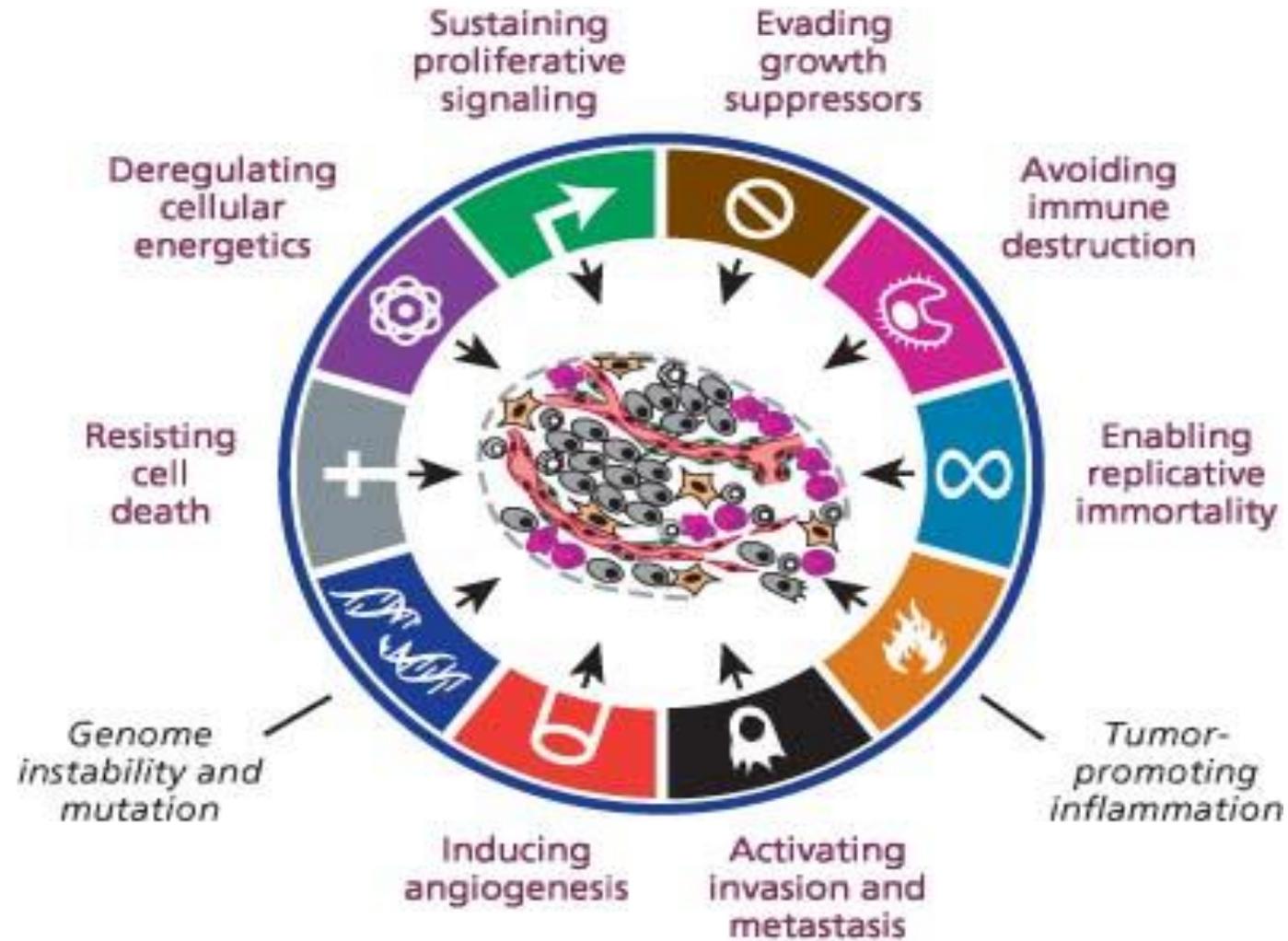
**Dr. Walid KHALILIA**

**Al- Istiqlal University- Palestine , 2021**

# Introduction

- GR, leads to a variety of cellular damages.
- Which leads to a network of signal transduction pathways involved in cell cycle arrest, DNA repair and Apoptosis.
- Apoptosis is the major mode of programmed cell death, and is characterized by a series of morphological hallmarks, including cell shrinkage, DNA condensation and fragmentation, followed by the formation of apoptotic bodies.
- Ionized radiation leads to a modulation of the expression of many genes. PERP induces apoptosis when it is overexpressed.

# Introduction



The Hallmarks of Cancer

# Purpose

- To determine the expressing of genes in response to GR processing.
- Novel treatment strategy to increase the cancer cell sensitivity to radiotherapy by modulation of the PERP expression could be developed.

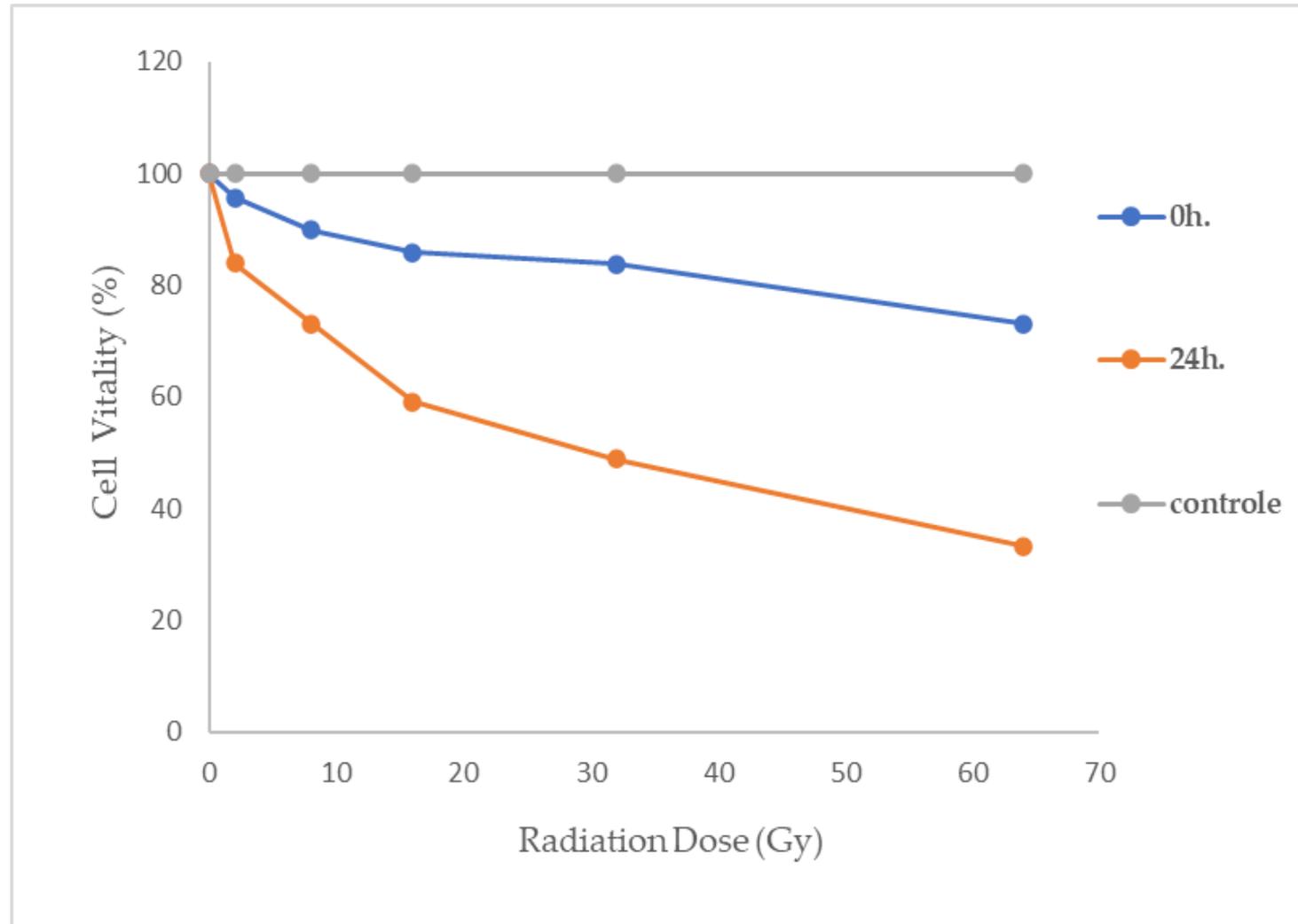
# Methodology

- HeLa cells were exposed to **GR**.
- **Proliferation** of cells were investigated by **MTT assay**.
- **Apoptotic Index (AI)** and morphological features were assessed by **fluorescent microscopy**.
- Gene expression was evaluated using **micro-array** technology, followed by **signalling pathway** analysis.

# Key Findings

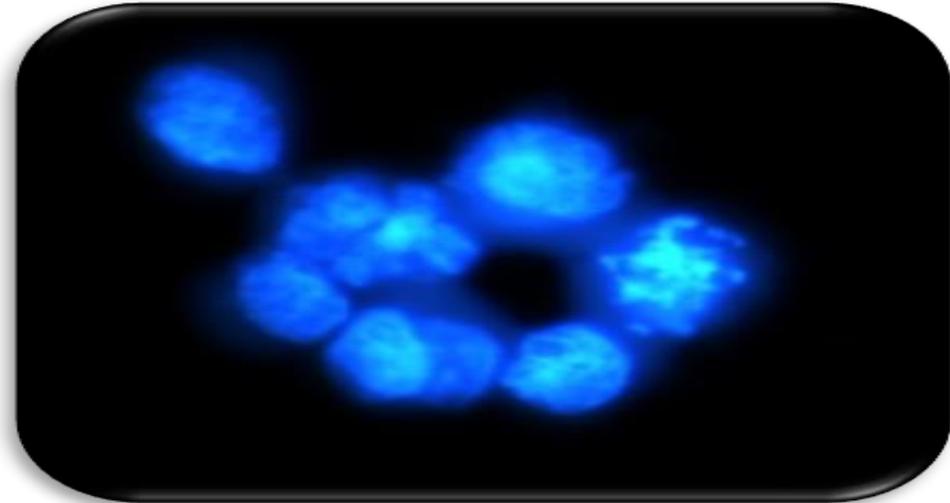
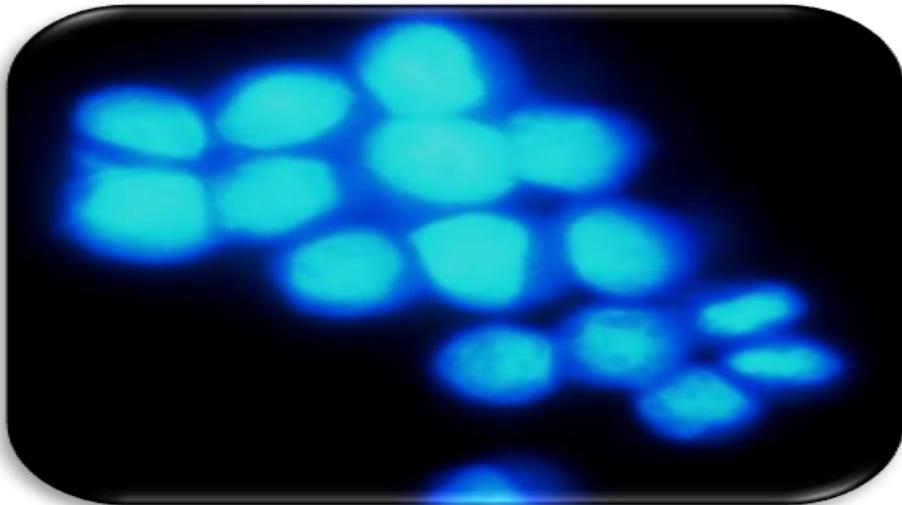
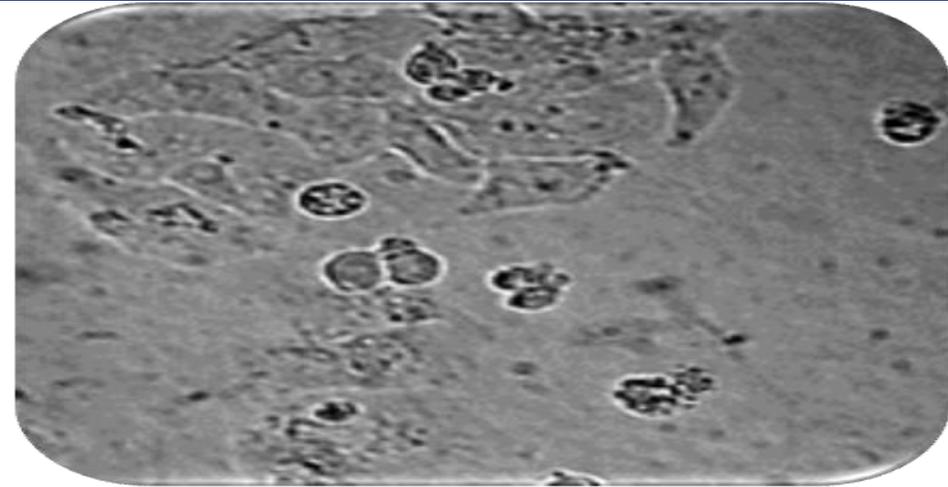
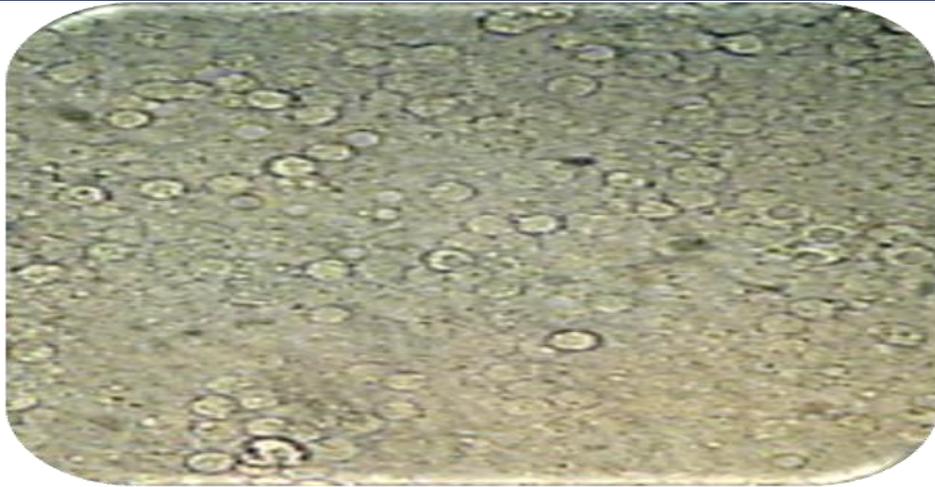
- ✓ GR inhibits proliferation of HeLa cells in a time- and dose- dependent manner.
- ✓ GR induced apoptosis of HeLa cells in a time- and dose- dependent manner.
- ✓  $IC_{50}$  and AI dose for HeLa cells were 32 Gy.

# Key Findings



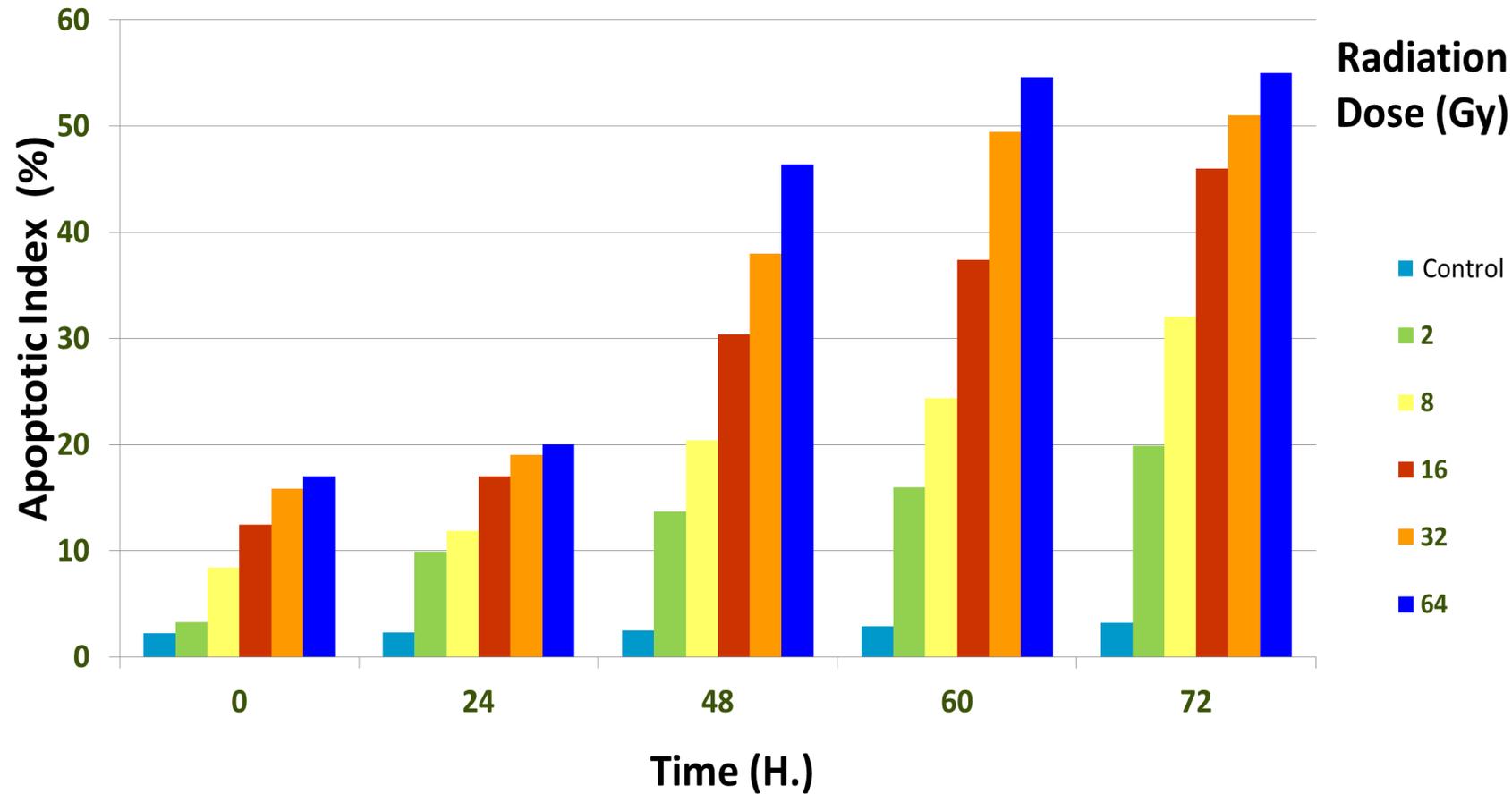
Effect of GR on HeLa cells survival at 0- and 24-hours post-irradiation time using MTT essay.

# Key Findings



Representative fluorescent images (X1000) of the nuclear morphology of HeLa cells in the control (left) and 32Gy irradiated groups at 48 hours post-irradiation time following DAPI staining; Description of control (left) and irradiated (right) HeLa cells appearance under the phase contrast microscope after 48 hours incubation (X100).

# Key Findings: AI

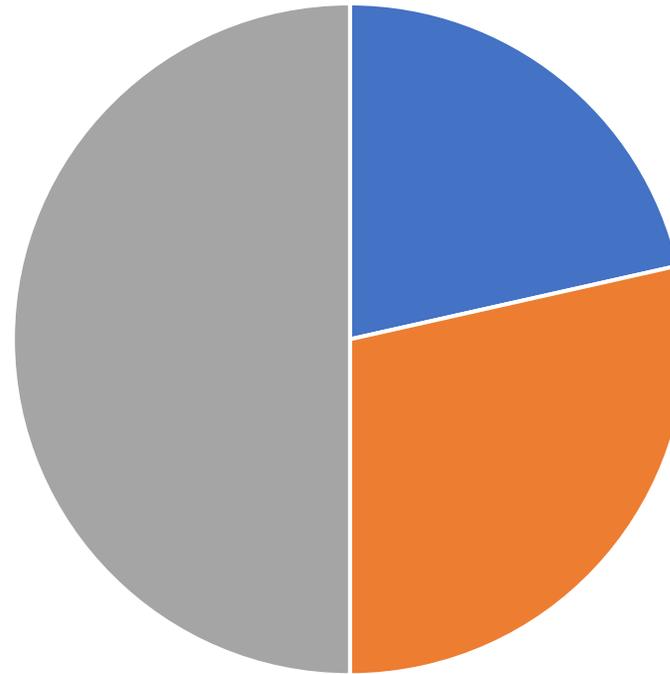


Measure of apoptotic index by counting 100 of HeLa cells in the control and all irradiated (2, 8, 16, 32 and 64 Gy) groups at 0, 24, 48, 60, and 72 hours post-irradiation time, following DAPI staining under fluorescence microscope ( $\times 1000$ ).

# Key Findings

Microarray results monitored the expression of some factors that are known apoptosis activators were up regulated by gamma radiation treatment, whereas some anti-apoptosis members were down regulated.

## Gene Expression



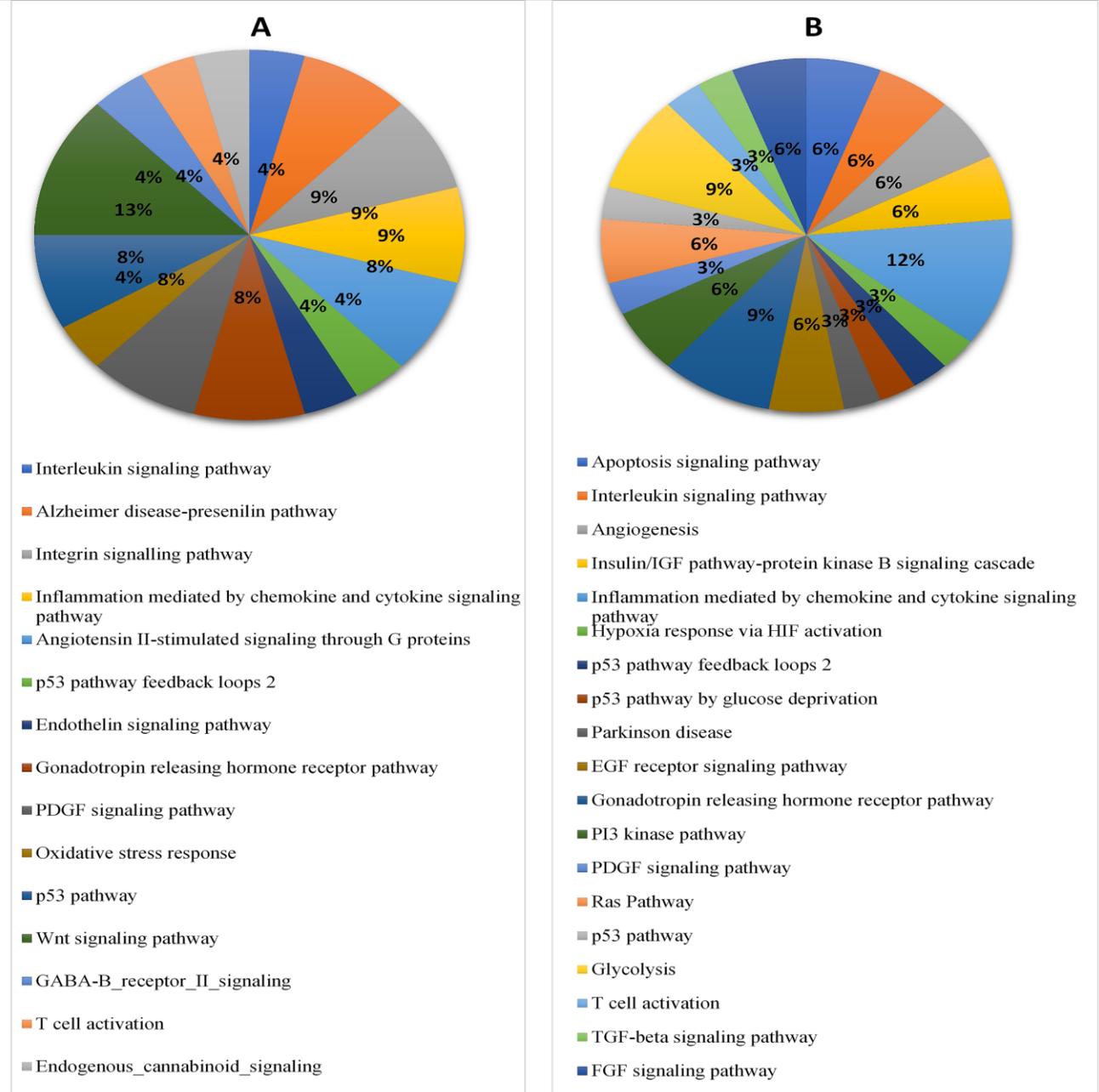
■ Up-regulated genes ■ Down-regulated genes ■ Total

mRNA levels of pro-apoptotic genes such as, PERP; BAX; CASP9; TRAF3 and other factors detected by microarray after treatment with gamma radiation were up-regulated. Whereas, many anti-apoptosis factors were down-regulated.

# Key Findings

## Pathway analysis

Pie charts showing pathways altered in **HeLa cells** at 48 hours after exposure to 32 Gy single dose of gamma radiation, as compared to control cells. Chart was generated from the microarray data analysis according to PANTHER pathway enrichment analysis. (A) Upregulated genes. While, (B) down-regulated genes.



# Conclusion

- Results of this study provide evidence that GR decreases survival of cervical carcinoma HeLa cells by altering the expression of some genes associated with cell proliferation and apoptosis.
- It was shown that PERP expression triggers the death of HeLa cells through the P53-dependent apoptotic pathway.
- Our study is a kind of screening rather than detailed research. We need further investigation to define these identified genes *in vitro* and *in vivo*.
- There is now a very large body of evidence supporting a role for membrane-induced apoptosis in the response to ionized radiation at least in some cells. The major challenges now are to clarify how these pathways progressing.



**THANK YOU ..**