

- **Chemical agents and radiation**



- **Stress to cells:**

ROS, charged particles, chemical modifications.

Damage to biomolecules (DNA/RNA, proteins etc)

- **Induction of protective stress responses**

- **Modifications of chromatin and DNA (epigenetics):**

Posttranslational modifications of proteins (PTM): phosphorylation, ubiquitylation, acetylation, methylation etc. (afterhigh/ low dose IR response). The induction of PTM's results in functional changes, activation or degradation of proteins.

Chromatin remodelling (4 classes remodelling enzyme complexes)

Chromatin remodelling by insertion of histone variants in chromatin

DNA methylation

- **PTMs exert effects on:** transcription, DNA repair, translation, noncoding DNA, apoptosis

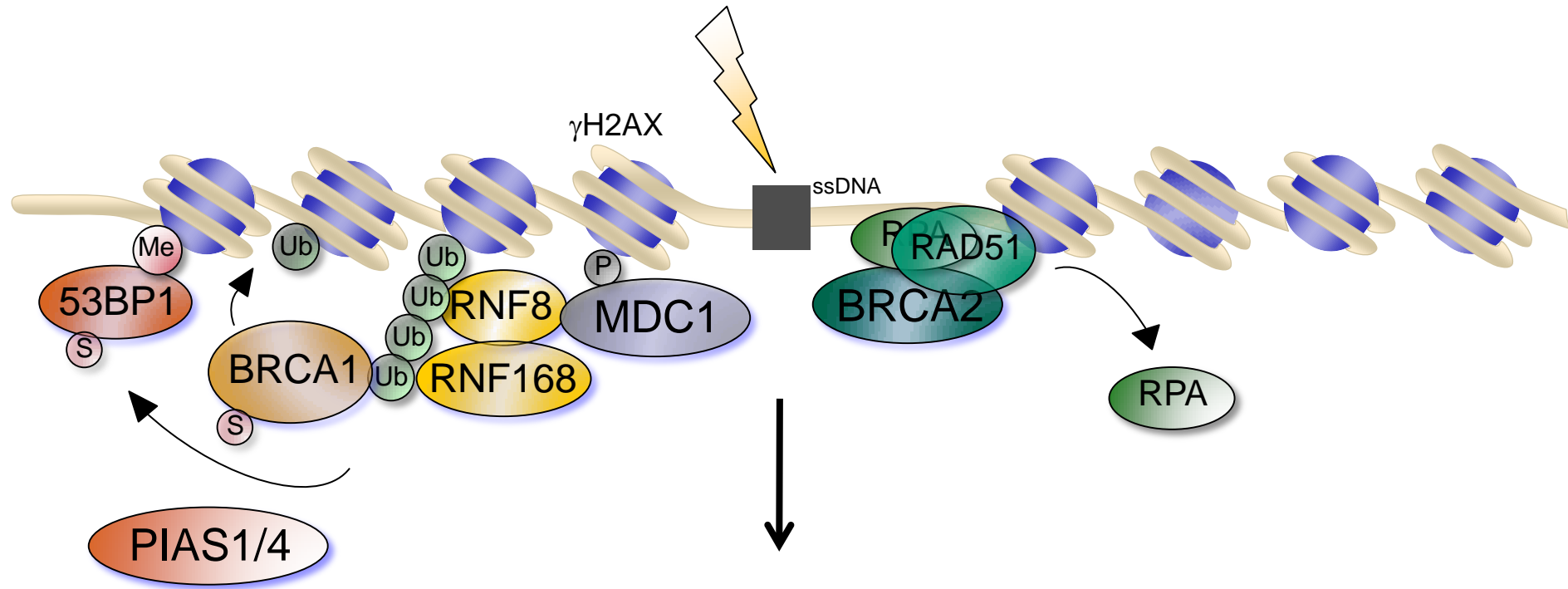
- **Alteration of transcription and modification of proteins:**

Silencing /overexpression of key factors in chromatin maintenance and methylation leading to radiosensitivity, repair defects and disease (cancer, development, progeria).

For example BRCA (breast cancer), ATM (cancer, neurological abnormalities)

CHROMATIN AND THE DSB RESPONSE

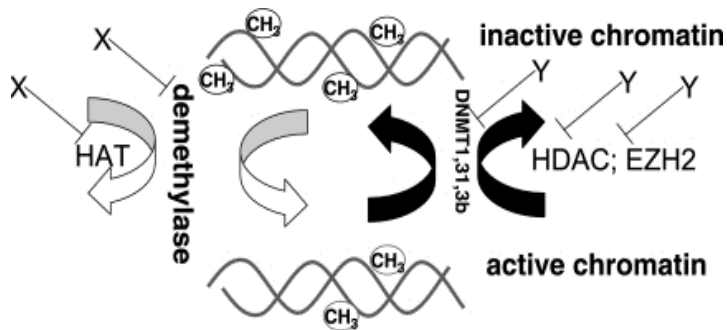
Double-strand break (DSB)



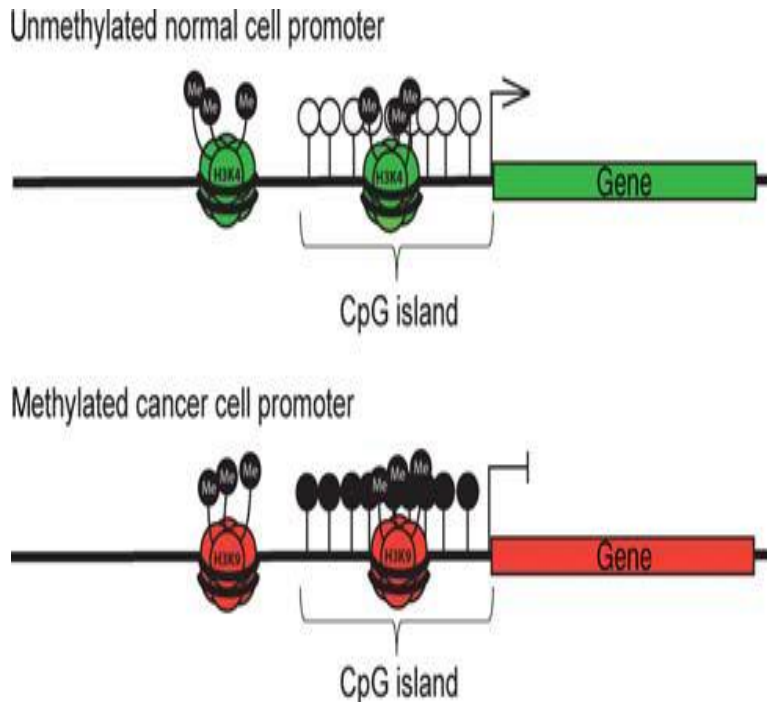
Cell cycle regulation and DSB repair

Legend: Repair of IR induced DNA double strand breaks requires many posttranslational modifications of chromatin proteins.

P= phosphorylation; Ubi=ubiquitylation; Me=methylation ;S=SUMOylation



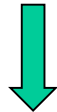
Legend: Chromatin structure alters DNA methylation



Legend: DNA methylation alters histone modifications

Unmethylated: Phospho H3 K4; Methylated: Phospho H3 K9

- **Chemical agents and radiation**
- **Stress to cells**
- **Induction of protective stress responses**
- **Modifications of chromatin and DNA (epigenetics) including posttranslational modification (PTM)**
- **PTMs exert effects on: transcription, DNA repair, translation, noncoding DNA, apoptosis**
- **Alteration of transcription and modification of proteins:**



Major impacts of defective epigenetical functions on Ionizing Radiation Response:

- **Defective DNA damage signaling after ionizing radiation**
- **Defective repair of DSB after ionizing radiation.**
- **Genome instability**