

# Lumiere Education

## Biochemistry: DNA, Proteins, and their Applications

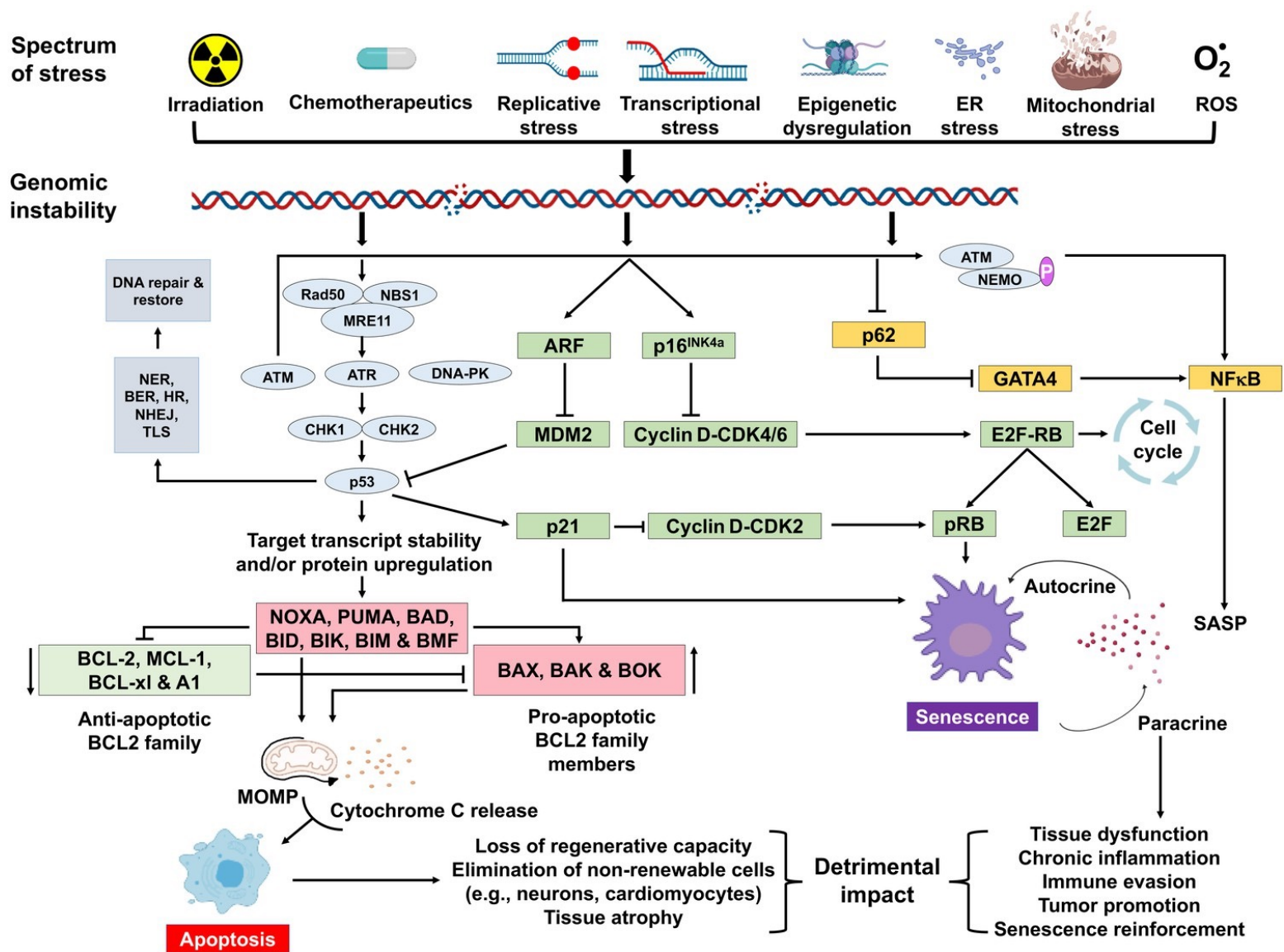
### Lecture 2

Proteins QC Continued & DNA Damage Response (DDR)

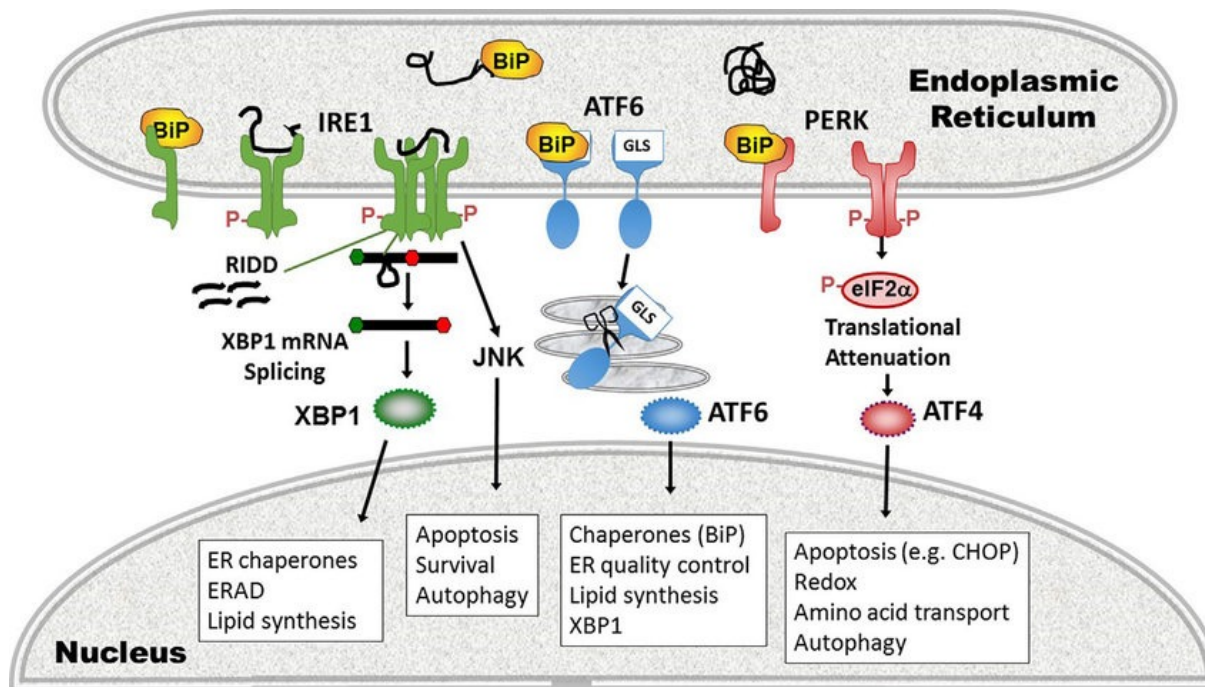
Ari Broad

Weill Institute for Cell and Molecular Biology (WICMB)

Cornell University

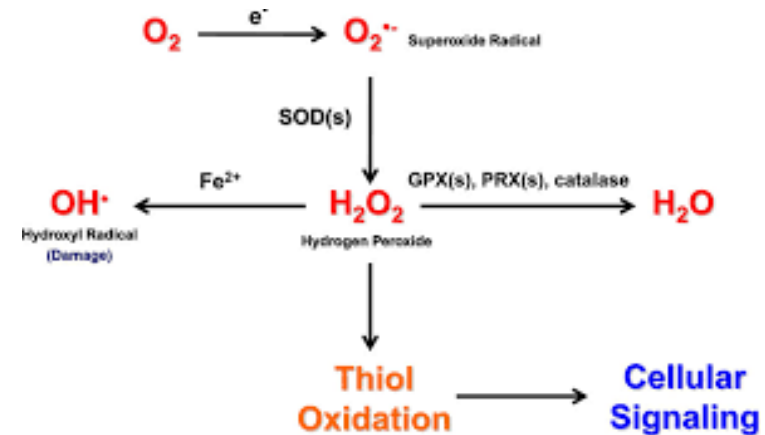


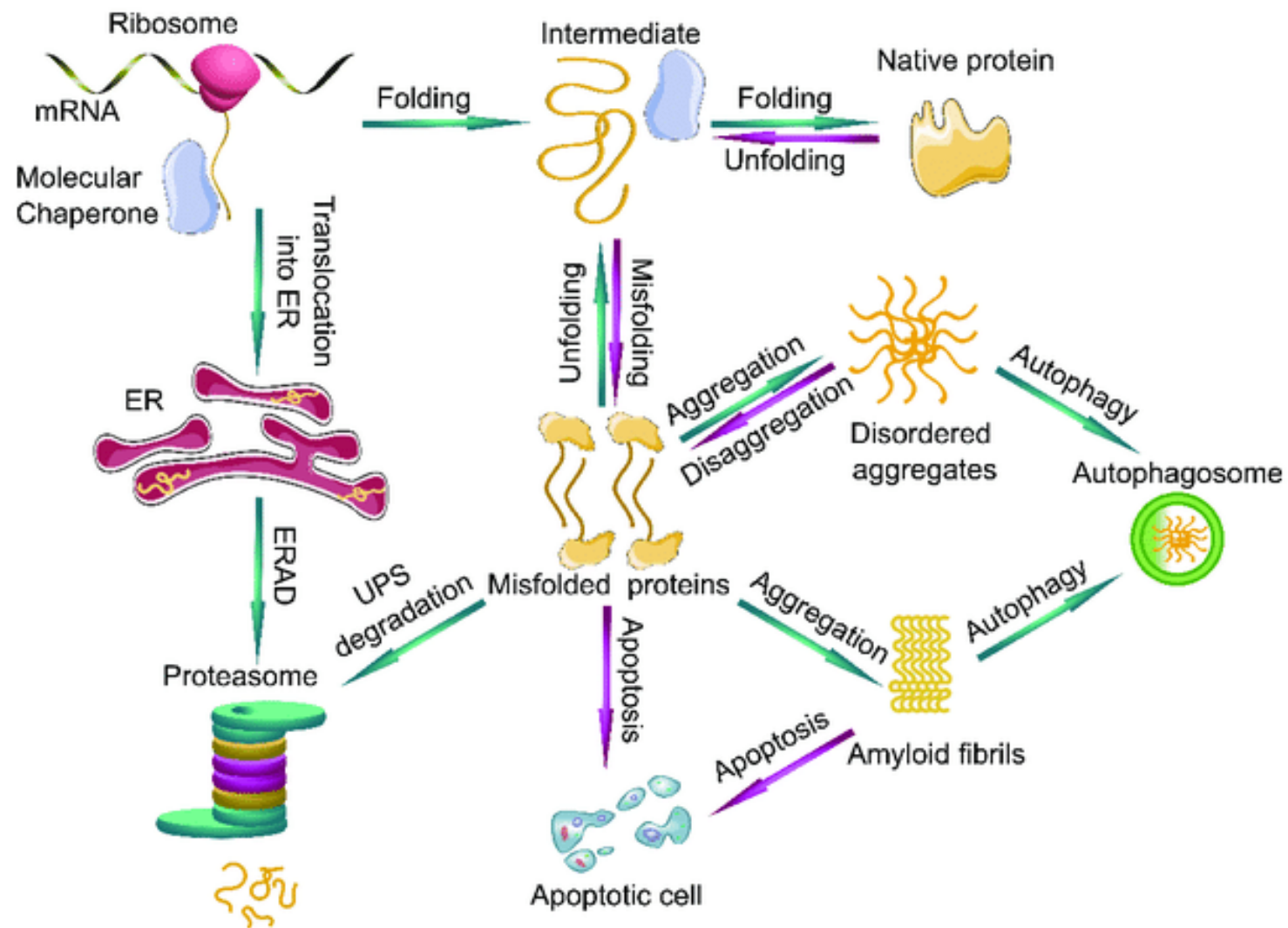
# Review of Protein Quality Control – aka Unfolded Protein Response



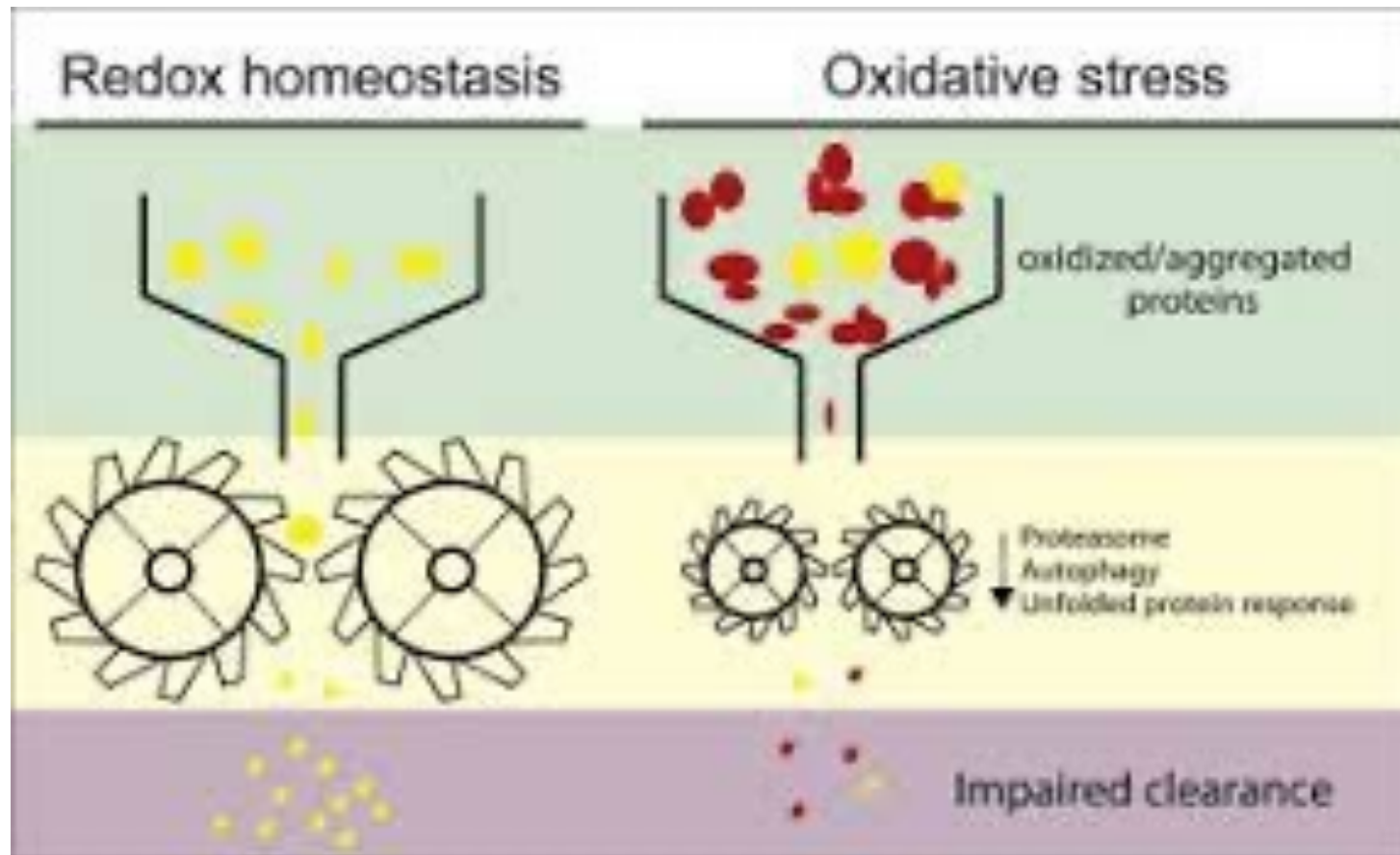
What can cause the UPR to be activated?

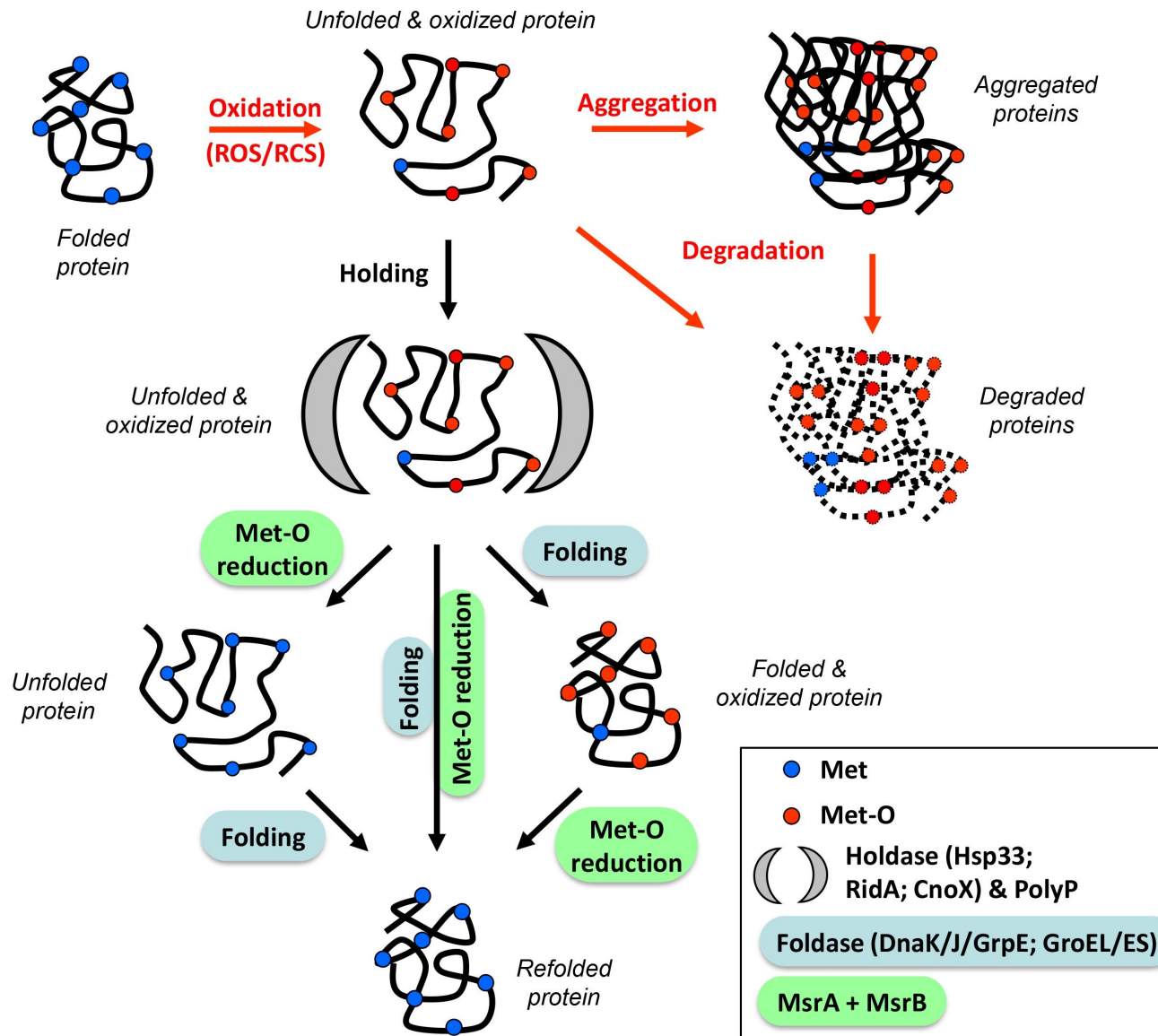
- Redox stress
- Osmotic stress
- Pathogen immune response





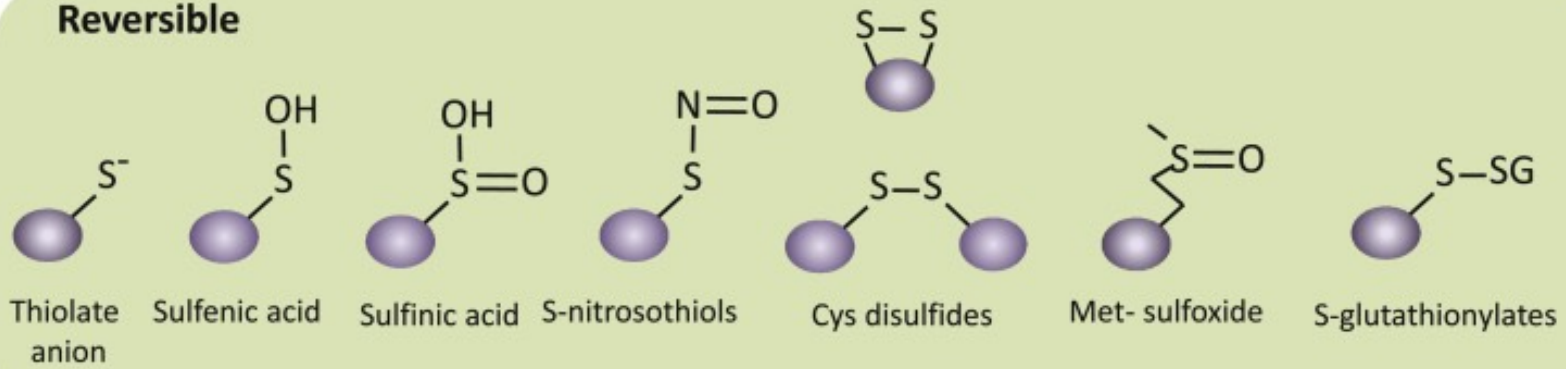
But how is the UPR activated?







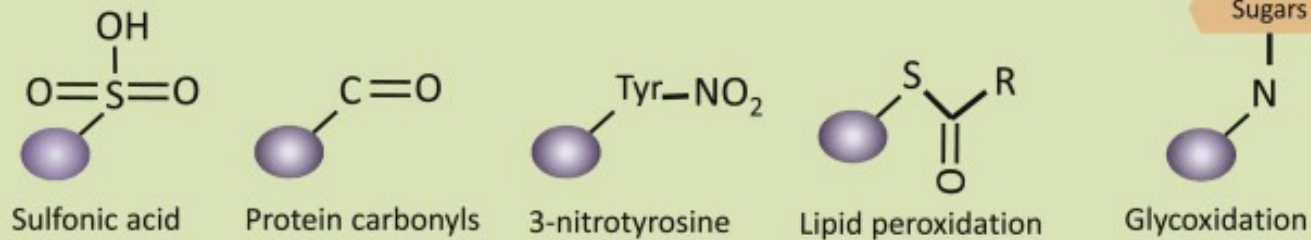
## Reversible



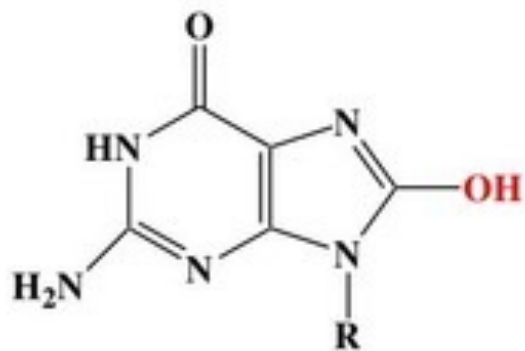
ROS  
RNS

Native  
Protein

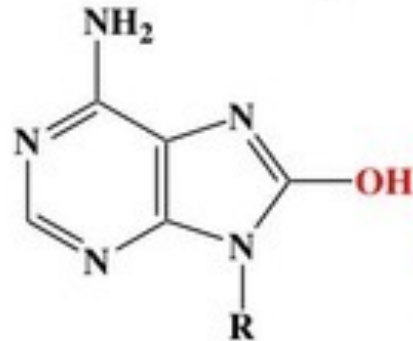
## Irreversible



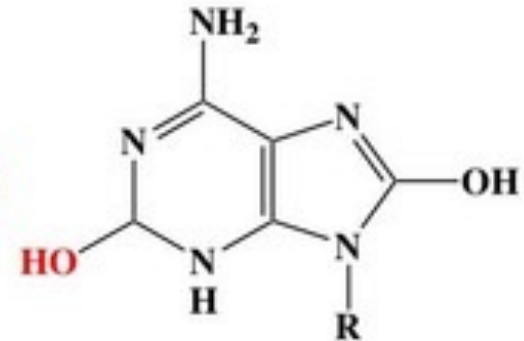
## DNA oxidation products



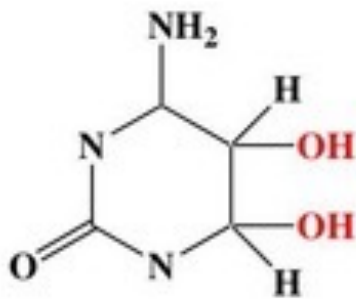
8-hydroxyguanine



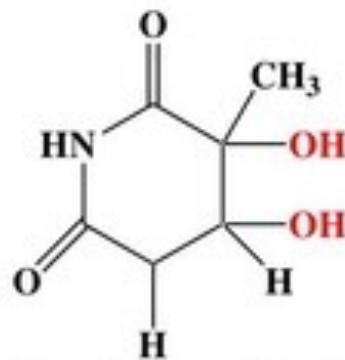
8-hydroxyadenine



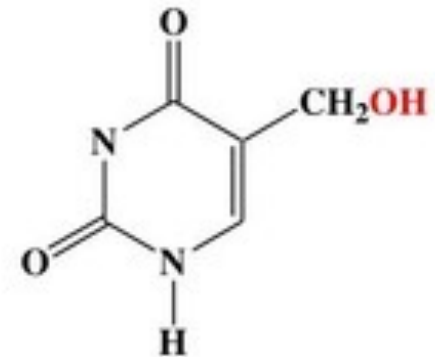
2-hydroxyadenine



5,8-dihydroxycytosine

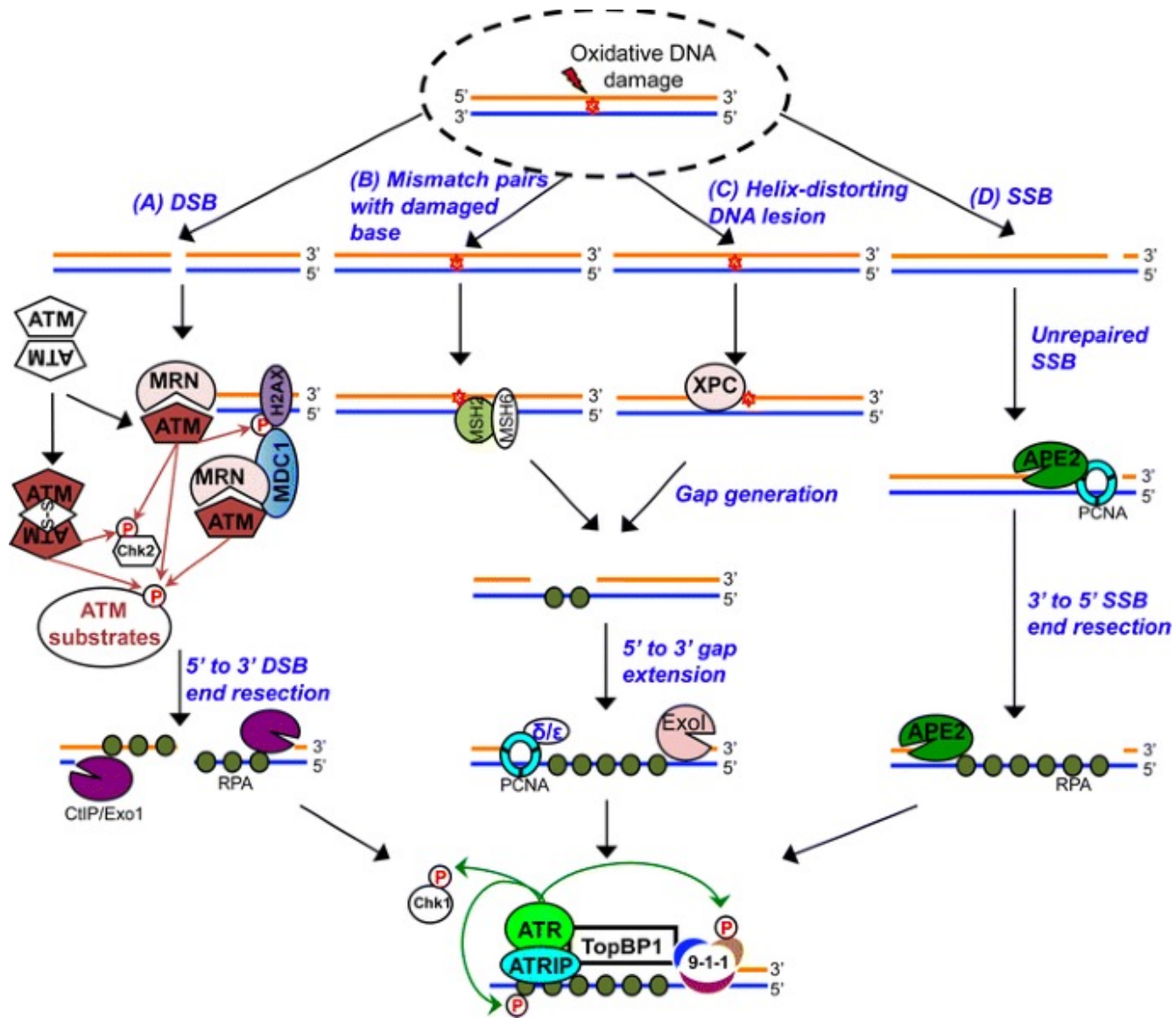


thymidine glycol

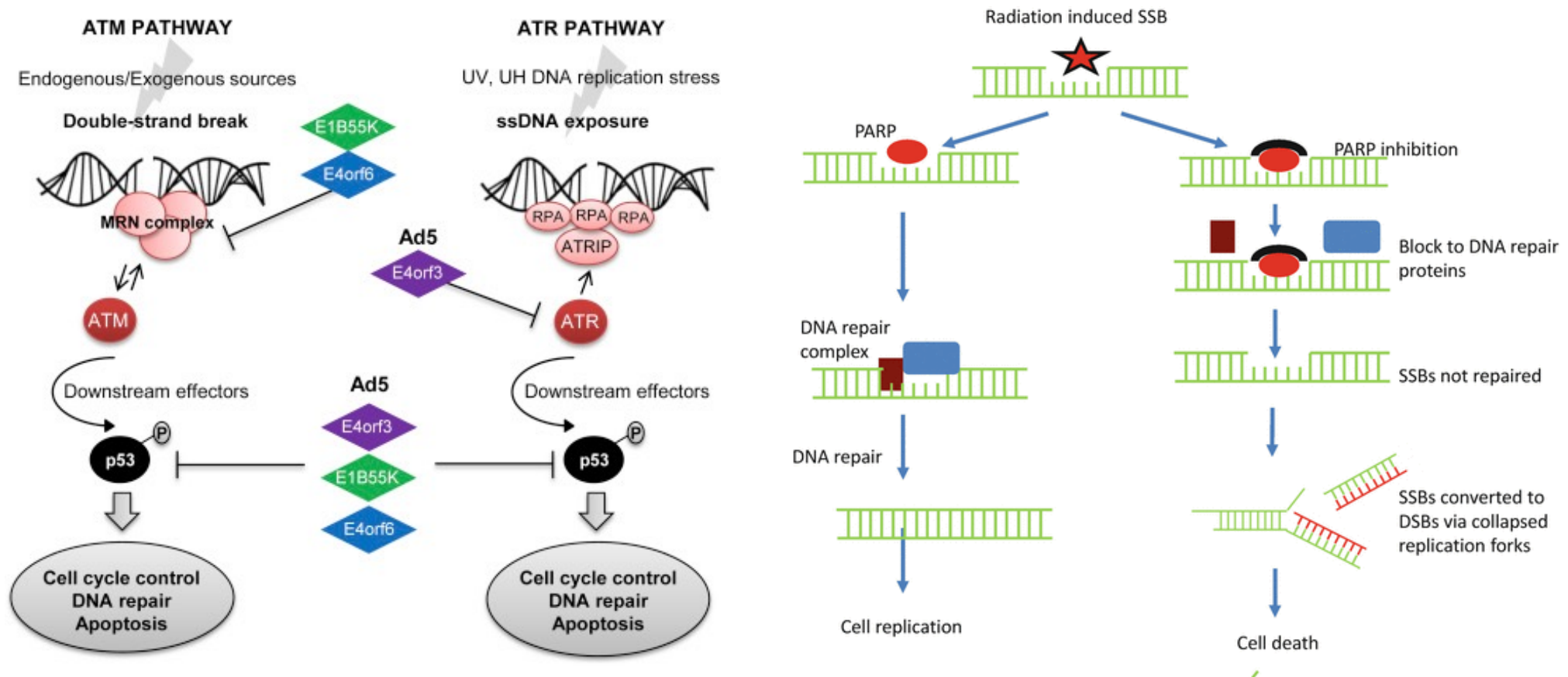


5-hydroxymethyluracil

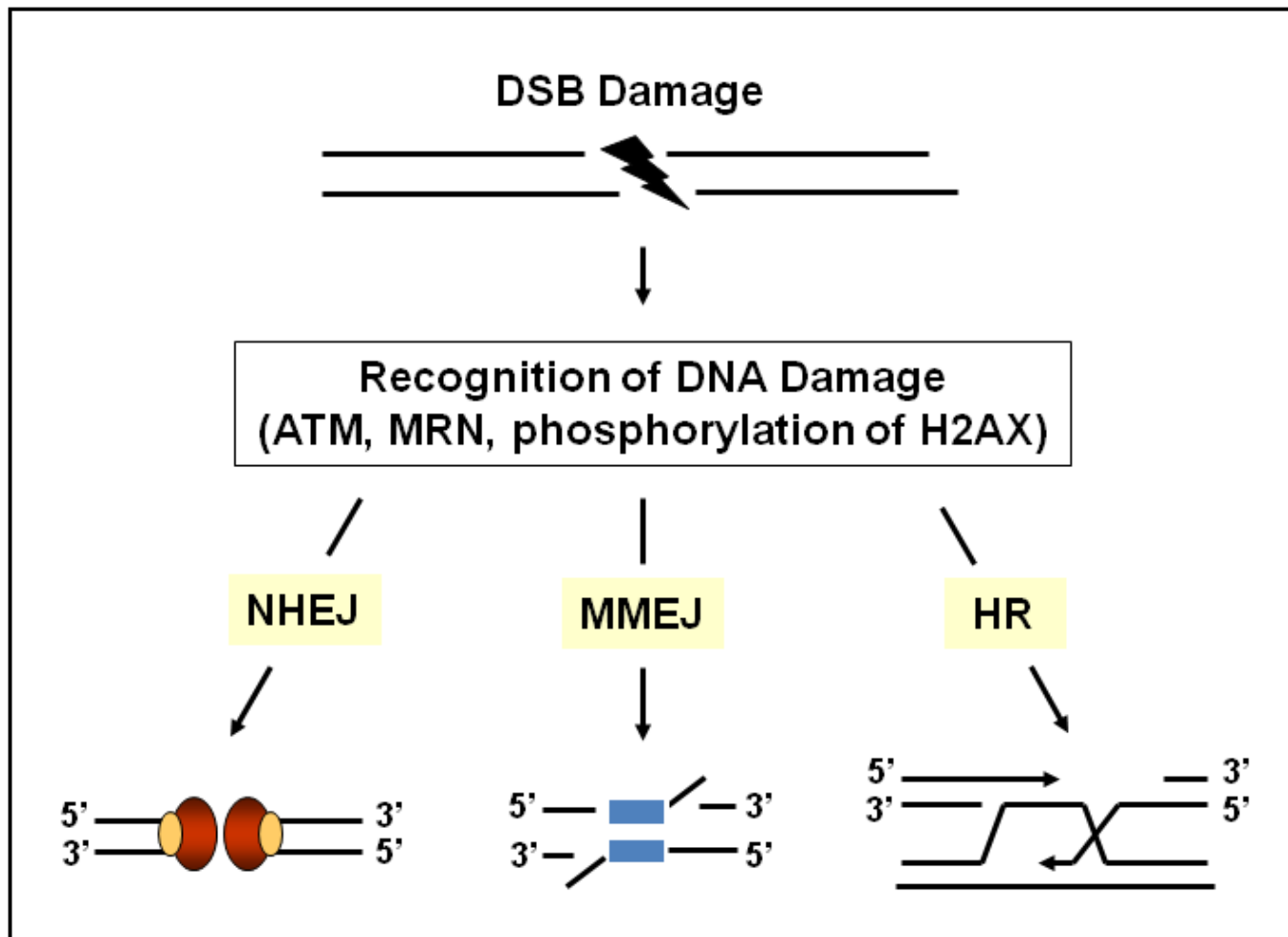




# DNA Damage Response vs DNA Damage Repair



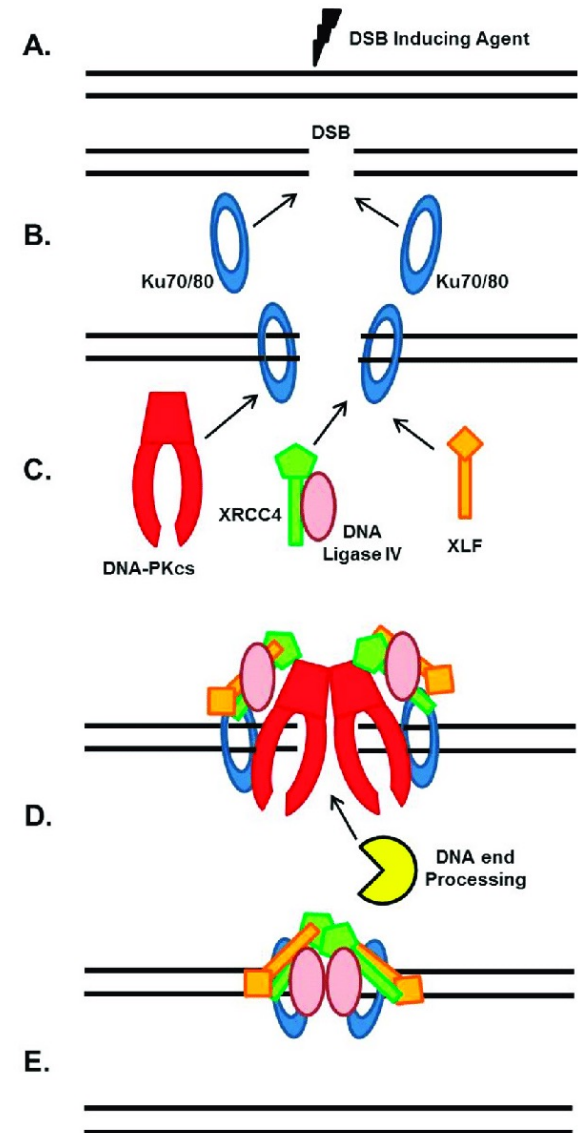
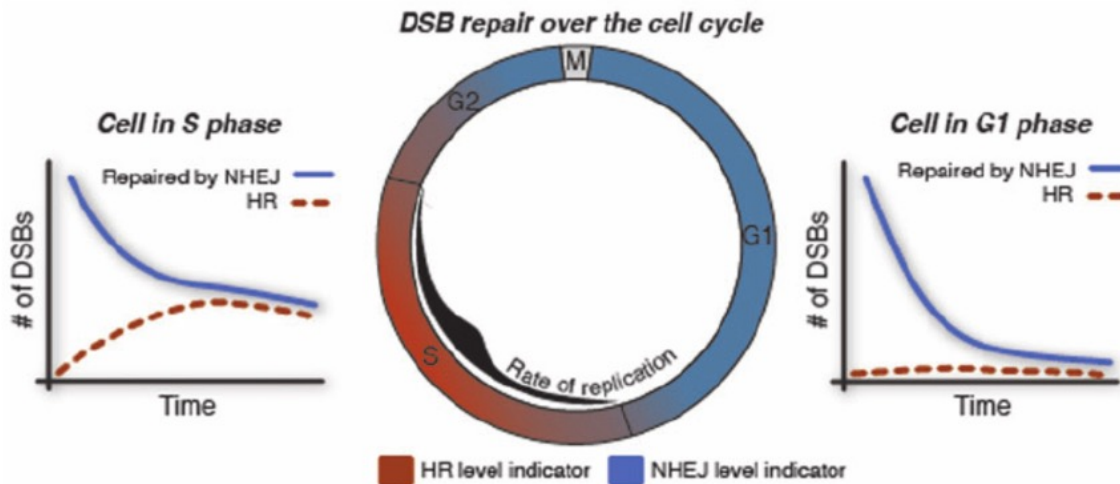
# DNA Damage Response vs DNA Damage Repair



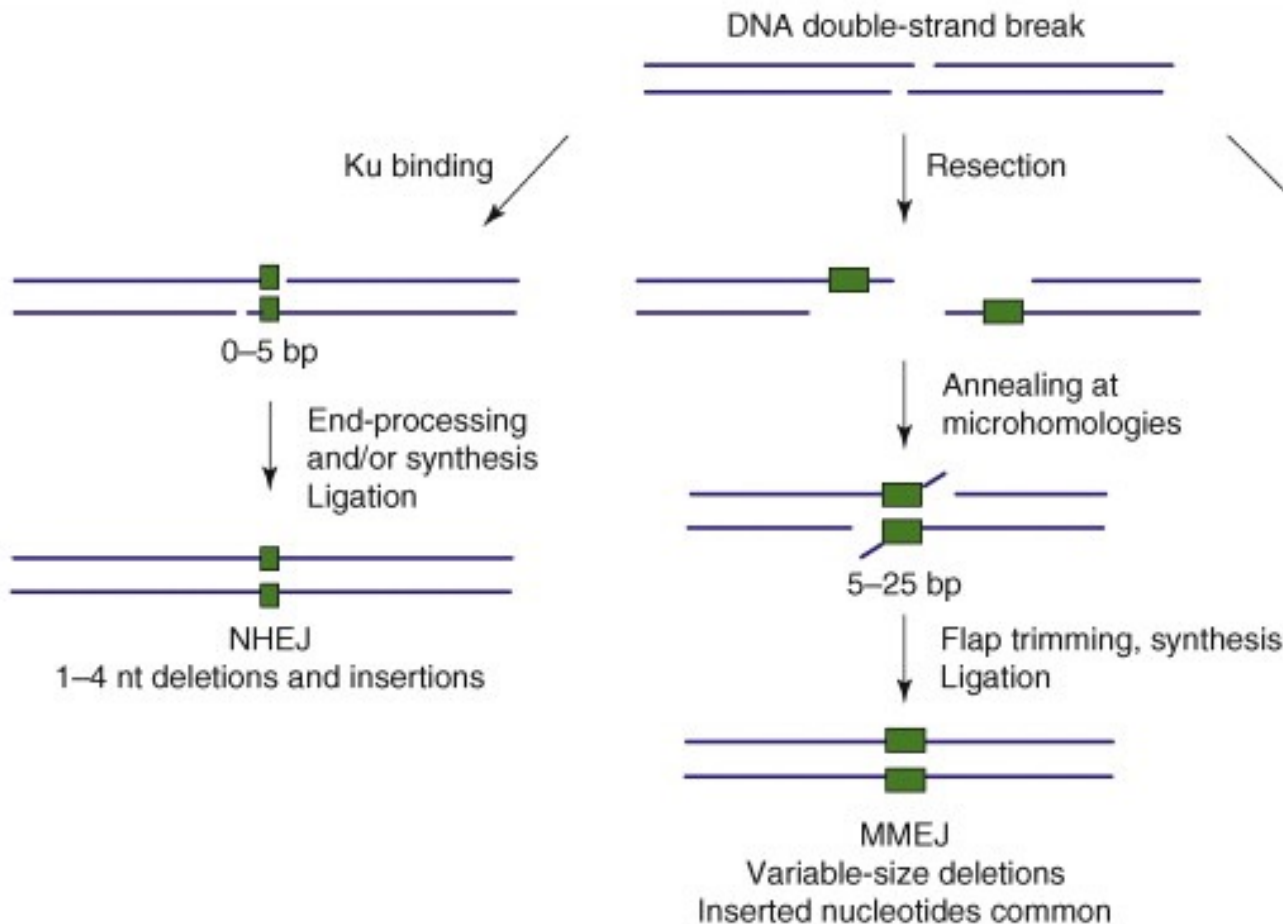
# NHEJ: Non-Homologous End Joining

Hallmarks of NHEJ:

- DSB must occur to repair via NHEJ
- Ku70/80 protects broken DNA ends and recruits DNA-PK
- DNA-PK recruits other repair factors
- Highly mutagenic
- Fast DNA repair
- Mostly done during G1&G2 for fast repair



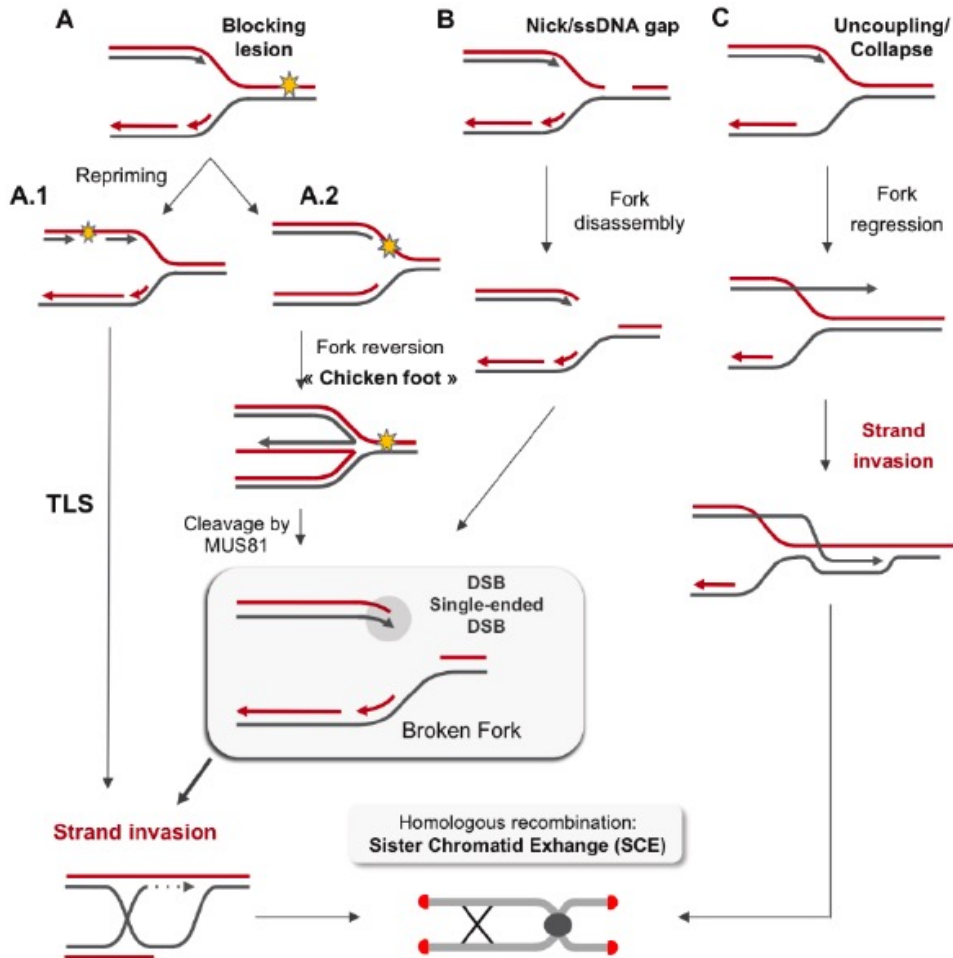
# MMEJ: Microhomology-Mediated End Joining



## MMEJ Hallmarks

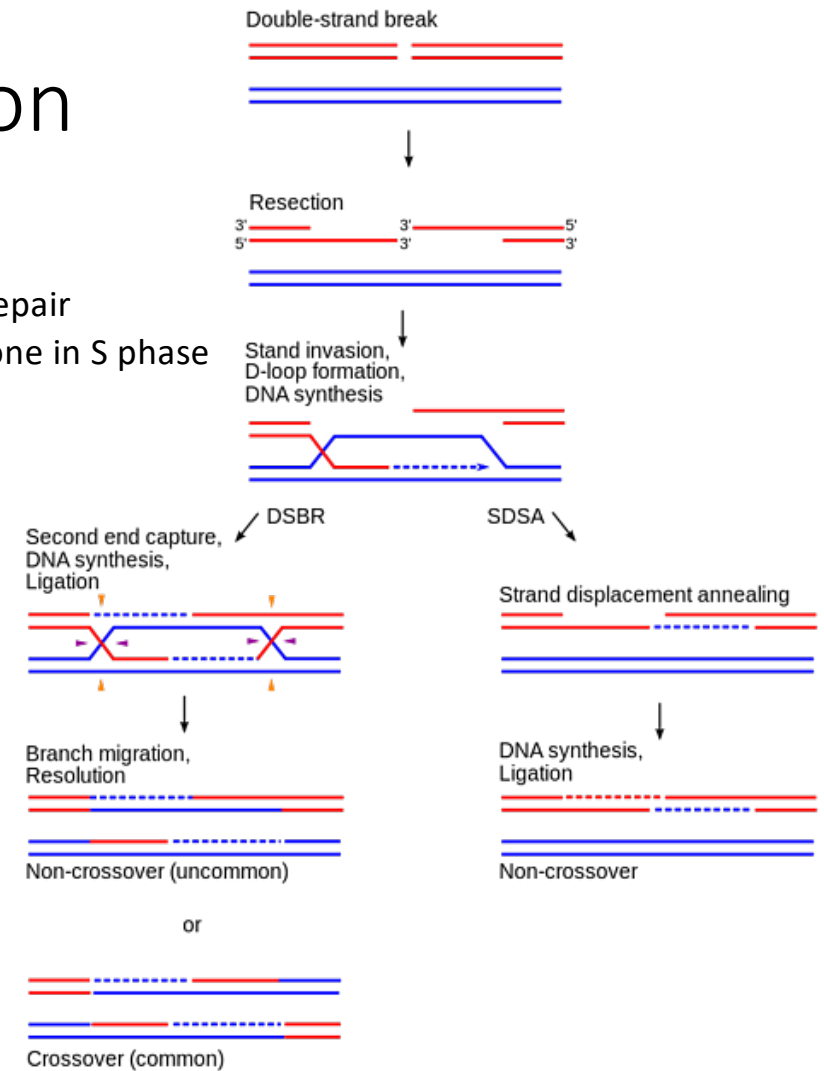
- Faster repair than NHEJ
- More mutagenic than NHEJ
- Occurs still even if NHEJ and HR is intact.

# HR: Homologous Recombination



## HR Hallmarks:

- Error-free
- Slow DNA repair
- Primarily done in S phase



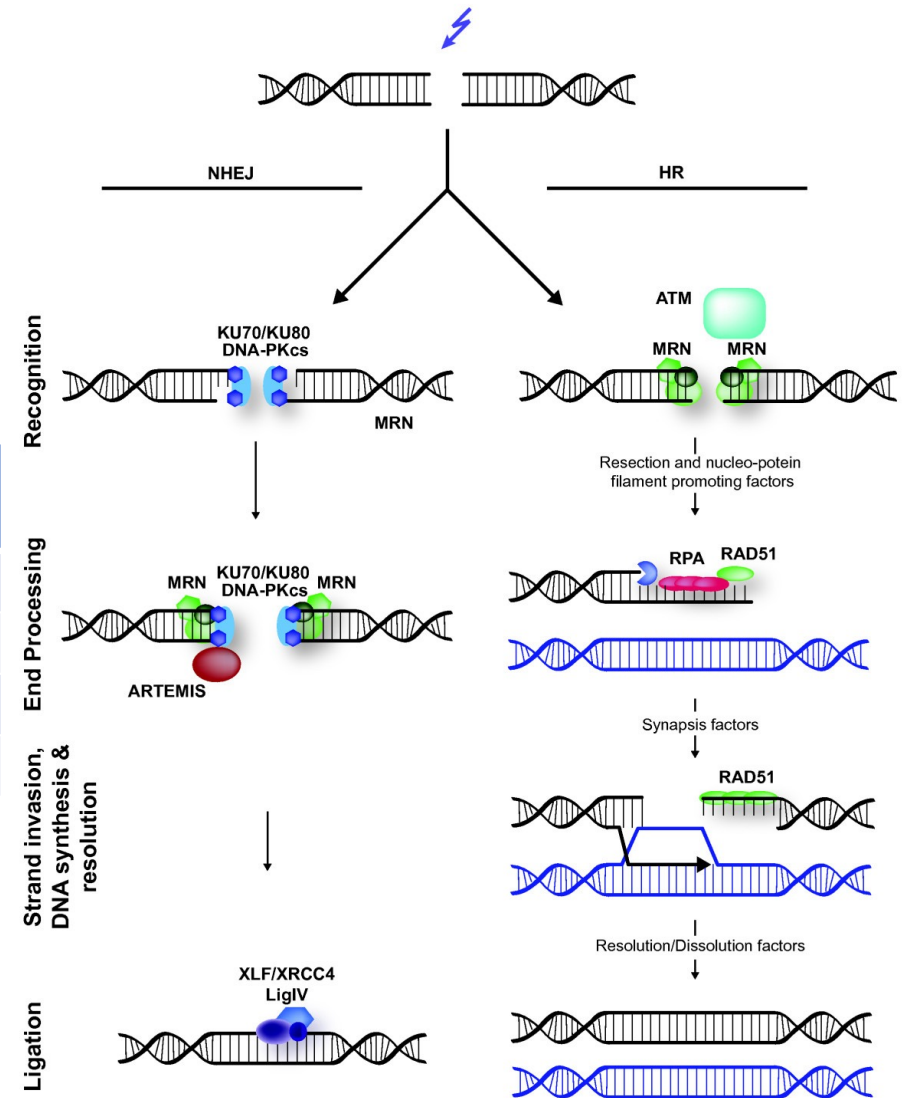
"HR schematic diagram" by Emw2012. Licensed under CC-BY-SA-3.0 via Wikimedia Commons.



# NHEJ vs HR

\*MMEJ is not considered a main repair pathway, as it occurs in the presence of HR and NHEJ as well.

Non-Homology End Joining (NHEJ)	Homologous Recombination (HR)
Error prone	Error free
Quick DNA repair	Slow DNA repair
Occurs during G1/G2 phases	Occurs during S phase
Does not require template	Requires homologous template



# Summary

You should now be briefly familiar with the following concepts:

- The importance of the Unfolded Protein Response (UPR).
- The severity of ROS stress on proteins and DNA.
- The difference between the DNA Damage Response and DNA Damage Repair.
- The differences between NHEJ, MMEJ, and HR repair.
- When NHEJ vs HR occurs during the cell cycle.

## Review Article

# Links between the unfolded protein response and the DNA damage response in hypoxia: a systematic review

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