

Nucleotide Excision Repair: Fighting Cancer & Aging

11^η Διημερίδα, ITE 2017, 13-14 Οκτωβρίου, Ηράκλειο, Κρήτη



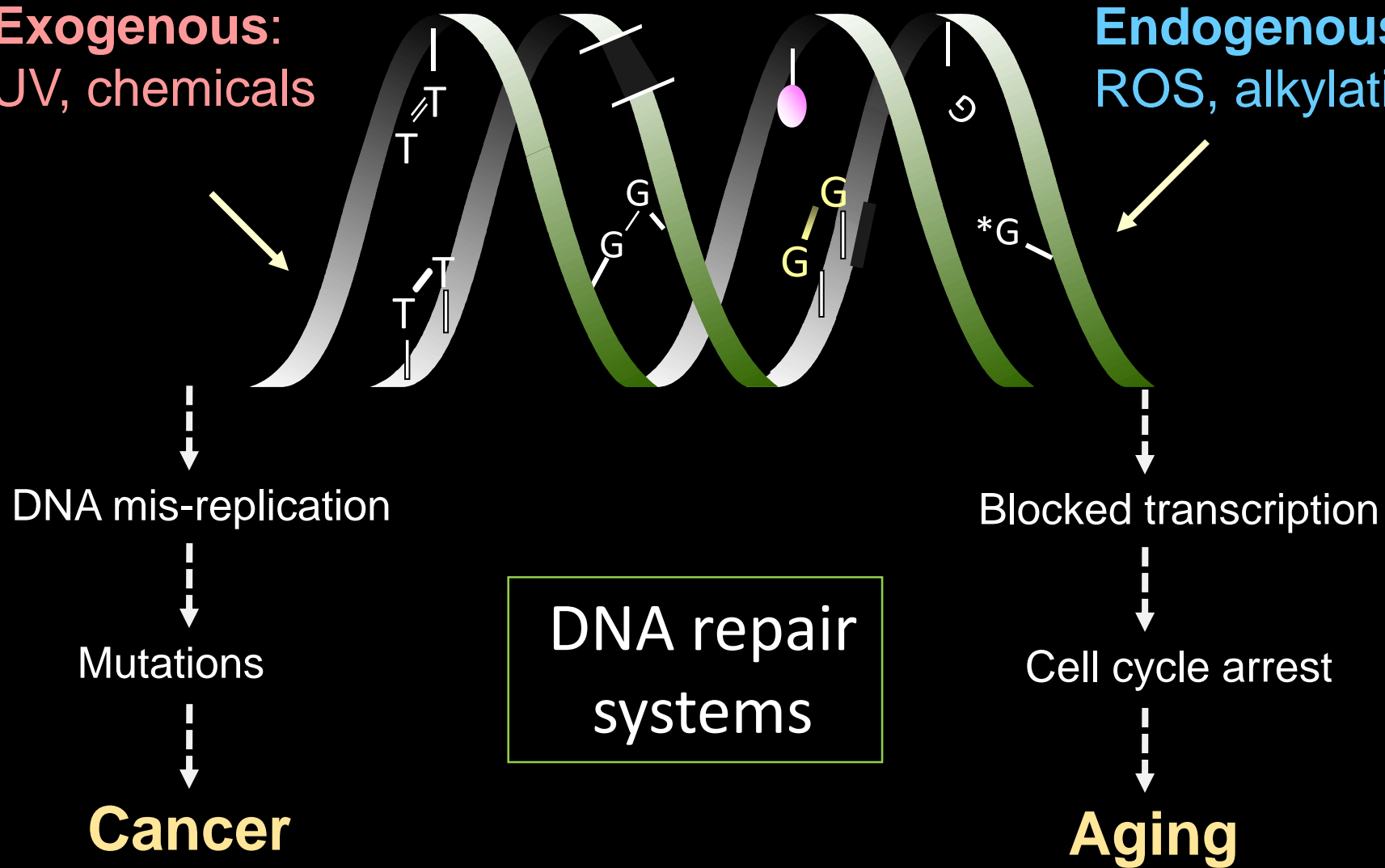
George A. Garinis

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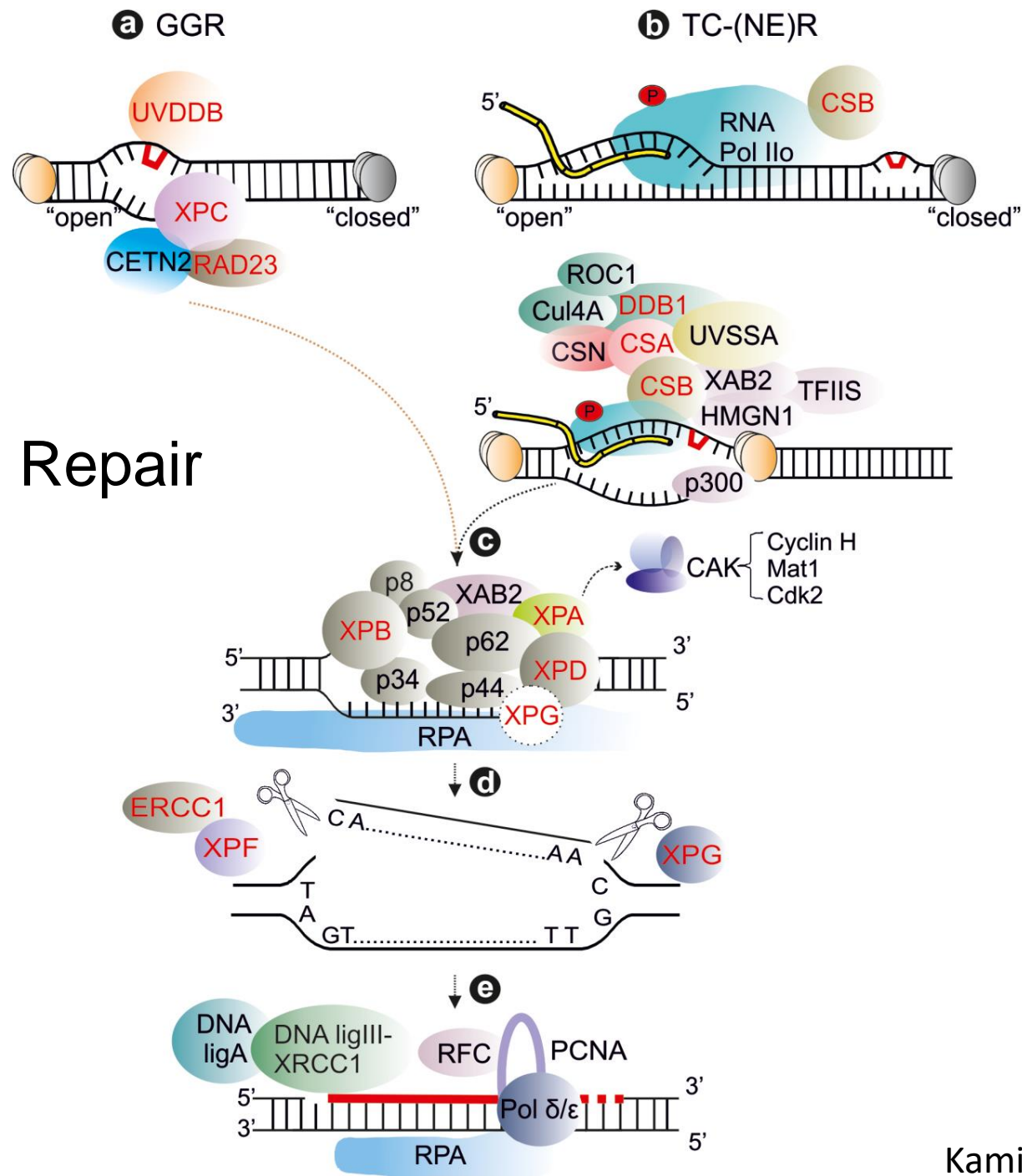
DNA damage

Exogenous:
UV, chemicals

Endogenous:
ROS, alkylation



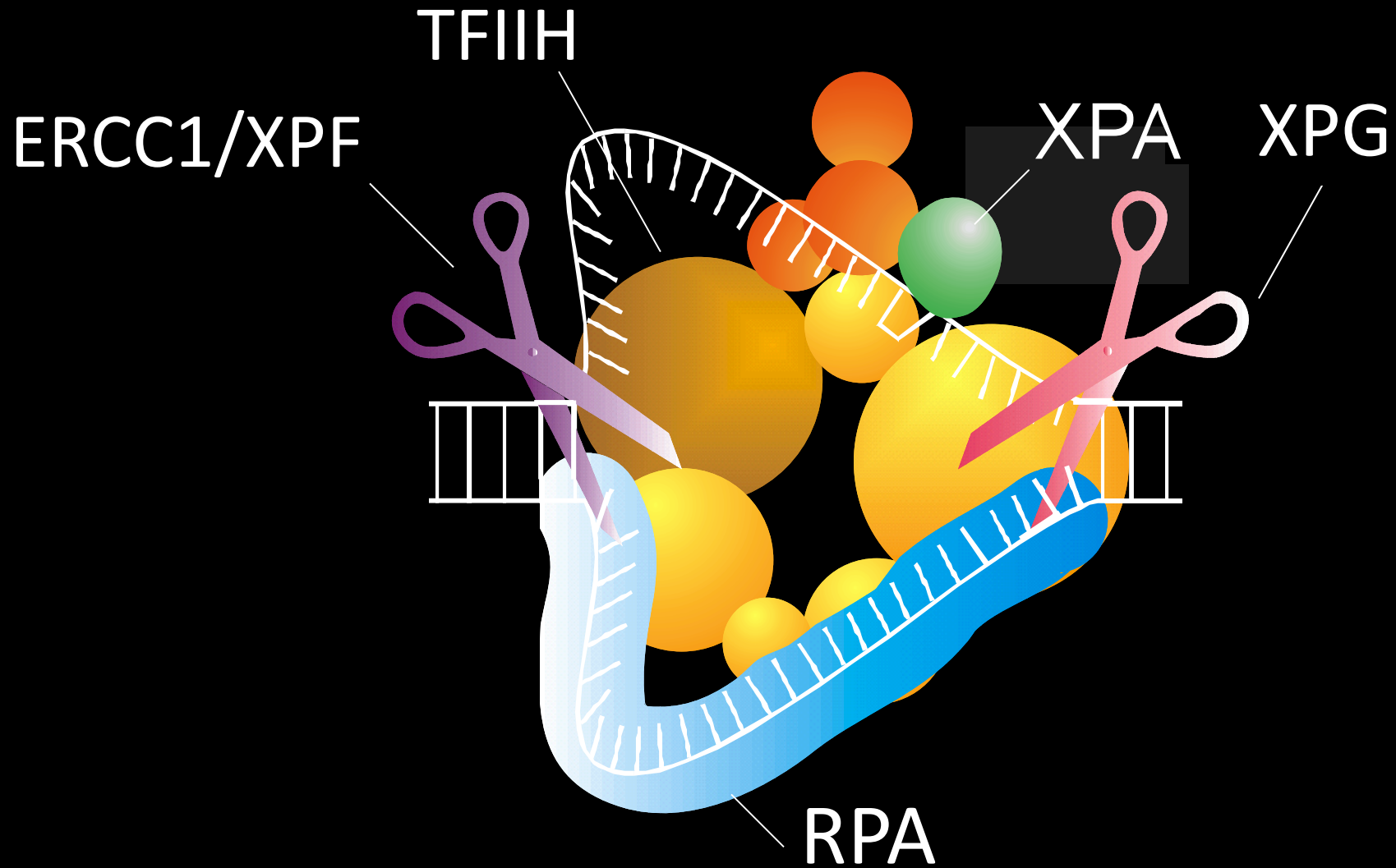
Nucleotide Excision Repair



Global genome nucleotide excision repair (GG-NER)

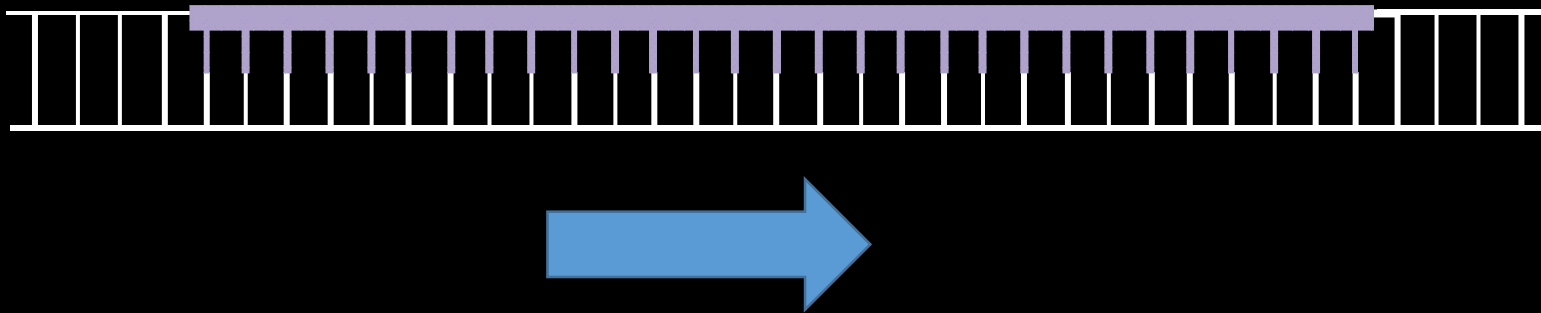


Global genome nucleotide excision repair (GG-NER)

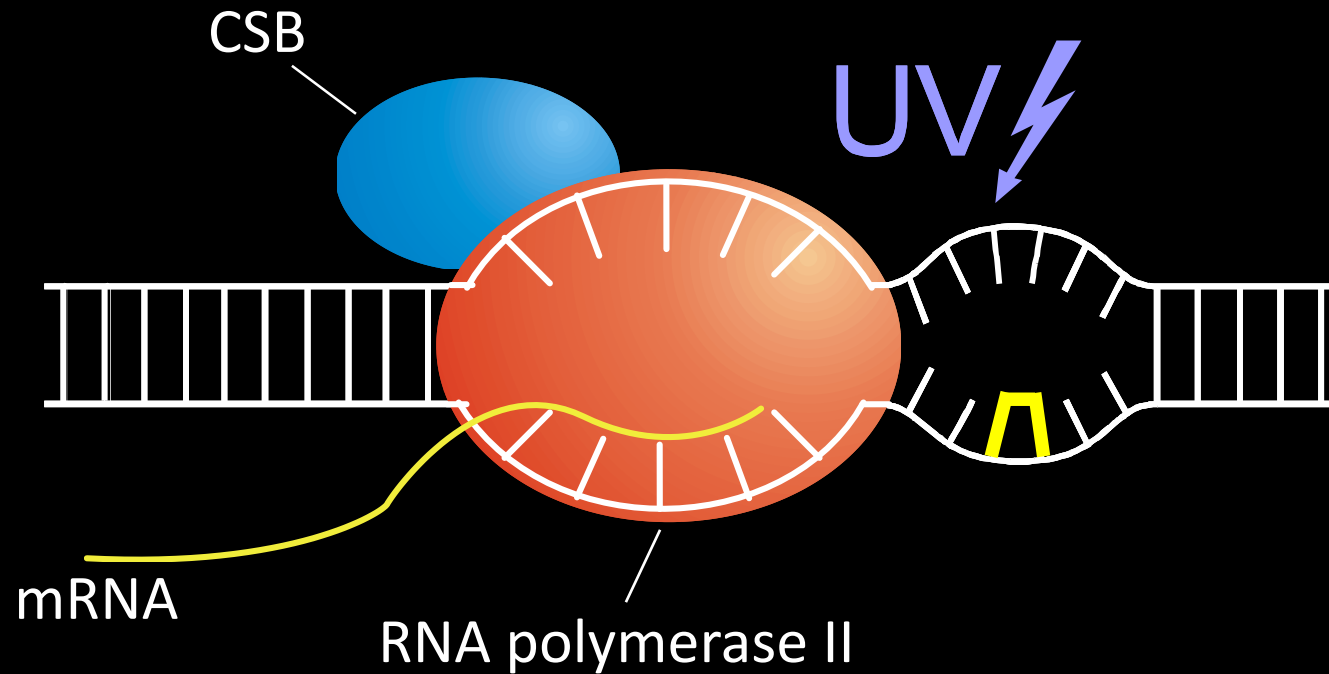


Global genome nucleotide excision repair (GG-NER)

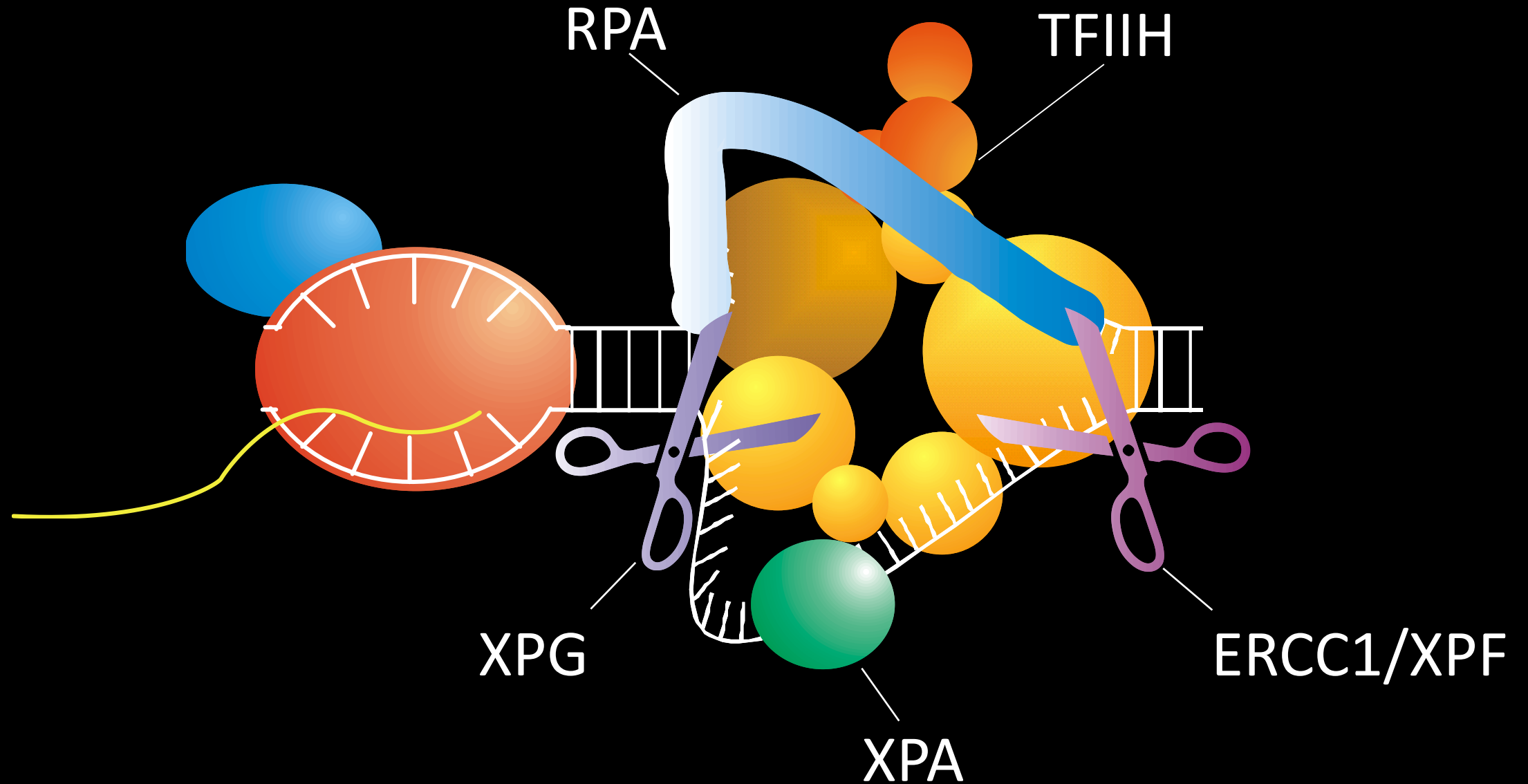
DNA polymerase δ/ϵ , RFC
PCNA and DNA ligase



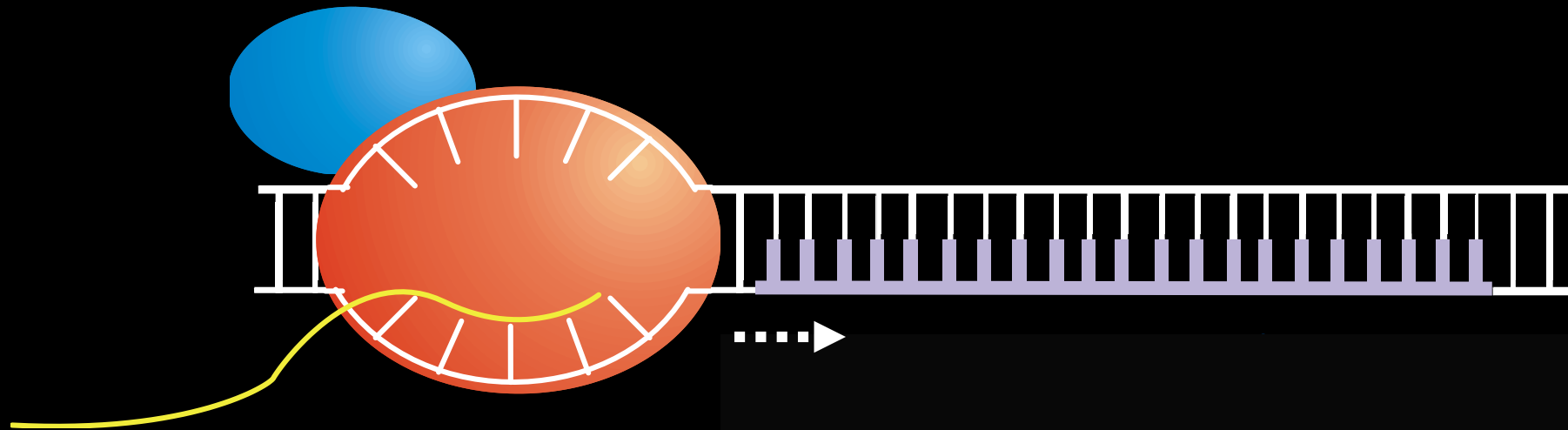
Transcription-coupled nucleotide excision repair (TC-NER)



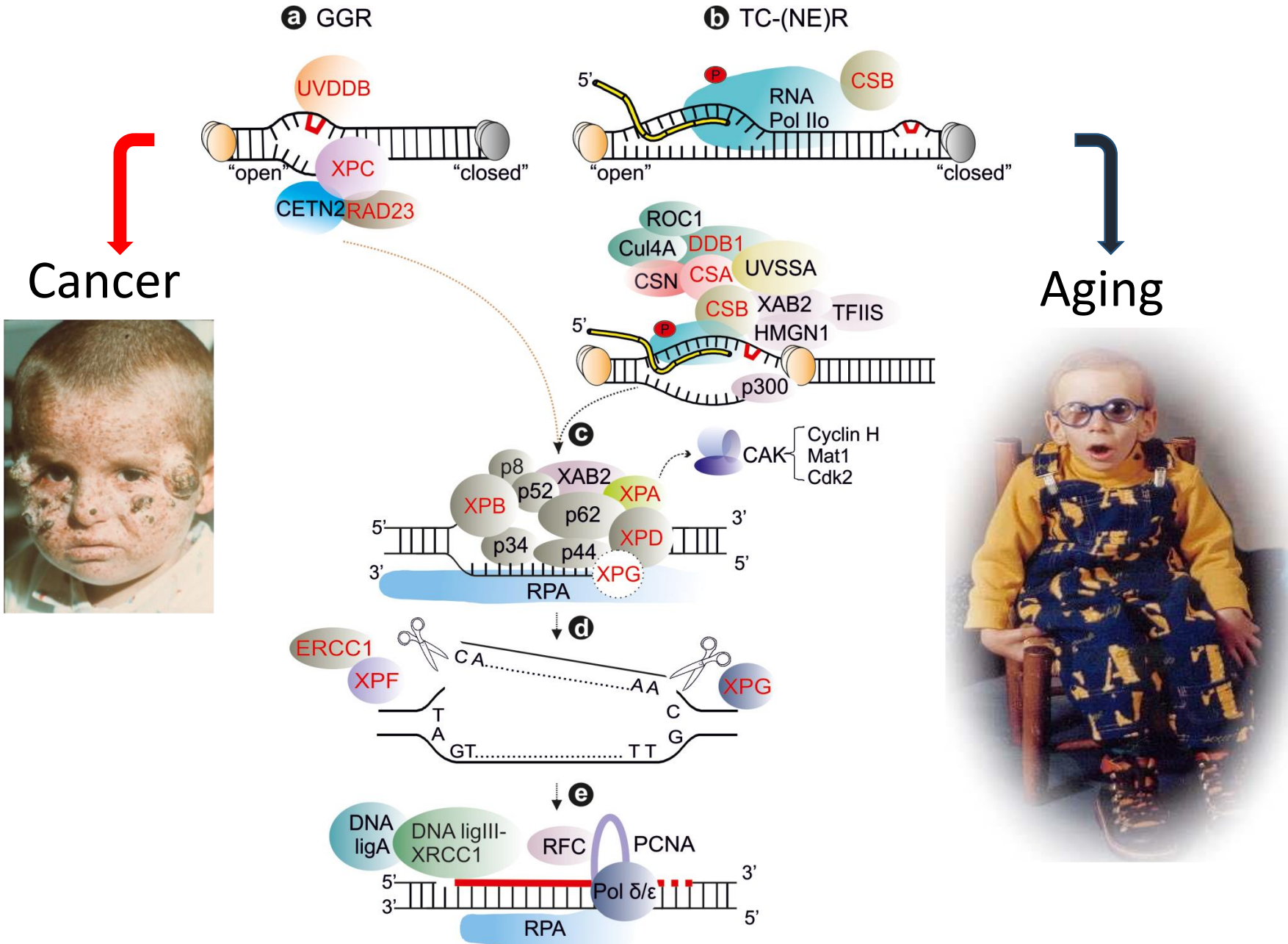
Transcription-coupled nucleotide excision repair (TC-NER)



Transcription-coupled nucleotide excision repair (TC-NER)



Nucleotide Excision Repair



Nucleotide Excision Repair (NER)

~30 genes

Mutations

Heterogeneity



Cancer

Ageing

DNA damage



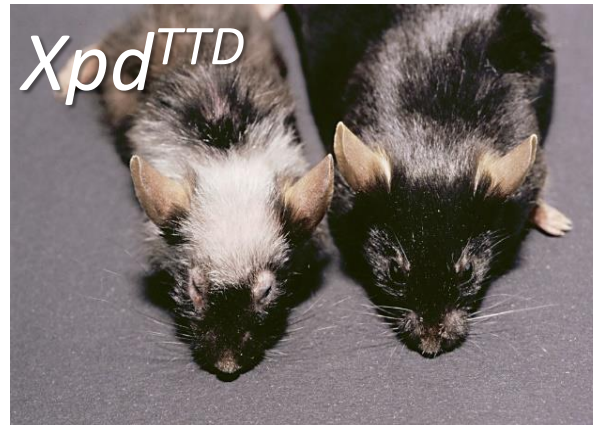
Developmental
defects



PLoS Biology 2007
Nature 2007



Premature
ageing



EMBO J 2005
PLoS Genetics 2008

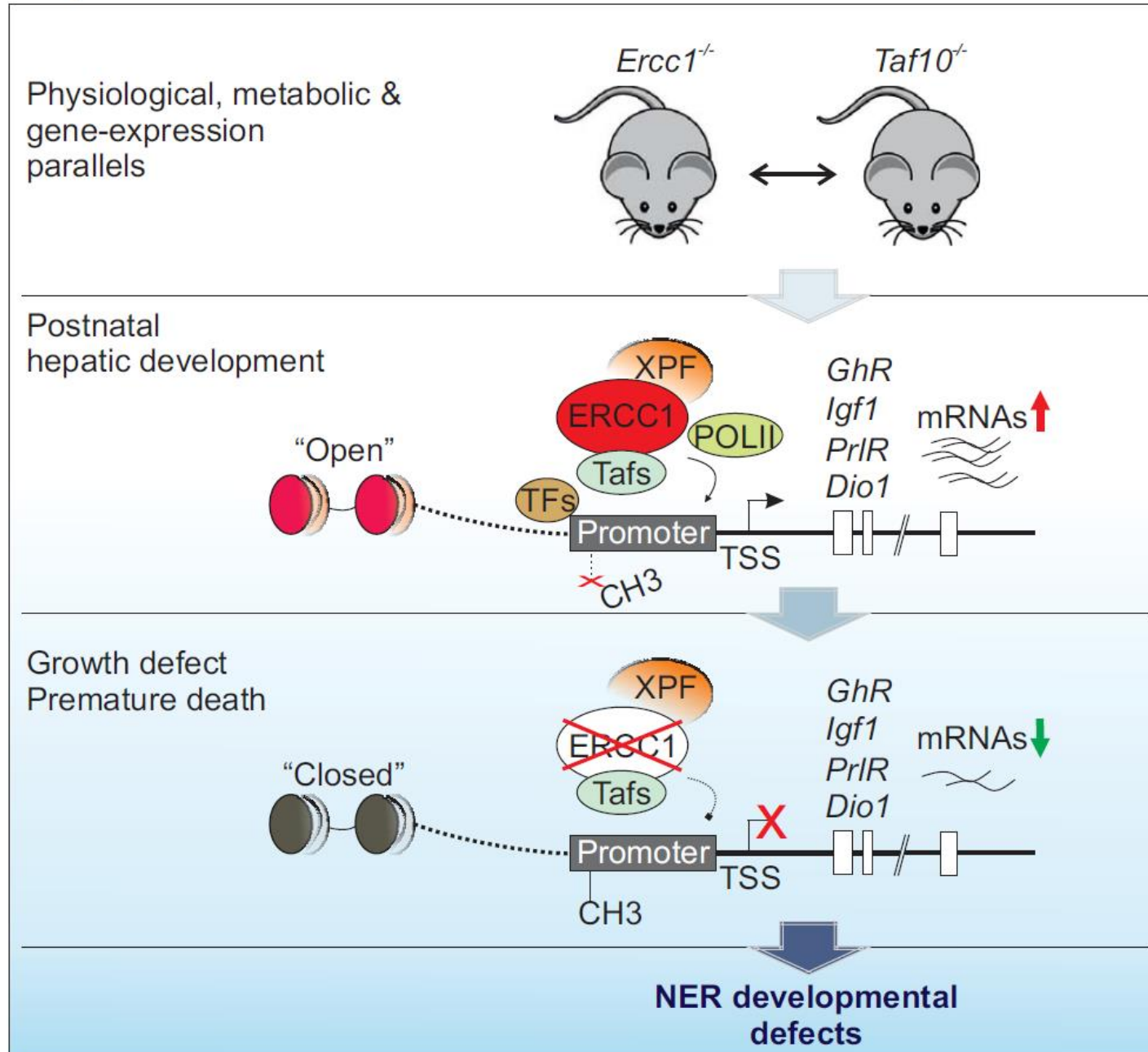


Skin
cancer

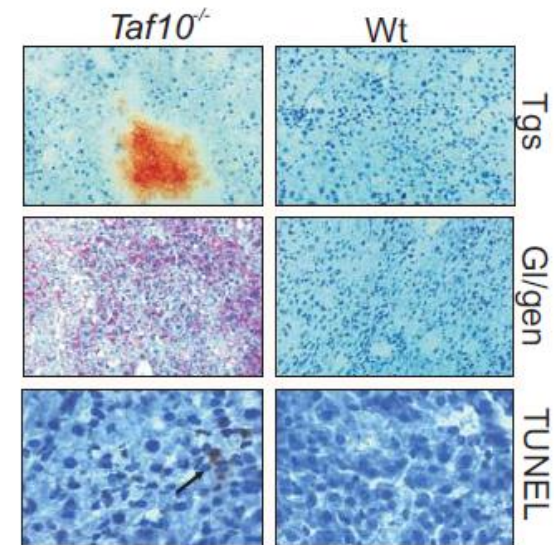
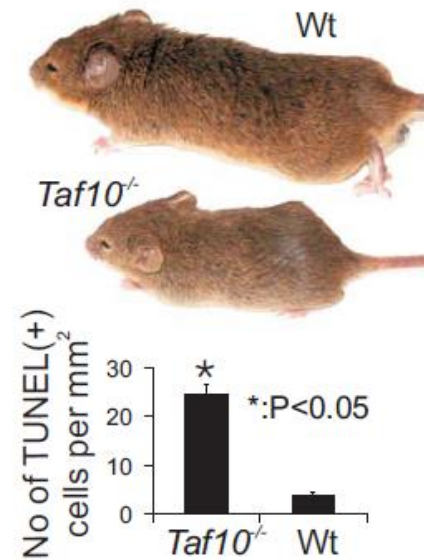
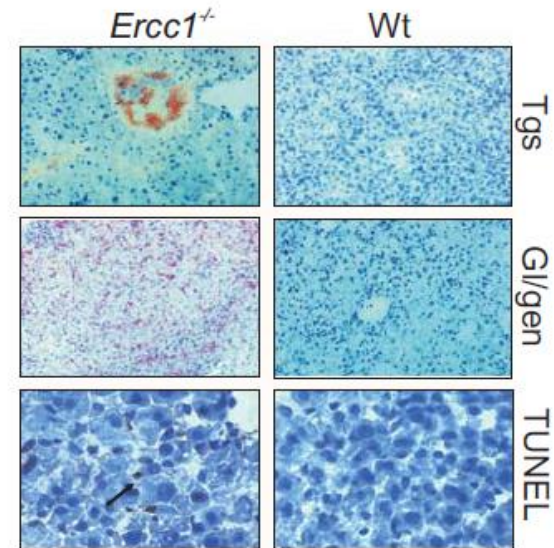
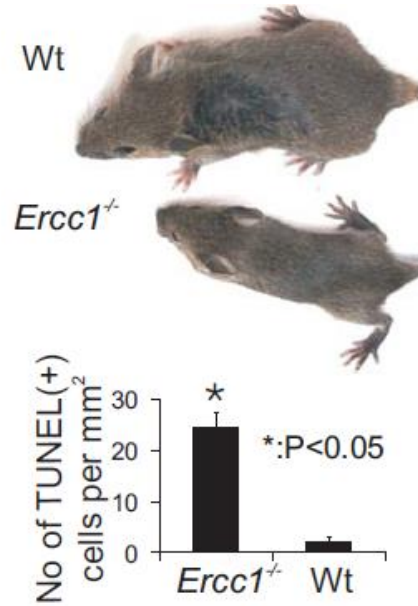
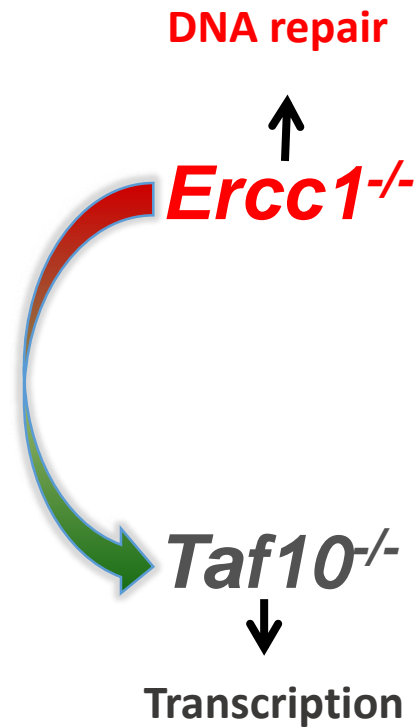


Nature Cell Biol 2009
Nature Cell Biol 2008

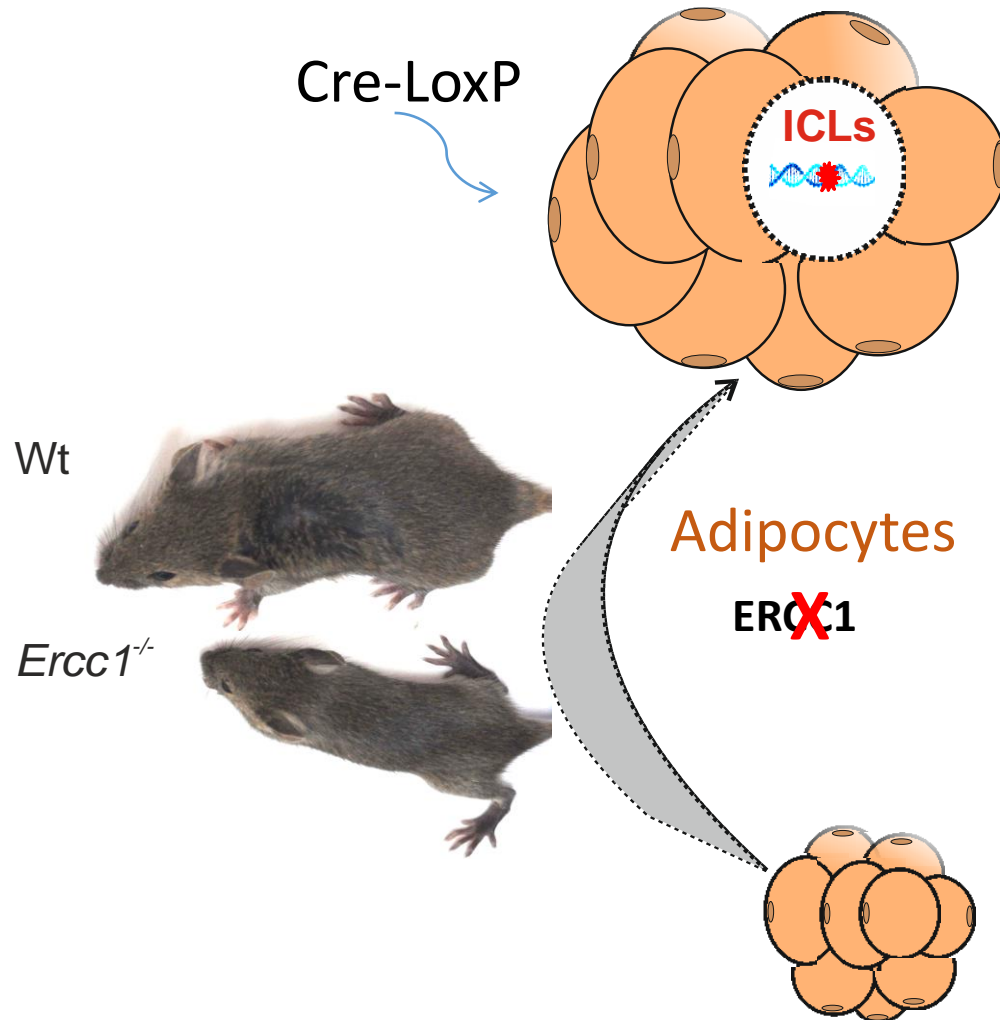
NER factors in transcription initiation



Taf10^{-/-} and *Ercc1*^{-/-} mice: striking parallels



Tissue-specific NER progeria: adipose tissue



Fat-specific *Ercc1^{f/-}* mice

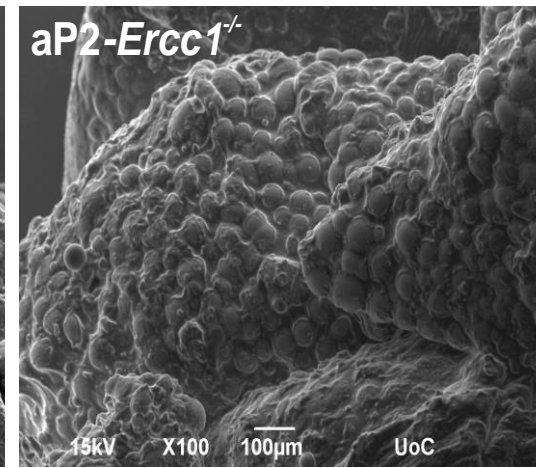
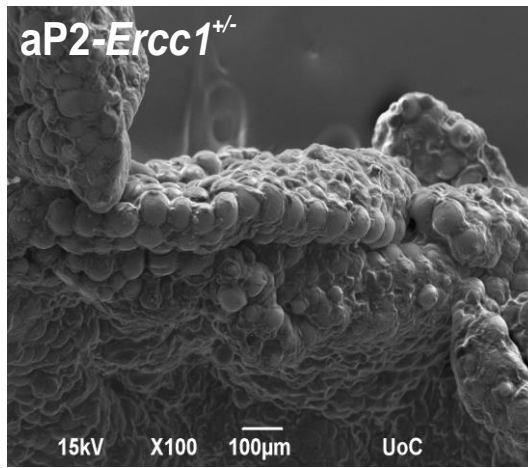


DNA damage

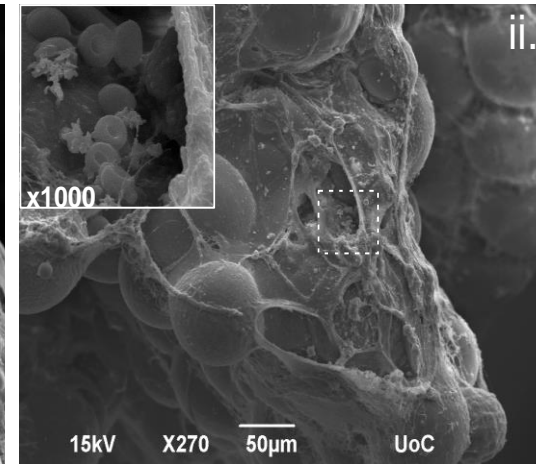
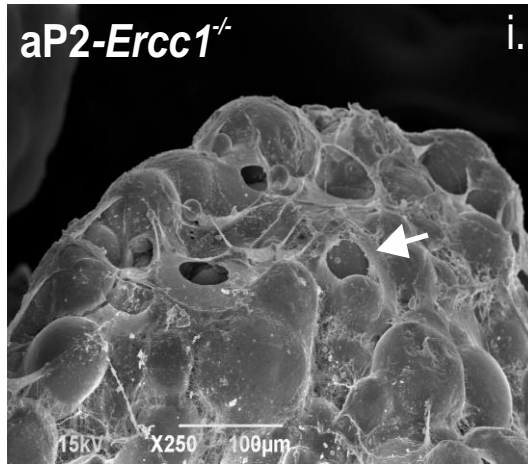


Fat degeneration

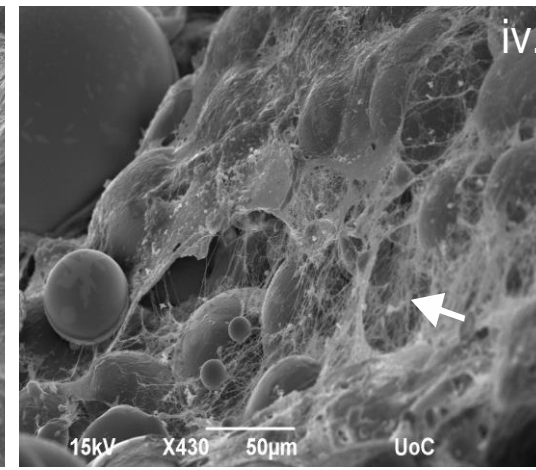
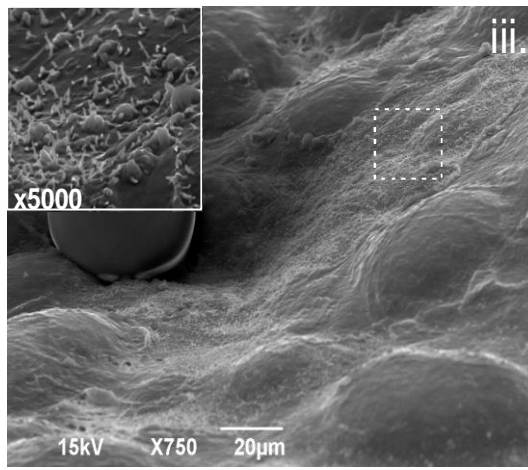
WAT

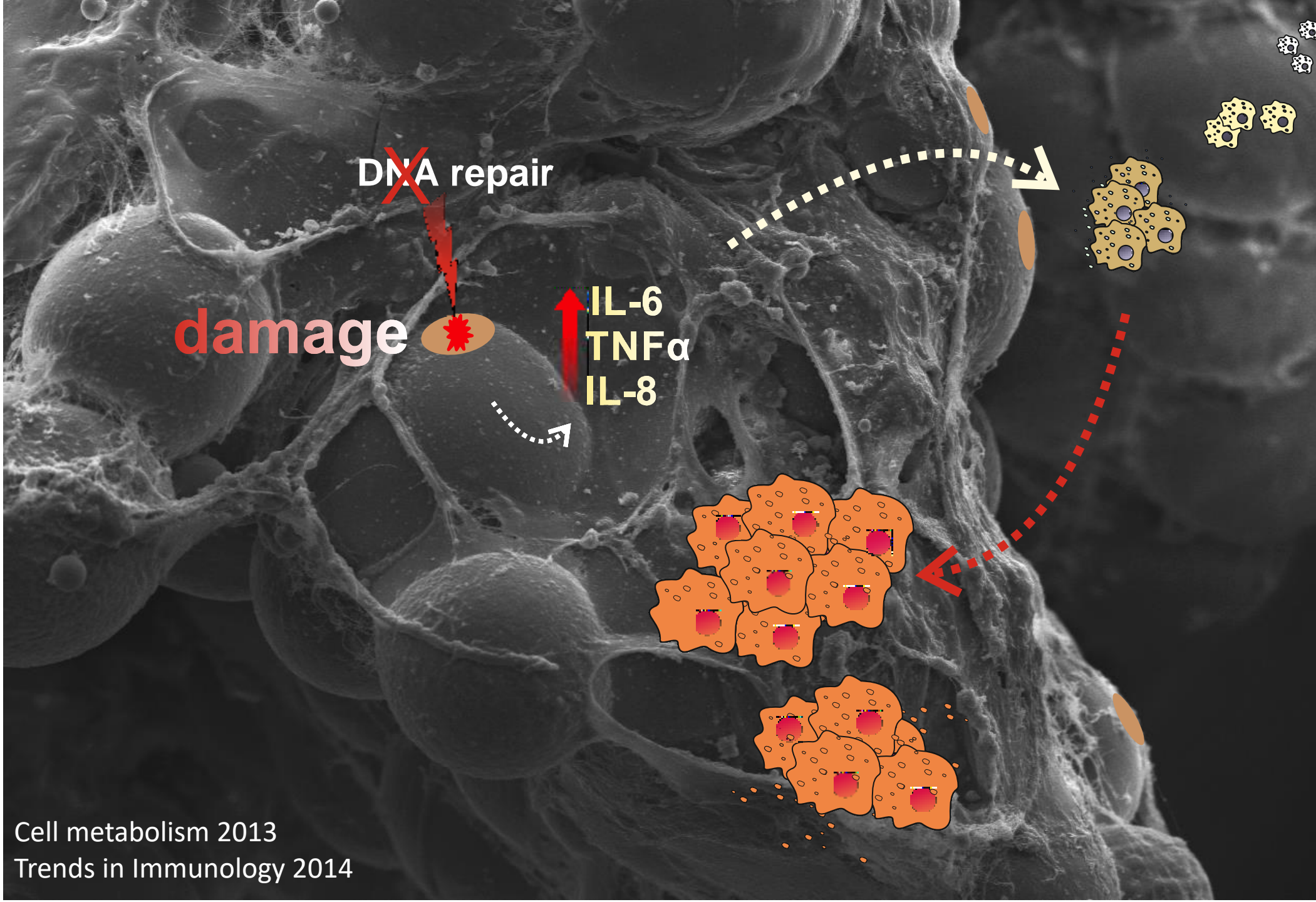


1.5-mo



5-mo





Tagging NER factors *in vivo*

Peptide



NER factor

Bacterial ligase

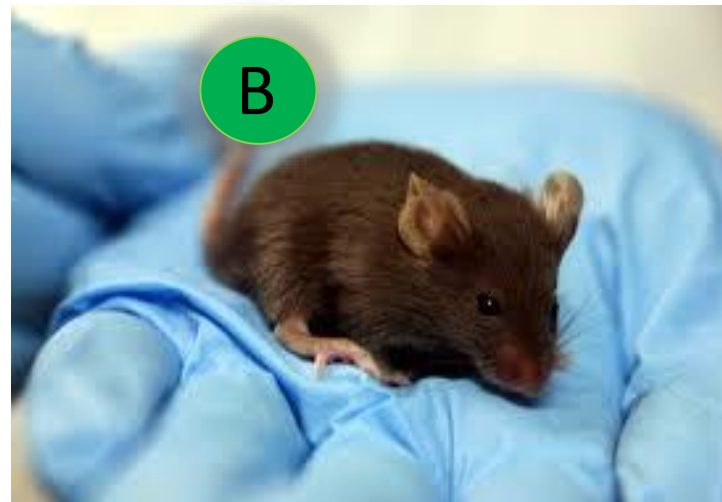


Knock-in



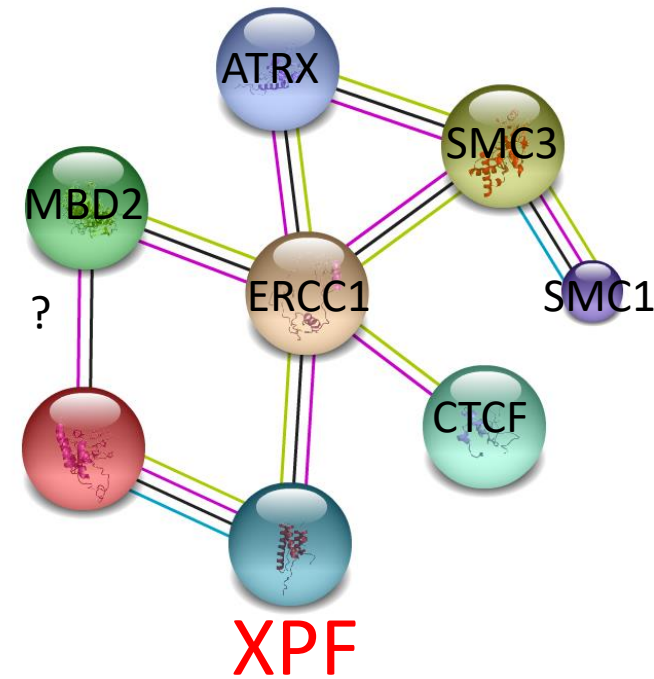
Transgenic

BioNER mice



NER factors in mammalian development

Fetus



Pup



Gene Silencing

“NER does more than its name implies”

NER factors

DNA repair

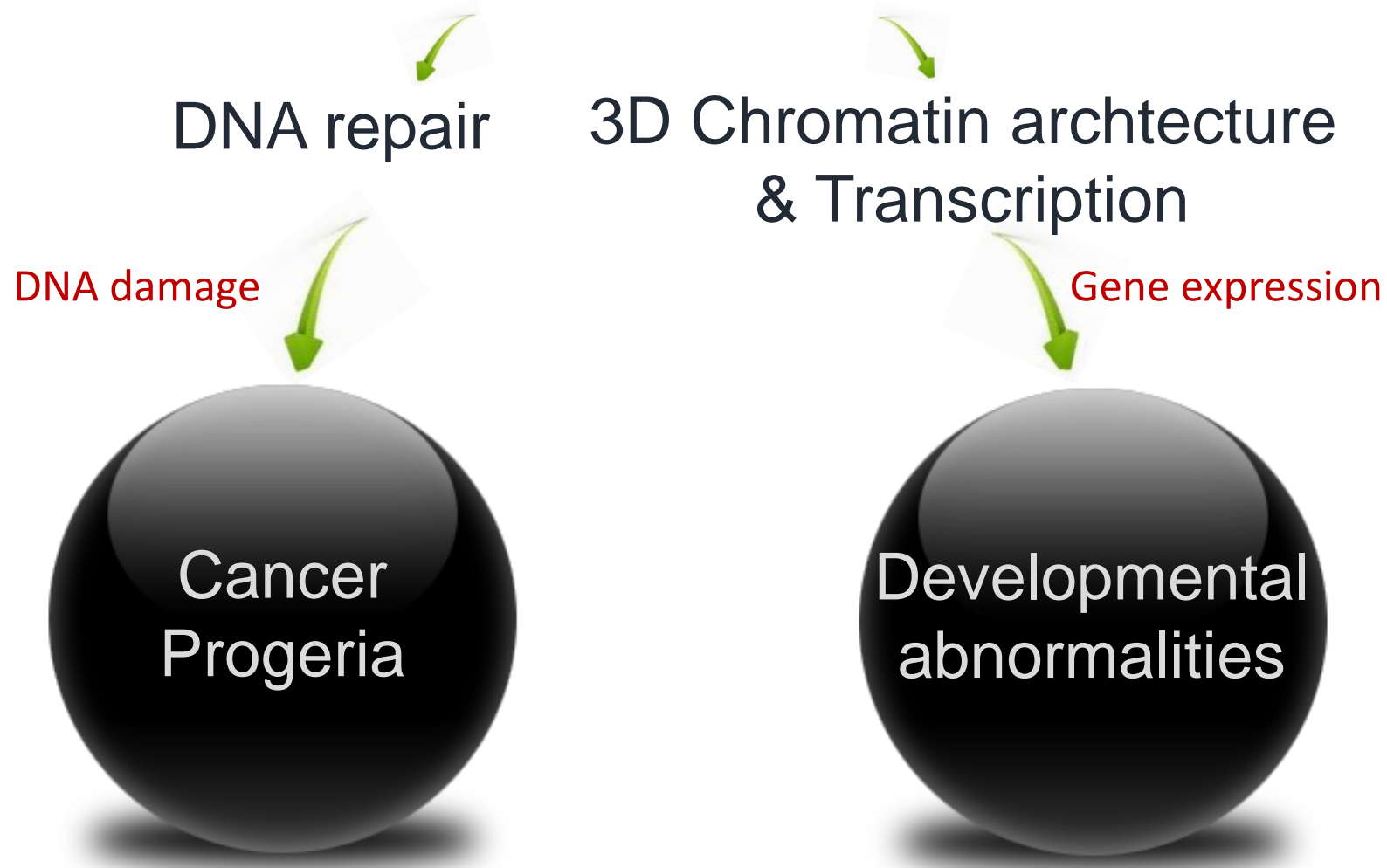
3D Chromatin architecture
& Transcription

DNA damage

Gene expression

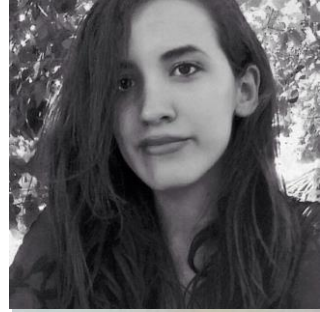
Cancer
Progeria

Developmental
abnormalities



Acknowledgements:

Garinis lab



Chromatin3D

aDDRess

CodeAge

MarriAge

