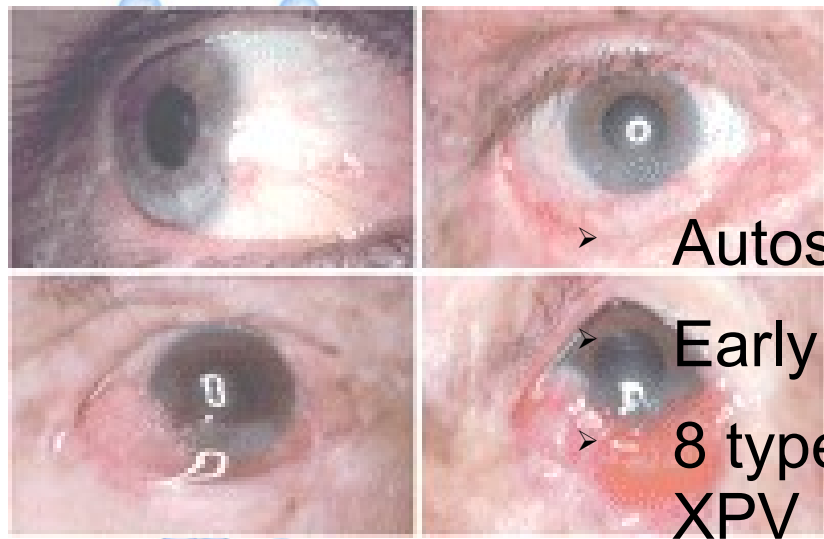


# **Xeroderma Pigmentosum**

Cindy Wu  
period 6

# Physiology



- Autosomal Recessive

- Early onset

- 8 types: XPA, XPB, XPC, XPD, XPE, XPF, XPG, XPV



- More common in North Africa and Middle East because of consanguinity

- Extremely sensitive to sunlight

- Causes basal cell carcinomas, poikiloderma, dry skin

- Eye problems, such as thin eyelids, or keratitis

- Sometimes causes neurological problems (De Sanctis-Cacchione)

- Cockayne's Syndrome, Trichothiodystrophy are diseases also related to the defects in XP

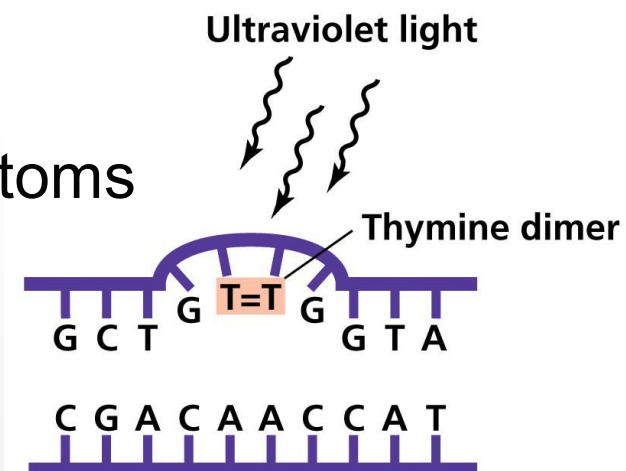
# Molecular Cause

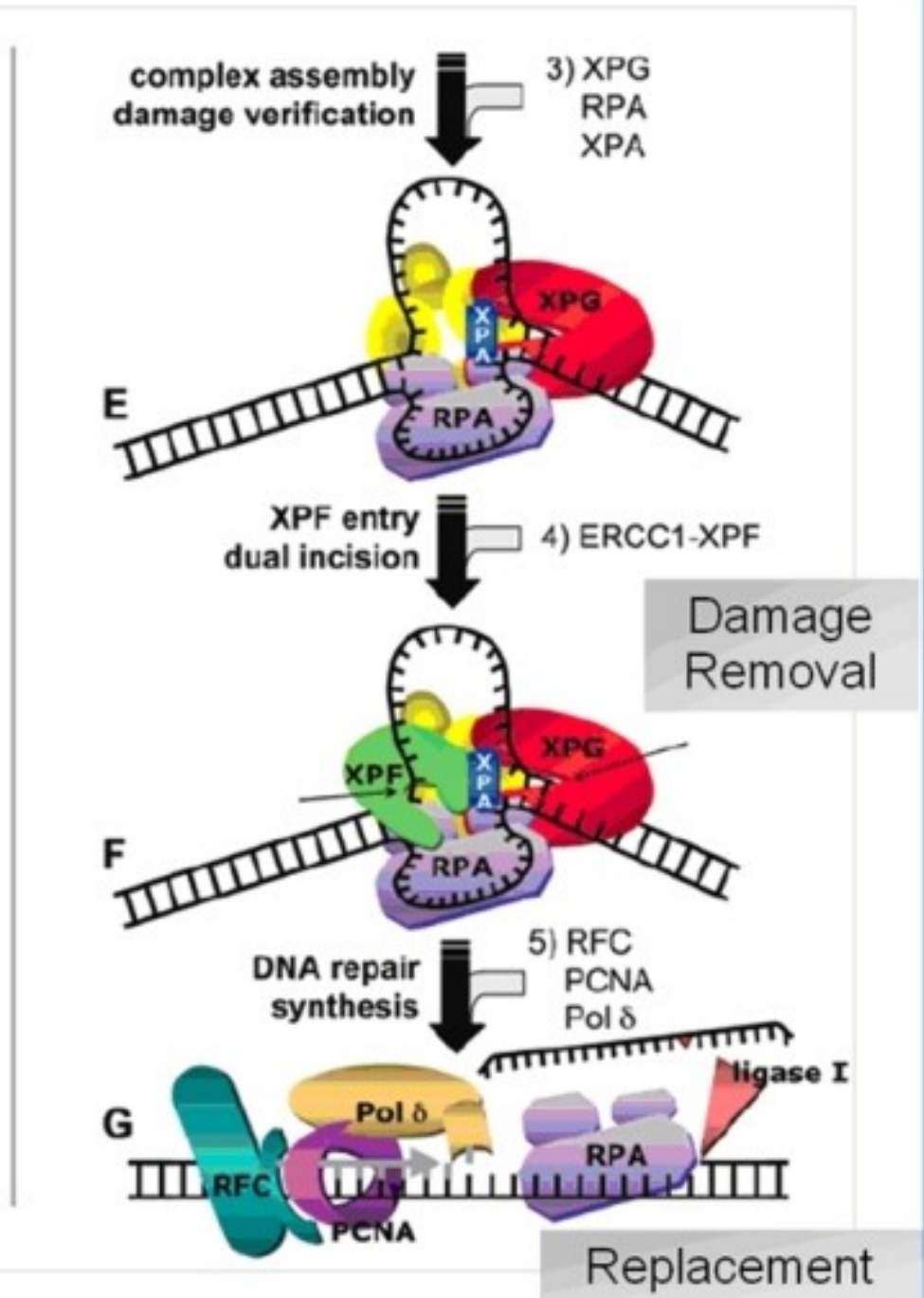
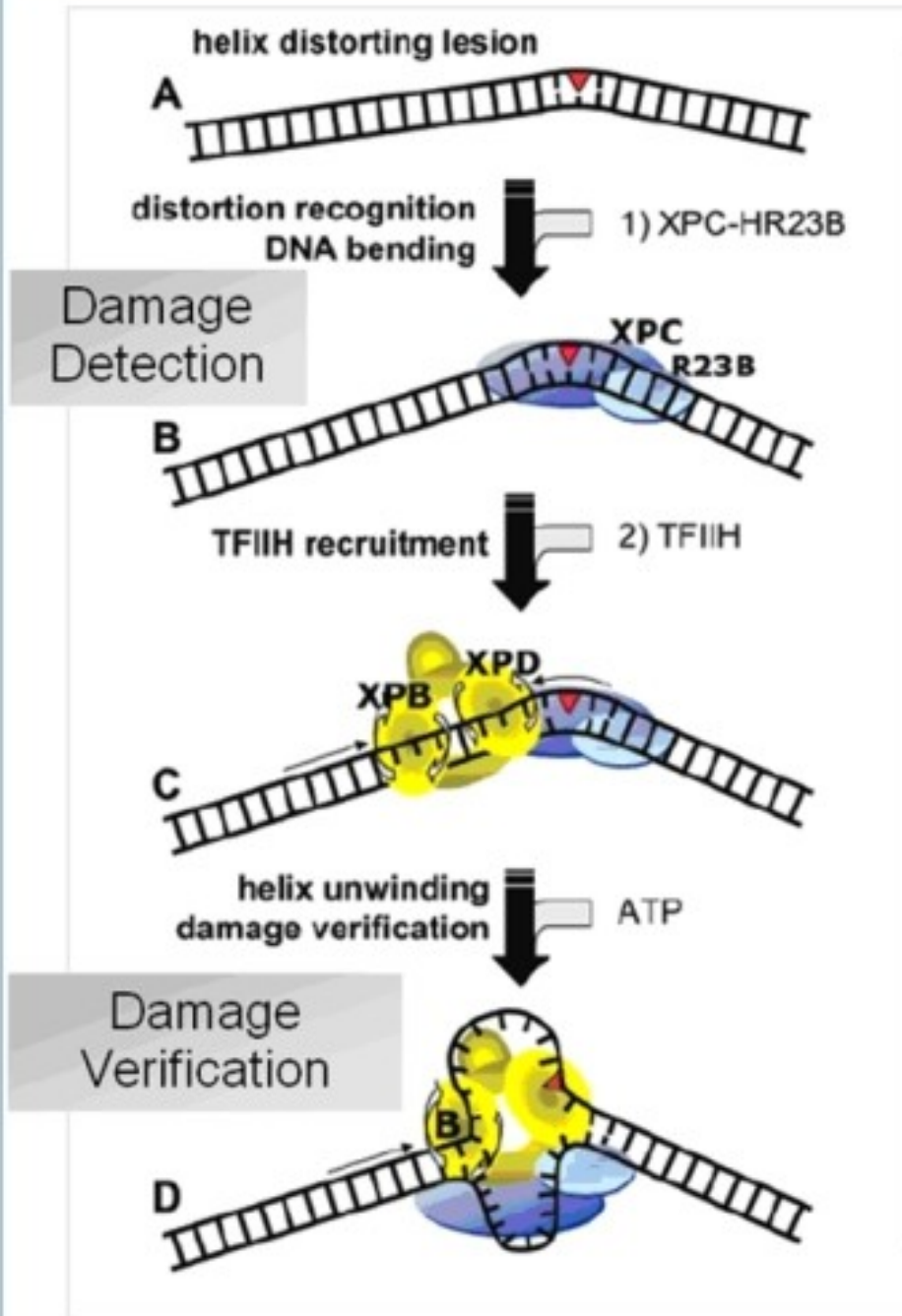
- XPA, ERCC3, XPC, ERCC2, DDB2, ERCC4, ERCC5, POLH mutations cause XP
- Each form of XP has a different gene that is mutated
- All are involved in nucleotide excision repair, which fixes thymine dimer errors caused by UV rays. This causes a build up in cancer cells

- POLH is responsible for DNA polymerase, unlike the other genes that are only responsible for NER related proteins.

- ERCC2 and ERCC3 can also cause TTD

- This results in some patients sharing XP symptoms and TTD symptoms





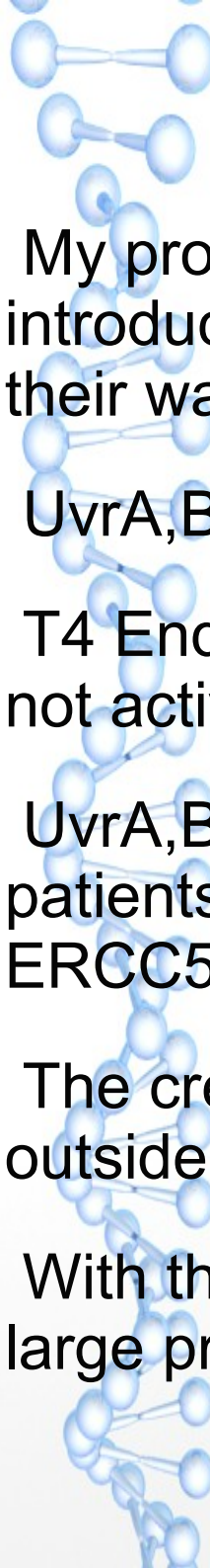
from: Gillet and Schärer, 2006



# Treatments/Risks and Limits

- Diagnosed with gene sequencing, hypersensitivity and chromosomal breakage studies, amniocentesis, chorionic villi sampling, unscheduled DNA synthesis (UDA), or alkaline comet assay (gel electrophoresis).
- Stay out of all sunlight, wear protective clothing, sunscreen
- Install special window films that block most UV rays, stay away from light bulbs that are not incandescent.
- Avoid any carcinogens, like cigarettes
- See the doctor(s) frequently.
- Isotretinoin, used to treat acne is effective in reducing skin cancer.
- Surgery or imiquimod 5% cream and oral acetretin (still under study) to treat tumors.
- T4 endonuclease V cream is being tested. T4 endonuclease is a bacterial DNA repair enzyme that examines the DNA and induces a glycosylic bond scission on the 5', and then the phosphodiester backbone is removed by beta-elimination.
- This treatment was tested on 30 XP patients, 20 with the cream and 10 with placebo. The test showed positive results.
- These treatments still need further testing

# Proposed Cure/Limits

- 
- My proposal is similar to the T4 Endonuclease V cream, I still want to introduce it with liposomes in cream, so that the liposomes can make their way to the skin easily, where the thymine dimers are.
  - UvrA,B,C,D are all involved in the NER of E.coli.
  - T4 Endonuclease is more similar to a photolyase (that require light), not active in mammals.
  - UvrA,B,C,D have similar functions to the defective NER proteins in XP patients. For example, UvrC makes an excision at the 3' first, just like ERCC5. T4 Endonuclease makes a 5' cut first.
  - The cream would have to be applied frequently and before going outside to prevent a severe buildup in thymine dimers.
  - With this treatment, XPV is not accounted for. Also, UvrA is a pretty large protein that might not be able to reach the nucleus.



## Information

- <http://www.photobiosci.info/CleaverNER.html>
- [http://www.touchbriefings.com/pdf/17/pt031\\_p\\_crommelin.pdf](http://www.touchbriefings.com/pdf/17/pt031_p_crommelin.pdf)
- <http://emedicine.medscape.com/article/1119902-workup>
- <http://emedicine.medscape.com/article/1119902-treatment>
- <http://www.ncbi.nlm.nih.gov/pubmed/14616811>
- <http://www.patient.co.uk/doctor/Xeroderma-Pigmentosum.htm>
- <http://www.ncbi.nlm.nih.gov/pubmed/3287161>
- <http://www.ncbi.nlm.nih.gov/books/NBK1397/#xp.molgen.TA>
- <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2288663/>
- <http://www.jbc.org/content/270/8/3765.full>
- <http://www.ojrd.com/content/6/1/70>
- <http://ijp.asm.org/content/182/20/5706.full>
- <http://www.ncbi.nlm.nih.gov/pubmed/11920746>
- <http://www.ncbi.nlm.nih.gov/pubmed/11289350>

# References

## ➤ Pictures

- [http://en.wikipedia.org/wiki/Xeroderma\\_pigmentosum](http://en.wikipedia.org/wiki/Xeroderma_pigmentosum)
- <http://brain.oxfordjournals.org/content/131/8/1979.full>
- [http://virchow.uni-wuerzburg.de/kiskerlab/pro\\_ener.html#euNER](http://virchow.uni-wuerzburg.de/kiskerlab/pro_ener.html#euNER)
- [http://academic.pgcc.edu/~kroberts/Lecture/Chapter%207/07-22\\_PyrimidineDimer\\_L.jpg](http://academic.pgcc.edu/~kroberts/Lecture/Chapter%207/07-22_PyrimidineDimer_L.jpg)