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TRANSLA-TION-II

TRANS-CRIPTION I

DNA Repair

Damage to DNA can occur due to errors of replication

Causes for damage

1) Environmental agents :- UV rays, ionising radiations, x rays
2) Chemical agents :- free radicals, alkalitic reagents
3) Repair enzymes identifying the incorrect bases and is corrected.
4) Defect in DNA repair leads to mutations.

Repair mechanisms

1. Mismatched Repair
2. Nucleotide excision repair.
3. Base excision repair
4. Double strand break repair

1. → This mechanism corrects a single mismatched base pair

→ Parent strand is identified by the presence of ~~unmethylated~~ Adenine in GATC sequence. methylated.

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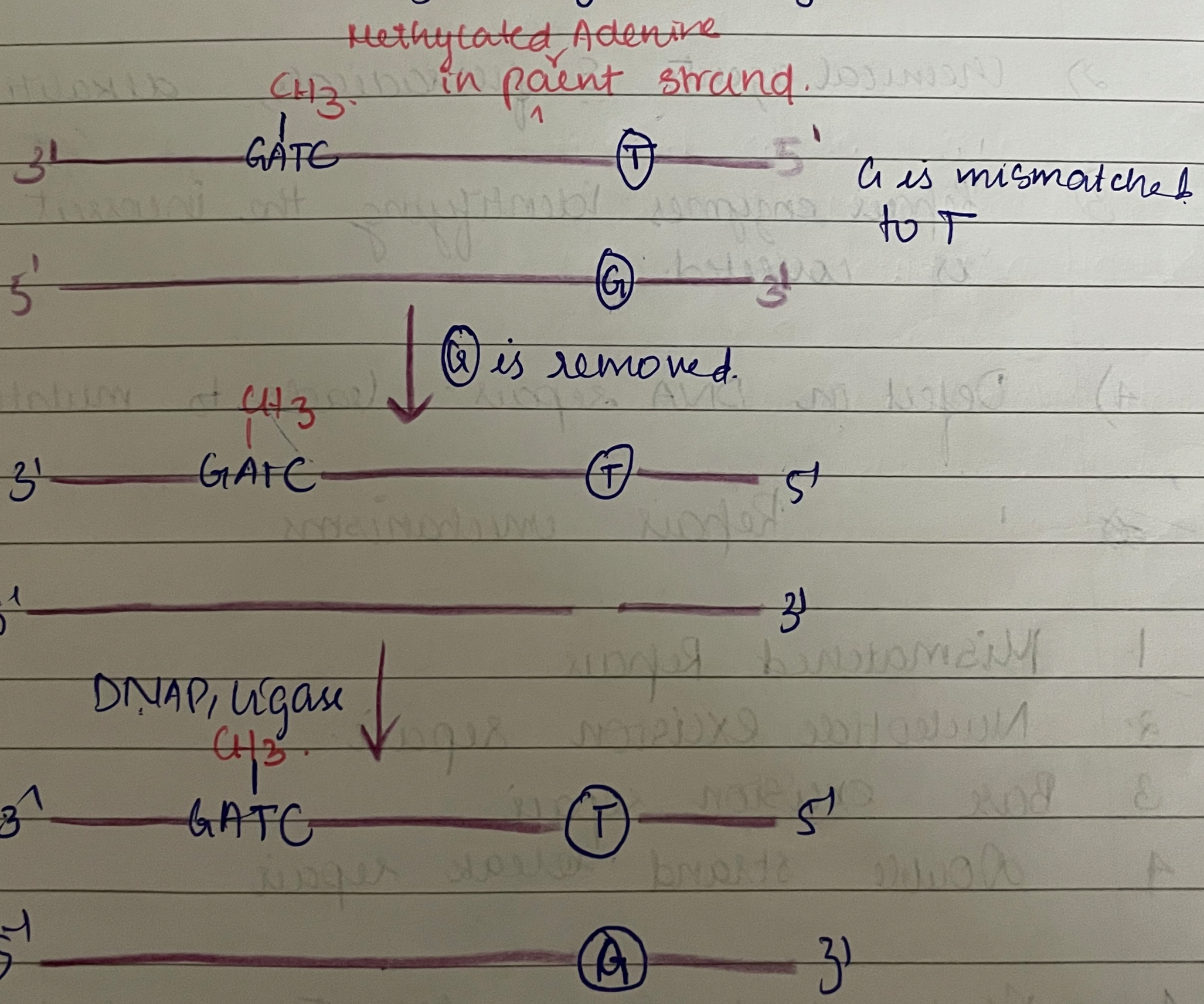
→ If a mismatch is found an endonuclease make a ~~longer~~ strand cut at the adjacent methylated GATC sequence

→ Defect is removed by exonuclease.

→ DNAP fill the gap using correct nucleotides.

→ This is then ligated by DNA ligase



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TRANSLA-TION II

2. NER

→ This mechanism repair the damage due to UV light

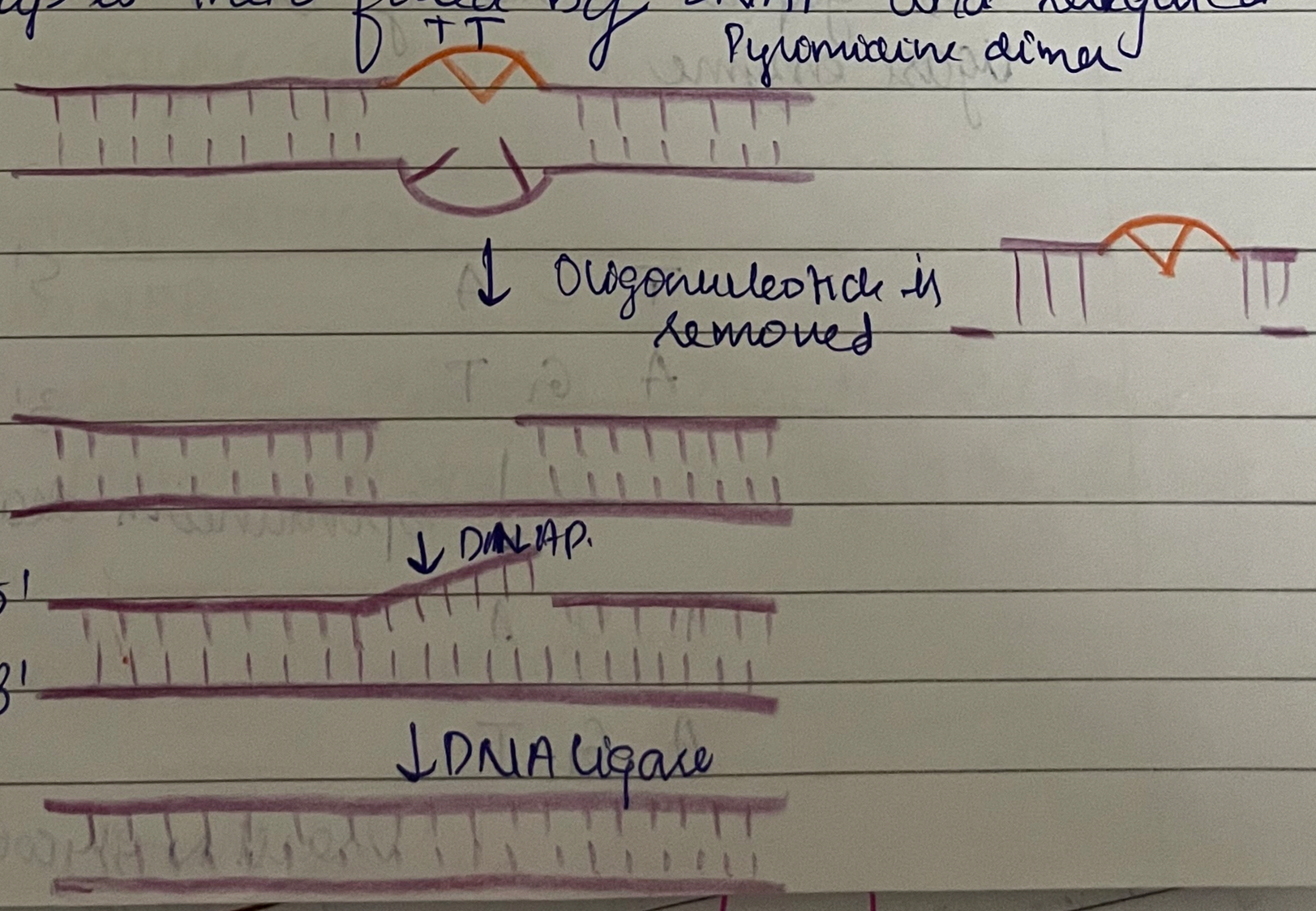
→ Exposure to UV light induce the formation of pyramidine-pyramidine dimer (usually thiamine-thiamine dimer.

→ NER also repair the defect due to ionising radiation, cancer chemotherapeutic agents and variety of chemicals.

→ After defect recognition an excision nuclease (exonuclease) cut the DNA at 2 sides.

→ An oligonucleotide (approx 30 bases in length) is removed.

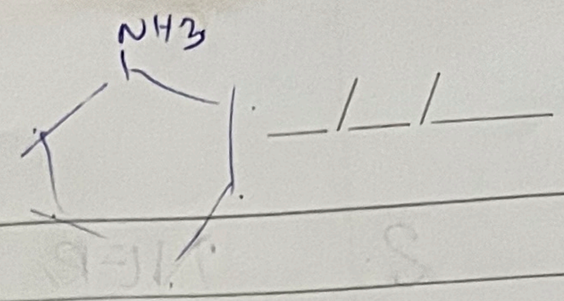
→ The gap is then filled by DNAP and religated.



TRANS-CRIPTION I

TCCAA

completes strand synthesis



3) BER

→ This repair mechanism corrects DNA damage from oxdn, deamination

Eg:- (Resulting from deamination of cytosine) and alkylation

→ Depurination is common & spontaneous damage occuring in DNA

This rep

→ N glycosilase recognise & remove the wrong base without altering the phosphodiester backbone. forming AP site. (A purinic or A pyramidinic)

→ AP endonuclease enzyme recognise the AP site & specifically cut the phosphodiester backbone. at 5' portion.

→ the gap is filled by DNAP and ligated by ligase enzyme

T C A 5'

A G T 3'

↓ spontaneous deamination

T U A

A G T

↓ Ukaii N-glycosylase

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TRANSLA-TION-II

T * A

A G T

↓ Apyrimidine endonuclease

T A

A G T

A

↓ DNAP + DNA ligase

T C A

A G T

TRANS-CRIPTION

Diseases associated with DNA repair

1. ~~Scbbt~~ Xerodeima pigmentosaum

⇝ Autosomal recessive

⇝ Defect in NER.

→ The ability to repair damage caused by UV light (T=T dimer) is deficient

→ Highly sensitive to sunlight (UV rays)

⇝ High risk of skin cancer

2. ~~Cccc~~ Cockayne syndrome

⇝ Autosomal recessive

⇝ Defect in NER.

→ Neurodegenerative disorder. Characterised by growth failure impaired develop of the nervous system.

⇝ Photosensitivity and eye disorders.

TCCAA

3 Ataxia - telangiectasia

→ AR
→ Ataxia (poor coordination)
→ telangiectasia (dilated blood vessels)
→ Caused by a defect in the ATMGr responsible for a protein required for DS Break Repair
→ ↑ sensitivity to damage by x rays
→ cerebellar ataxia and lymphoreticular neoplasma

4 Bloom syndrome

→ defect in DNA helicase.
→ disorder characterised by short stature, ↑ develop of cancer

5 Hereditary Non-polyposis (colorectal cancer)

→ Autosomal Dominant
→ Defect in DNA mismatched repair
→ High risk of choloncancer & endometrial cancer

6. Fanconi's Anemia

→ AR
→ Defective repair of cross-linking damage.
→ Anemia & ↑ frequency of cancer.

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Repair Mechanism

4. Double strand break repair

It repair DNA damage due to
- Ionizing radiation
- Free radical
- Chemotherapeutic agents

2 repair mechanism

(i) Homologous recombination:-
Joining of ends require sequence similarity

(ii) Non-homologous end joining:-
the break ends are directly ligated without the need for a homologous (sequence similarity) template