PIPADOR REVISION

MRCOG Part 1 Revision Notes

DNA Structure and Replication

MOLECULAR BIOLOGY • LECTURE 87

VISUAL EXAMINATION REVISION NOTES

2026 Edition

MRCOG Part 1 Revision Notes

Lecture 87: DNA Structure and Replication

Molecular biology • Visual revision edition

COLOUR CODE USED THROUGHOUT THESE NOTES

DNA / STRUCTURE	CHROMATIN / HISTONES	REPLICATION / REPAIR	MUTATION / DAMAGE	CLINICAL / DRUGS

LEARNING OBJECTIVES — tick off as you go

- ☐ Describe nucleotides, base pairing and the double helix.
- ☐ Outline the genome and chromatin packaging, including histone marks.
- ☐ Explain semi-conservative replication, the fork enzymes and telomeres.
- ☐ Match DNA repair pathways to the diseases caused when they fail.
- ☐ Classify mutations and link to drugs that target DNA (incl. PARP inhibitors).

1 DNA Structure

IN ONE LINE: *Two antiparallel sugar–phosphate strands, bases paired inside (A=T, G≡C), twisted into a right-handed helix. Avery (1944) showed DNA is the genetic material; Watson, Crick, Franklin and Wilkins solved the structure (1953).*

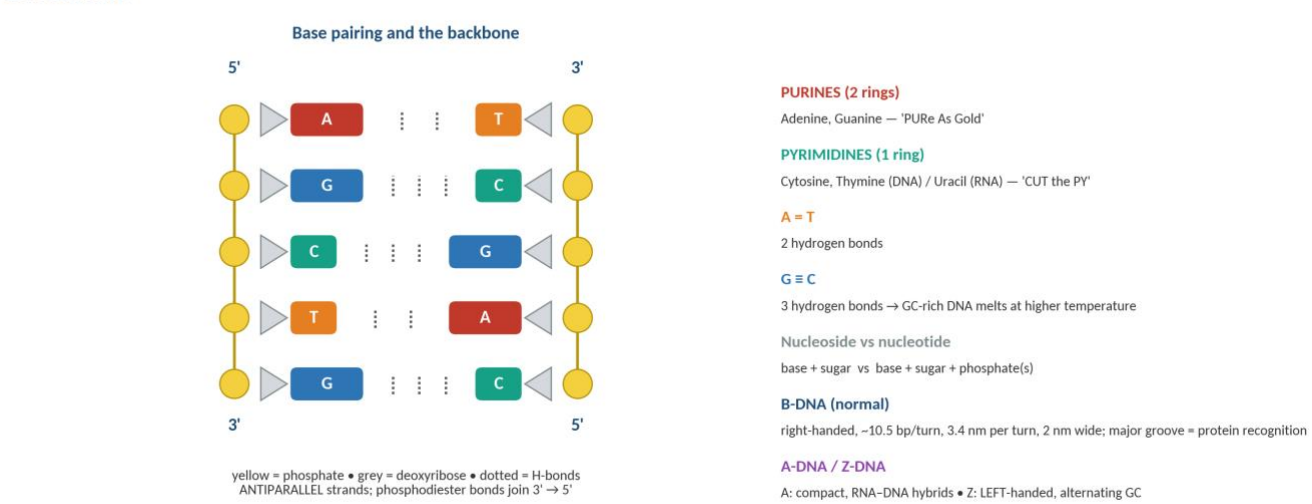


Figure 1. Base pairing and helix.

MNEMONIC / MEMORY HOOK

'PURe As Gold' (purines = A, G — two rings) • **'CUT the PY'** (pyrimidines = C, U, T — one ring).

2 Genome and Chromatin

Feature	Key points
Nuclear genome	~3.2 billion bp; 22 autosome pairs + XX/XY; ~20,000 protein-coding genes = ~1.5% of DNA
Mitochondrial genome	16,569 bp circle, 37 genes (Lecture 79)
Gene parts	Exons (coding), introns (spliced out), 5'/3' UTRs; promoters, enhancers, silencers, insulators
Repeats	Microsatellites (1–6 bp — QF-PCR, forensics, MSI), minisatellites, satellite (centromere); SINEs (Alu ~1 million copies), LINEs (L1)

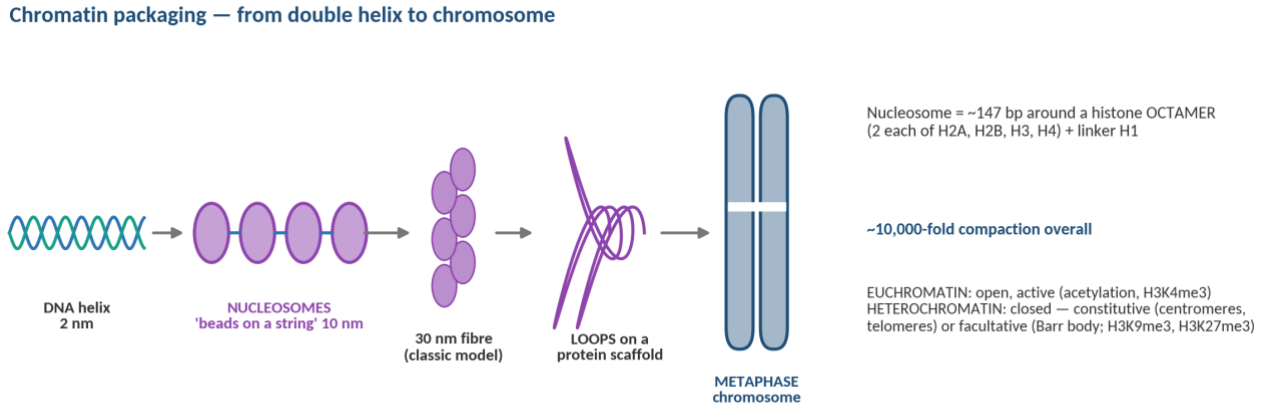


Figure 2. Chromatin packaging.

- The **30 nm fibre** is the textbook model; live-cell studies suggest chromatin is more irregular. **Histone code**: acetylation (H3K27ac) opens chromatin; H3K4me3 marks active promoters; H3K9me3 / H3K27me3 silence.

3 Replication

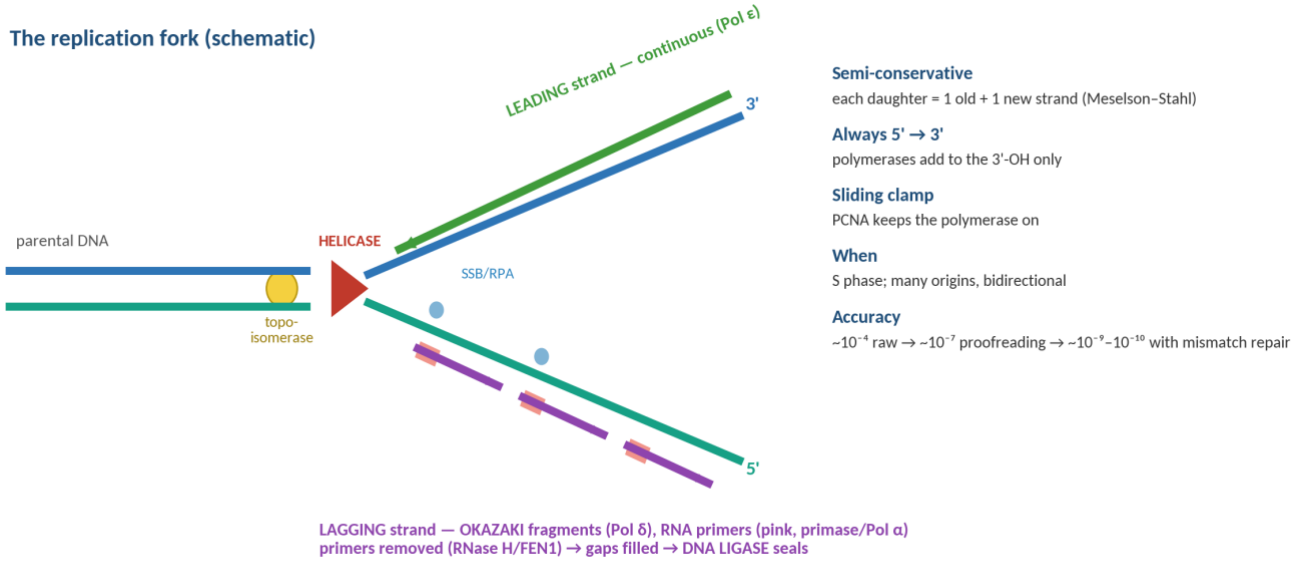


Figure 3. The replication fork.

Enzyme	Job
ORC + MCM helicase	Mark origins; unwind the helix
Topoisomerase	Relieve supercoiling ahead of the fork (target of etoposide, doxorubicin; bacterial gyrase → quinolones)
SSB / RPA	Keep single strands apart
Primase + Pol α	RNA primer + short DNA start
Pol ε / Pol δ	Leading / lagging strand; 3'→5' proofreading
PCNA	Sliding clamp
RNase H / FEN1 + ligase	Remove primers; seal Okazaki fragments

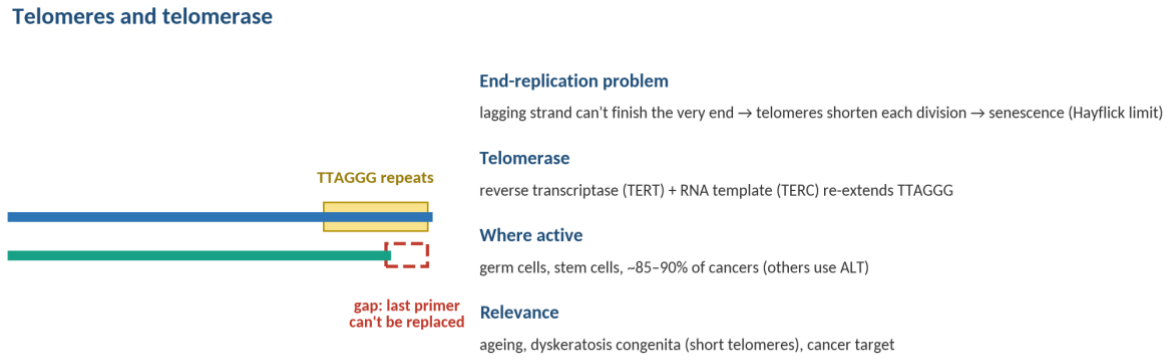


Figure 4. Telomeres.

4 DNA Repair

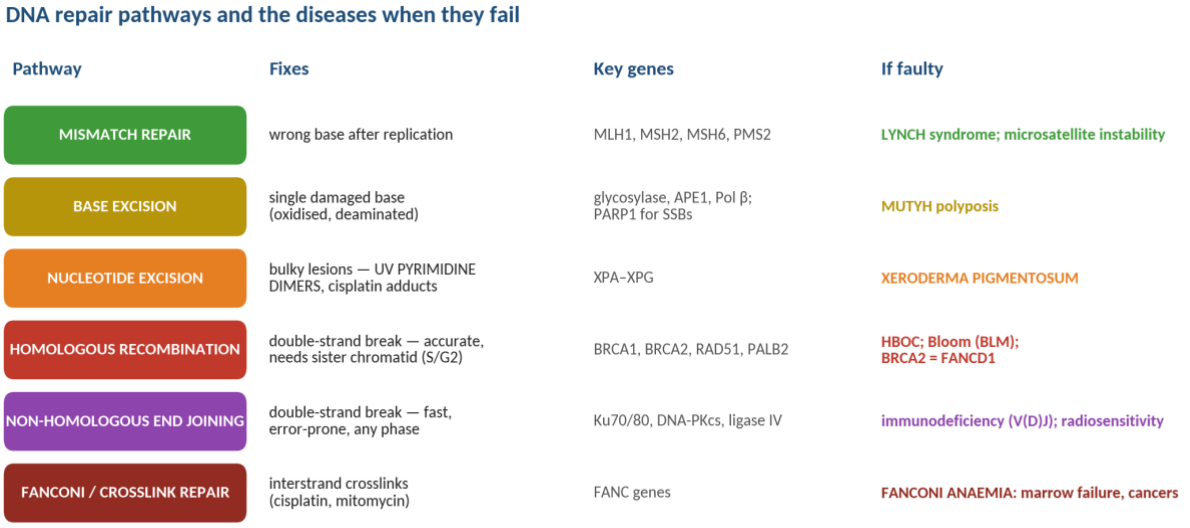


Figure 5. Repair pathways.

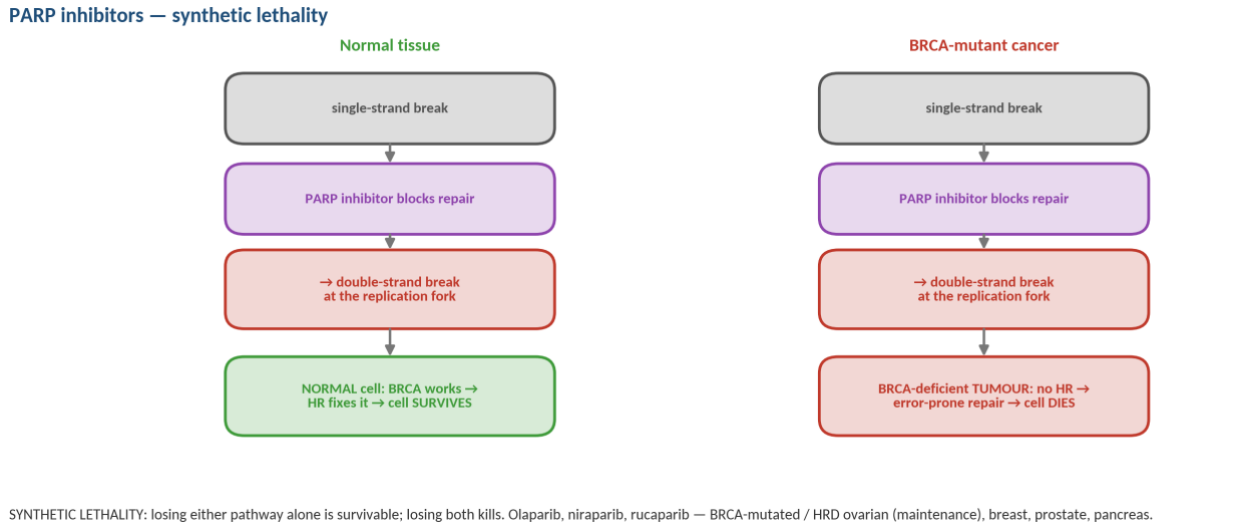


Figure 6. PARP inhibitors.

5 Mutations

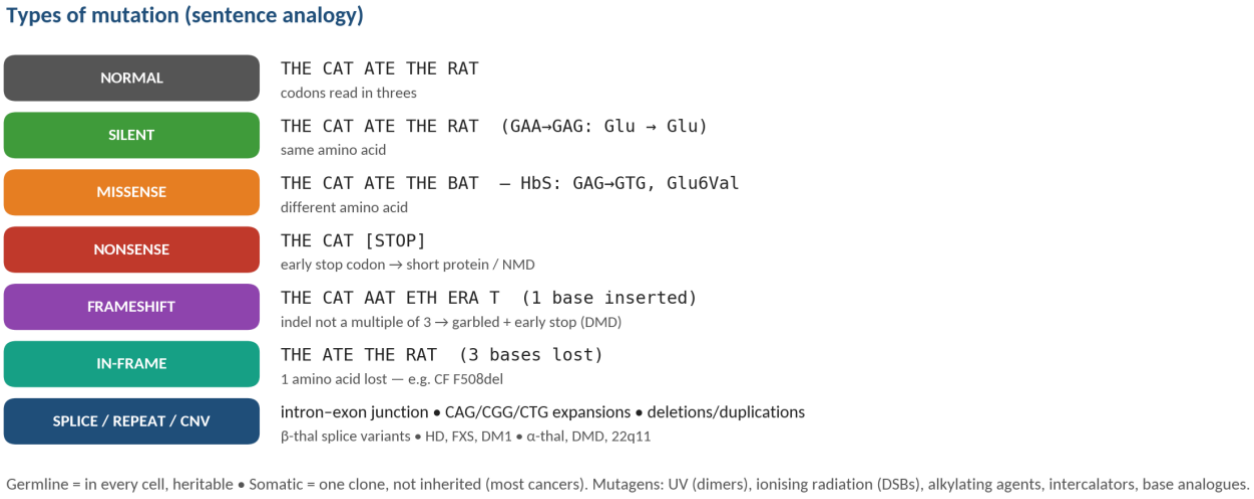


Figure 7. Mutation types.

6 Clinical Correlates

Drug	DNA mechanism / O&G use
Cisplatin / carboplatin	Cross-links DNA — ovarian, cervical, endometrial cancer; BRCA/HRD tumours more sensitive
Doxorubicin / etoposide	Topoisomerase II inhibitors (doxorubicin also intercalates) — sarcoma, GTN (EMA-CO)
Methotrexate	Dihydrofolate reductase inhibitor → stops nucleotide synthesis — ectopic pregnancy, GTN
5-Fluorouracil	Thymidylate synthase inhibitor — VIN/VAIN topical, GI cancers
PARP inhibitors	Olaparib, niraparib, rucaparib — maintenance in BRCA/HRD ovarian cancer
Quinolones / rifampicin	Bacterial DNA gyrase / bacterial RNA polymerase

★ PEARL

MMR → Lynch (MSI); NER → xeroderma pigmentosum; HR → BRCA; crosslink repair → Fanconi anaemia. PARP inhibitor + BRCA loss = synthetic lethality. Leading strand continuous, lagging strand in Okazaki fragments.

7 MRCOG Exam Pearls — Last-Minute Page

Numbers to know

2 / 3 H-bonds A=T / G≡C	**~10.5** bp per turn (B-DNA)	**2 nm** Helix width	**~3.2×10^9** bp in genome
~20,000 Protein-coding genes	**~147 bp** DNA per nucleosome	**~10^{-9}–10^{-10}** Final error rate	**TTAGGG** Telomere repeat

HIGH-YIELD CHECKLIST

- ☐ Purines A, G; pyrimidines C, T, U; A=T (2), G≡C (3).
- ☐ Antiparallel, right-handed B-DNA; major groove for proteins.
- ☐ ~3.2 Gb, ~20,000 genes (~1.5% coding); Alu, LINEs, microsatellites.
- ☐ Nucleosome: octamer (2× H2A, H2B, H3, H4) + H1; ~147 bp.
- ☐ Acetylation opens; H3K9me3/H3K27me3 close.
- ☐ Semi-conservative; leading (ε) vs lagging (δ, Okazaki); ligase; PCNA.
- ☐ Telomerase: germ/stem/cancer cells.
- ☐ Repair pathways ↔ Lynch, XP, BRCA, Fanconi, Bloom.
- ☐ Mutations: silent, missense (HbS), nonsense, frameshift, in-frame (F508del), splice, repeat, CNV.
- ☐ Drugs: platinum, topo II inhibitors, methotrexate, PARP inhibitors.

Self-assessment — cover the right-hand column

Question	Answer
Which bases are purines?	Adenine and guanine
Why is GC-rich DNA more stable?	Three hydrogen bonds per G–C pair
Composition of the histone octamer?	Two each of H2A, H2B, H3 and H4
What does 'semi-conservative' mean?	Each daughter helix has one old and one new strand
Which strand is made in Okazaki fragments?	The lagging strand
Enzyme that seals Okazaki fragments?	DNA ligase
What does telomerase use as a template?	Its own RNA component (TERC)
Repair pathway defective in xeroderma pigmentosum?	Nucleotide excision repair
Type of mutation in sickle cell (HbS)?	Missense (Glu6Val)
Why do PARP inhibitors kill BRCA-mutant cells?	Synthetic lethality — no homologous recombination back-up

8 References

- Alberts B et al. Molecular Biology of the Cell. 7th ed. 2022.
- Turnpenny P, Ellard S. Emery's Elements of Medical Genetics. 16th ed. 2021.
- Lord CJ, Ashworth A. PARP inhibitors: synthetic lethality in the clinic. Science 2017.