PIPADOR REVISION

MRCOG Part 1 Revision Notes

Cell Cycle Control and Development of Cancer

BIOCHEMISTRY • LECTURE 211

VISUAL EXAMINATION REVISION NOTES

2026 Edition

MRCOG PART 1 REVISION NOTES | BIOCHEMISTRY

211 Cell Cycle Control and Development of Cancer

Cell cycle and checkpoints, apoptosis, oncogenes, tumour suppressors and DNA repair genes, carcinogenesis and therapy

G1/S	p53	2 hits	1 hit
Restriction point (Rb–E2F)	'Guardian of the genome'	Tumour suppressor inactivation (Knudson)	Oncogene activation (gain of function)

■ KEY FACTS: Learning objectives

- Describe the phases of the cell cycle, cyclins/CDKs and checkpoints.
- Describe apoptosis and the regulation of cell number.
- Describe oncogenes, tumour suppressor genes, DNA repair genes and the hallmarks of cancer.
- Apply these to gynaecological cancers (HPV/cervix, BRCA/ovary, Lynch/endometrium) and to cytotoxic drugs.

211.1 The cell cycle

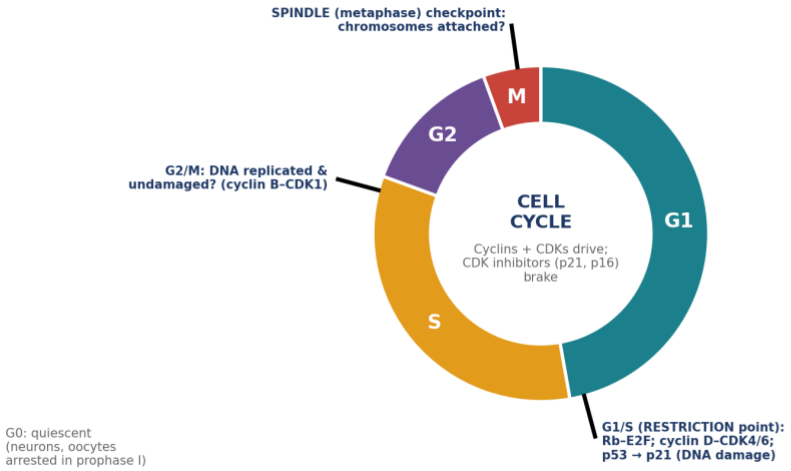


Figure 211.1 — Cell cycle phases and checkpoints

Phase	Events	Control
G1	Growth, preparation; decision to divide	Cyclin D–CDK4/6 phosphorylates Rb → releases E2F → S-phase genes; CDK inhibitors p16 (INK4a), p21 (induced by p53)
S	DNA replication	Cyclin E/A–CDK2
G2	Check replication; prepare for mitosis	Cyclin A/B–CDK1; DNA damage checkpoint (ATM/ATR, CHK1/2)
M	Mitosis (prophase → metaphase → anaphase → telophase) + cytokinesis	Cyclin B–CDK1; spindle assembly checkpoint (APC/C)
G0	Quiescence / terminal differentiation	Neurons, cardiomyocytes; oocytes arrested in prophase I

211.2 Apoptosis

Pathway	Mechanism
Intrinsic (mitochondrial)	DNA damage/stress → p53 → BAX/BAK (pro-) vs BCL-2 (anti-) → cytochrome c release → apoptosome → caspase-9 → caspase-3
Extrinsic (death receptor)	FasL/TNF → death receptors → caspase-8 → caspase-3
Features	Cell shrinkage, chromatin condensation, blebbing, apoptotic bodies, no inflammation (vs necrosis); phosphatidylserine exposure → phagocytosis
Reproductive examples	Follicular atresia, luteolysis, endometrial shedding, Müllerian regression (AMH), syncytiotrophoblast turnover

211.3 Genes in cancer

Class	Behaviour	Examples (gynaecological relevance)
Proto-oncogenes → oncogenes	Gain of function; dominant (one hit)	KRAS (mucinous/low-grade serous ovarian), HER2/ERBB2 (breast; serous endometrial), PIK3CA (endometrial, ovarian clear cell), MYC, BRAF
Tumour suppressor genes	Loss of function; recessive at cell level — two hits (Knudson)	TP53 (high-grade serous ovarian ≈ 96%; serous endometrial), RB1, PTEN (endometrioid endometrial), ARID1A (clear cell/endometrioid, endometriosis-associated), CDKN2A (p16)
DNA repair (caretaker) genes	Loss → genomic instability	BRCA1/2 (homologous recombination — ovarian, breast; PARP inhibitor sensitivity — synthetic lethality); mismatch repair MLH1, MSH2, MSH6, PMS2 (Lynch syndrome — endometrial, colorectal, ovarian; microsatellite instability)

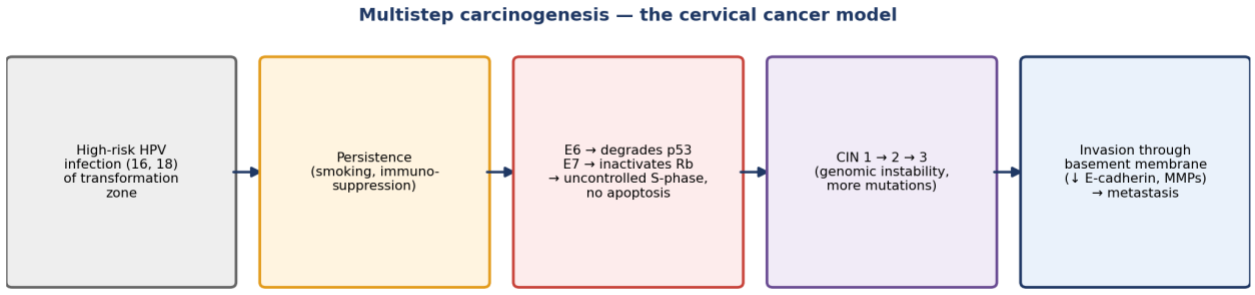
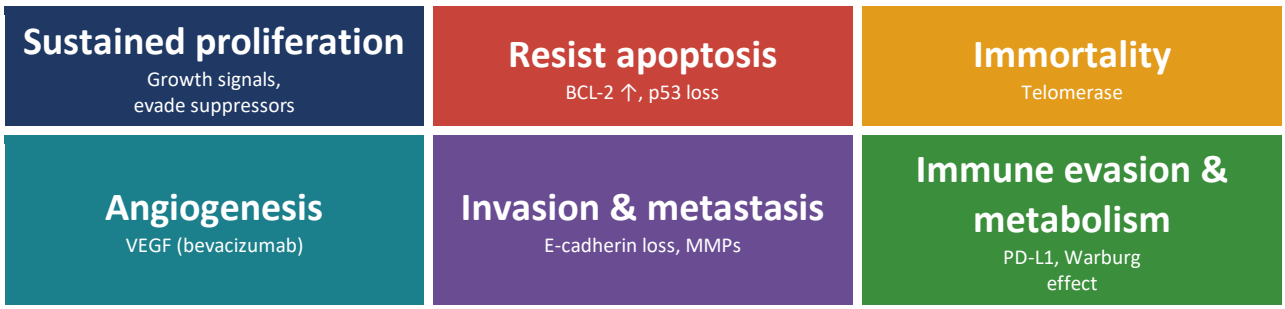


Figure 211.2 — Multistep carcinogenesis in the cervix



211.4 Cell-cycle-targeted therapy

Drug	Phase / target	Use in O&G
Platinum (carboplatin, cisplatin)	DNA cross-links (cell-cycle non-specific)	Ovarian, cervical (chemoradiation), endometrial

Drug	Phase / target	Use in O&G
Taxanes (paclitaxel)	M phase — stabilise microtubules	Ovarian, endometrial, cervical
Methotrexate	S phase — dihydrofolate reductase	Ectopic pregnancy, low-risk GTN
Actinomycin D, etoposide	Transcription / topoisomerase II	GTN (EMA-CO)
PARP inhibitors (olaparib, niraparib)	Synthetic lethality with HR deficiency	BRCA-mutated / HRD ovarian cancer maintenance
CDK4/6 inhibitors (palbociclib)	G1 arrest	ER+ breast cancer
Immune checkpoint inhibitors (pembrolizumab, dostarlimab)	PD-1	MMR-deficient endometrial, cervical cancer

211.5 Must-know summary

■ EXAM TIP

- G1/S restriction point: **cyclin D–CDK4/6 phosphorylates Rb → E2F**; p53 → p21 arrests damaged cells.
- Oncogenes = one hit gain of function (KRAS, HER2); tumour suppressors = two hits (TP53, RB1, PTEN); caretakers = DNA repair (BRCA, MMR).
- **HPV E6 → p53 degradation; E7 → Rb inactivation**.
- HGSOC ≈ TP53; endometrioid endometrial ≈ PTEN; Lynch = MMR; BRCA → PARP inhibitors.
- Methotrexate (S phase) for ectopic; taxanes (M phase).

■ MNEMONIC / MEMORY AID

HPV — 'E6 Sinks p53, E7 Severs Rb'. Lynch genes — 'MLH1, MSH2, MSH6, PMS2'.