PIPADOR REVISION

MRCOG Part 1 Revision Notes

Cell Surface Receptors

BIOCHEMISTRY • LECTURE 206

VISUAL EXAMINATION REVISION NOTES

2026 Edition

206

MRCOG PART 1 REVISION NOTES | BIOCHEMISTRY

Cell Surface Receptors

Receptor families, G-protein-coupled receptors and the G-protein cycle, Gs/Gi/Gq pathways, regulation and disorders

7-TM	≈ 30–40%	Gs / Gi / Gq	4 classes
GPCR — largest receptor family	Of drugs target GPCRs	Main α-subunit classes	Surface receptors: GPCR, RTK, JAK–STAT, ion channel

■ KEY FACTS: Learning objectives

- Classify cell surface receptors: G-protein-coupled, ion channel-linked, enzyme-linked (receptor tyrosine kinase, serine/threonine kinase, guanylyl cyclase) and cytokine (JAK–STAT).
- Describe GPCR structure, the G-protein cycle and the main G-protein pathways.
- Describe receptor regulation and disorders, with obstetric pharmacology.

206.1 Families of cell surface receptors

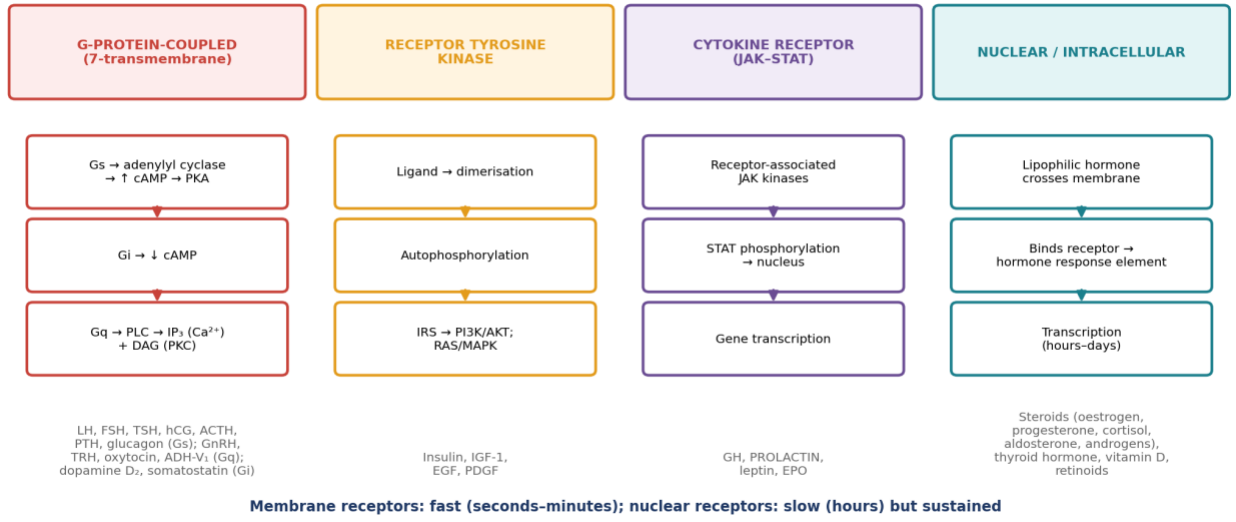


Figure 206.1 — Receptor families and signalling pathways

Receptor class	Mechanism	Examples
Ion channel-linked (ionotropic)	Ligand opens a channel — milliseconds	Nicotinic ACh (NMJ), GABA-A (benzodiazepines, allopregnanolone), NMDA (Mg^{2+} block), 5-HT_3 (ondansetron)
G-protein-coupled (7-TM)	G protein → second messengers	LH, FSH, TSH, hCG, oxytocin, ADH, GnRH, adrenergic, muscarinic, dopamine, prostaglandin, opioid receptors
Receptor tyrosine kinase	Dimerisation, autophosphorylation → PI3K/AKT, RAS/MAPK	Insulin, IGF-1, EGF, VEGF, PDGF; HER2 (trastuzumab)
Cytokine receptors (JAK–STAT)	Associated JAK kinases → STATs	GH, prolactin, EPO, leptin, interferons, interleukins
Serine/threonine kinase	SMAD phosphorylation	TGF-β family: activin, inhibin (antagonist), AMH, BMPs
Guanylyl cyclase	Membrane (ANP/BNP) or soluble (NO) → cGMP	ANP; NO (GTN, sildenafil via PDE5)

206.2 G-protein-coupled receptors

A single polypeptide crossing the membrane **seven times** (N-terminus outside, C-terminus inside). Ligand binding to the extracellular/transmembrane pocket changes conformation, allowing coupling to a **heterotrimeric G protein (α, β, γ)**. The glycoprotein hormone receptors (LH/hCG, FSH, TSH) have large extracellular leucine-rich domains for ligand binding.

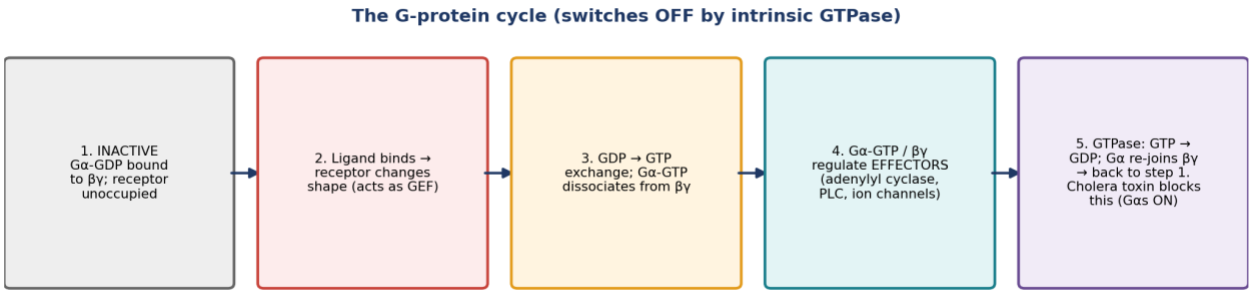


Figure 206.2 — The G-protein cycle

Gα class	Effector	Second messenger	Receptor examples (O&G)
Gαs	↑ Adenylyl cyclase	↑ cAMP → PKA	LH/hCG, FSH, TSH, ACTH, β_1/β_2 (terbutaline tocolysis), ADH-V_2, PGE_2-EP2/EP4 (cervical ripening), CRH
Gαi	↓ Adenylyl cyclase; opens K^+ channels	↓ cAMP	Dopamine D_2 (prolactin inhibition — cabergoline), α_2 (methyldopa), M_2 (heart), opioid, somatostatin
Gαq	Phospholipase C-β	IP_3 (Ca^{2+}) + DAG (PKC)	Oxytocin, $PGF_2\alpha$ (FP), GnRH, TRH, α_1 (phenylephrine), ADH-V_1, M_3, angiotensin II (AT_1)
βγ subunits	K^+ channels, PI3K	—	Vagal slowing of heart (GIRK)

206.3 Regulation and disorders

Process / disorder	Mechanism / example
Desensitisation	GRKs phosphorylate occupied receptor → β-arrestin uncouples and internalises — tachyphylaxis to β-agonist tocolysis; prolonged oxytocin infusion ↓ receptor responsiveness (PPH after long augmentation)
Downregulation	Continuous GnRH agonist → loss of pituitary GnRH receptors
Activating mutations	McCune–Albright (Gsα, mosaic) — precocious puberty; LH receptor activating mutation (familial male precocious puberty); TSH receptor (toxic adenoma)
Inactivating mutations	Nephrogenic DI (V_2), Leydig cell hypoplasia (LHR), FSHR mutations (ovarian dysgenesis), pseudohypoparathyroidism (Gsα)
Autoantibodies	TRAb stimulate TSHR (Graves'); AT_1 receptor agonistic antibodies (pre-eclampsia)
Bacterial toxins	Cholera toxin (Gαs permanently active → cAMP → secretory diarrhoea); pertussis toxin (blocks Gαi)

206.4 Must-know summary

■ EXAM TIP

- Surface receptors: **ion channel, GPCR, RTK, JAK–STAT, Ser/Thr kinase (TGF-β), guanylyl cyclase**.
- GPCR = 7-TM; heterotrimeric G protein; **GTPase** switches off.
- **Gs → cAMP** (LH, FSH, TSH, hCG, β_2); **Gi → ↓ cAMP** (D_2, α_2); **Gq → IP_3/DAG/Ca^{2+}** (oxytocin, $PGF_2\alpha$, GnRH, α_1).
- Insulin/IGF = RTK; GH/prolactin = JAK–STAT; activin/AMH = SMAD.
- Desensitisation (β-arrestin), downregulation (GnRH agonists); McCune–Albright, cholera toxin.

■ MNEMONIC / MEMORY AID

'QISS QIQ SI QS QS': α_1 q, α_2 i, β_1 s, β_2 s; M_1 q, M_2 i, M_3 q; D_1 s, D_2 i; H_1 q, H_2 s; V_1 q, V_2 s.