PIPADOR REVISION

MRCOG Part 1 Revision Notes

Activin

ENDOCRINOLOGY • LECTURE 175

VISUAL EXAMINATION REVISION NOTES

2026 Edition

MRCOG PART 1 REVISION NOTES | ENDOCRINOLOGY

175 Activin

TGF-β superfamily, receptors and SMAD signalling, actions in reproduction and pregnancy, and clinical correlations

β + β	↑ FSH	Follistatin	SMAD2/3
Homo/heterodimers (βA, βB)	Pituitary action	Binding protein — neutralises activin	Intracellular signalling

■ KEY FACTS: Learning objectives

- Describe the structure of activins and their place in the TGF-β superfamily.
- Describe activin receptors, SMAD signalling and the roles of follistatin and inhibin.
- Describe the actions of activin in the pituitary, ovary, endometrium, pregnancy and non-reproductive tissues.
- Relate activin to pre-eclampsia, preterm labour and emerging therapeutics.

175.1 The TGF-β superfamily

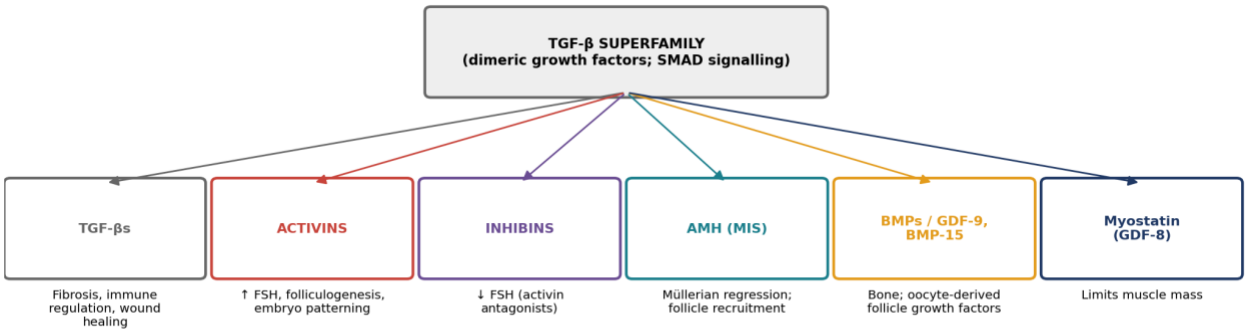


Figure 175.1 — Reproductively important members of the TGF-β superfamily

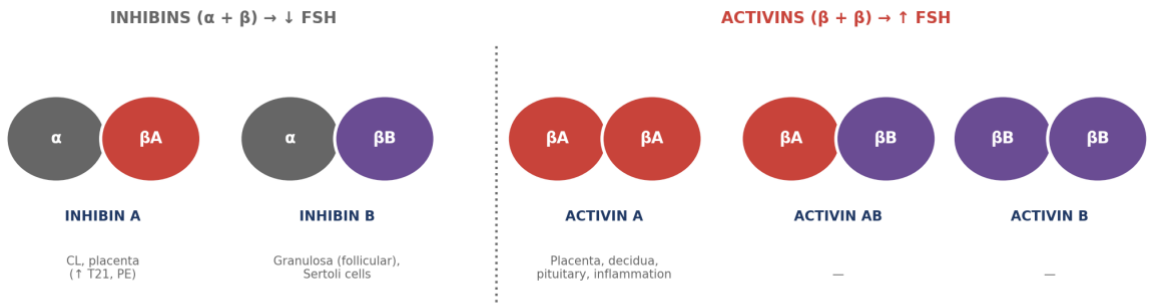


Figure 175.2 — Activins (β + β) compared with inhibins (α + β)

Activin	Subunits	Notes
Activin A	βA–βA	Most studied; placenta, decidua, ovary, pituitary, inflammatory cells, bone marrow
Activin AB	βA–βB	—
Activin B	βB–βB	Ovary, pituitary

175.2 Receptors and signalling

Activin binds **type II receptor** (ActRII / ActRIIB — serine/threonine kinase) ▶ Recruits & phosphorylates **type I receptor** (ALK4 — ActRIB) ▶ **SMAD2/3** phosphorylated → complex with **SMAD4** ▶ Nuclear translocation → **gene transcription** (e.g. FSHβ) ▶ Antagonists: **follistatin** (binds activin), **inhibin** (blocks ActRII via betaglycan), inhibitory SMAD7

175.3 Actions

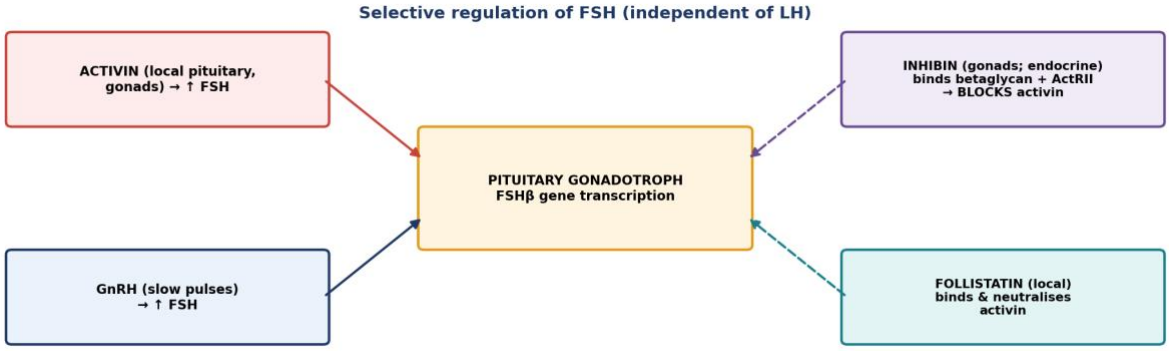


Figure 175.3 — Activin, inhibin and follistatin in FSH regulation

Site	Actions of activin
Pituitary	Originally isolated as an FSH-releasing protein — ↑ FSHβ transcription (autocrine/paracrine), ↑ GnRH receptor expression; opposed by follistatin and gonadal inhibin
Ovary	↑ Granulosa proliferation, FSH receptor and aromatase expression; ↓ theca androgen production; ↓ premature luteinisation; promotes oocyte maturation — supports follicular development
Endometrium	Decidualisation, endometrial repair after menstruation; implicated in endometriosis
Placenta / pregnancy	Activin A from placenta, decidua and membranes rises with gestation; modulates hCG and progesterone production, trophoblast invasion
Embryo	Mesoderm induction, left–right patterning (Nodal related)
Other	Erythropoiesis (first called erythroid differentiation factor), wound healing, fibrosis, inflammation (acute-phase rise in sepsis), muscle mass (with myostatin), bone

175.4 Clinical correlations

Condition	Activin link
Pre-eclampsia	Activin A (and inhibin A) markedly ↑ — placental hypoxia/oxidative stress, endothelial dysfunction; research biomarker
Preterm labour / infection	Activin A ↑ in amniotic fluid and maternal serum with intra-amniotic inflammation
Menopause transition	Loss of inhibin with relatively preserved activin/follistatin balance contributes to the monotropic FSH rise
PCOS	Altered activin/follistatin ratio proposed (↑ follistatin → arrested follicles) — inconsistent
Granulosa cell tumours	Dysregulated TGF-β/activin signalling (inhibin-α loss in mouse models; FOXL2 mutation in humans)

Condition	Activin link
Therapeutics	Activin ligand traps: luspatercept (anaemia in β-thalassaemia/MDS — promotes late erythropoiesis), sotatercept (pulmonary arterial hypertension); myostatin/activin blockade studied for muscle wasting

Feature	Activin	Inhibin
Structure	β + β	α + β
Effect on FSH	↑	↓
Mode	Mainly autocrine/paracrine	Mainly endocrine (gonads → pituitary)
Binding protein / antagonist	Follistatin	Betaglycan co-receptor
Pregnancy	↑; ↑↑ in pre-eclampsia	Inhibin A ↑ in trisomy 21 and pre-eclampsia

175.5 Must-know summary

■ EXAM TIP

- Activins are **β–β dimers** (TGF-β family); inhibins share the β-subunit with an α-subunit.
- Signalling: ActRII → ALK4 → **SMAD2/3 + SMAD4**; neutralised by **follistatin**, antagonised by **inhibin**.
- **↑ FSH** synthesis; supports granulosa proliferation, FSH receptor and aromatase expression.
- Activin A ↑ in **pre-eclampsia** and intra-amniotic infection; activin ligand traps (luspatercept, sotatercept) are licensed drugs.

■ MNEMONIC / MEMORY AID

'Activin Activates FSH; Inhibin Inhibits FSH; Follistatin Freezes activin'.