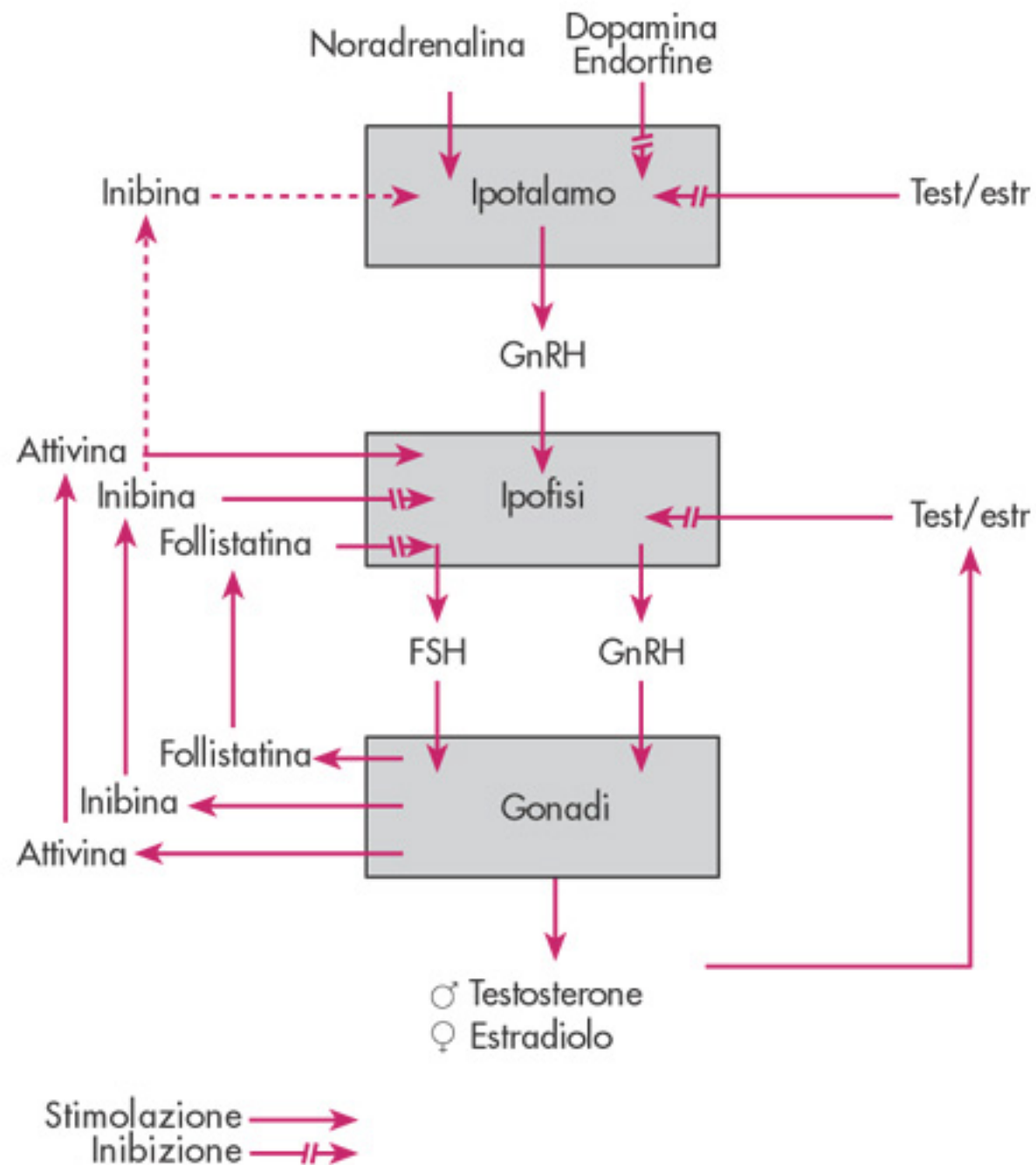
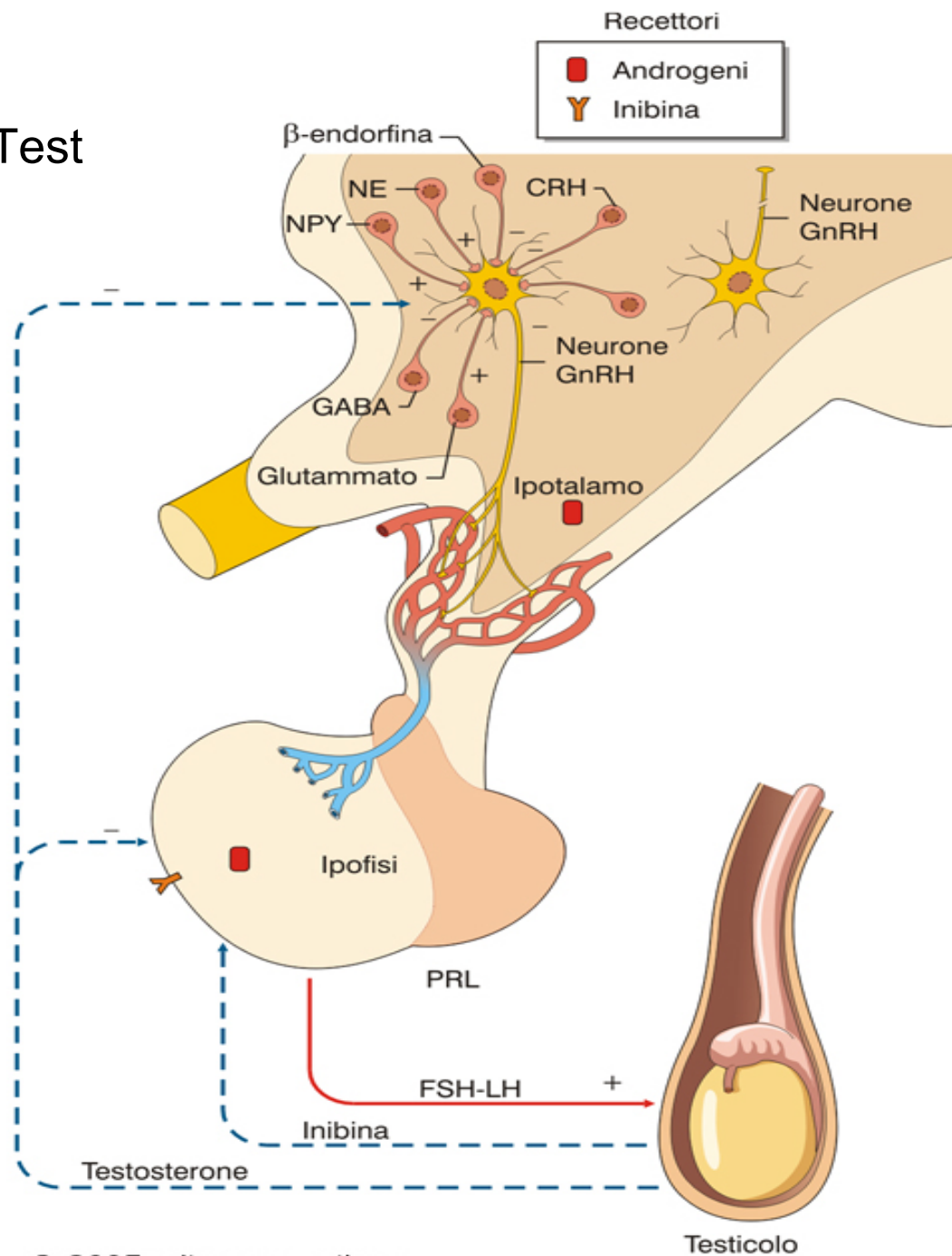


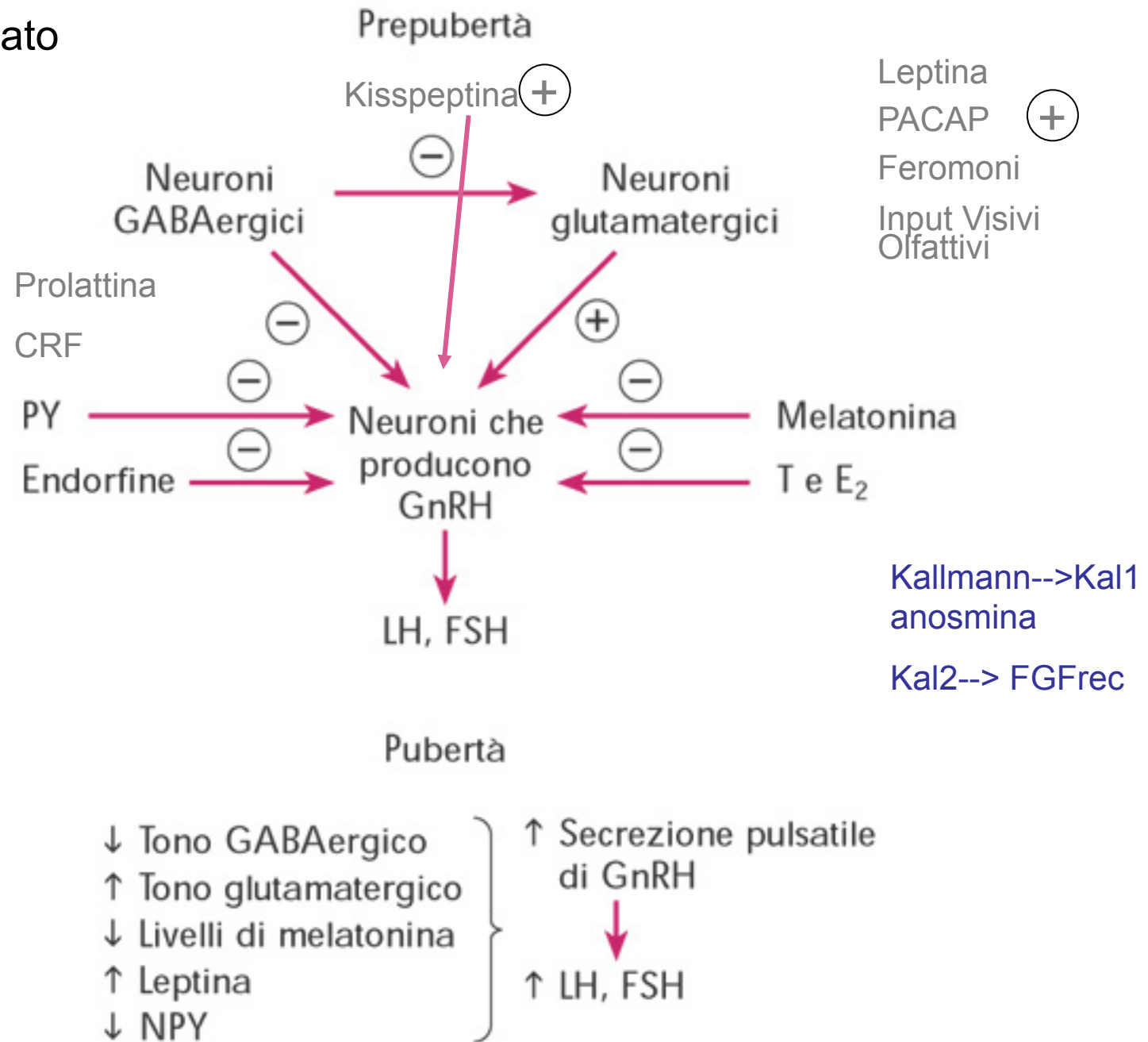
Asse HPG



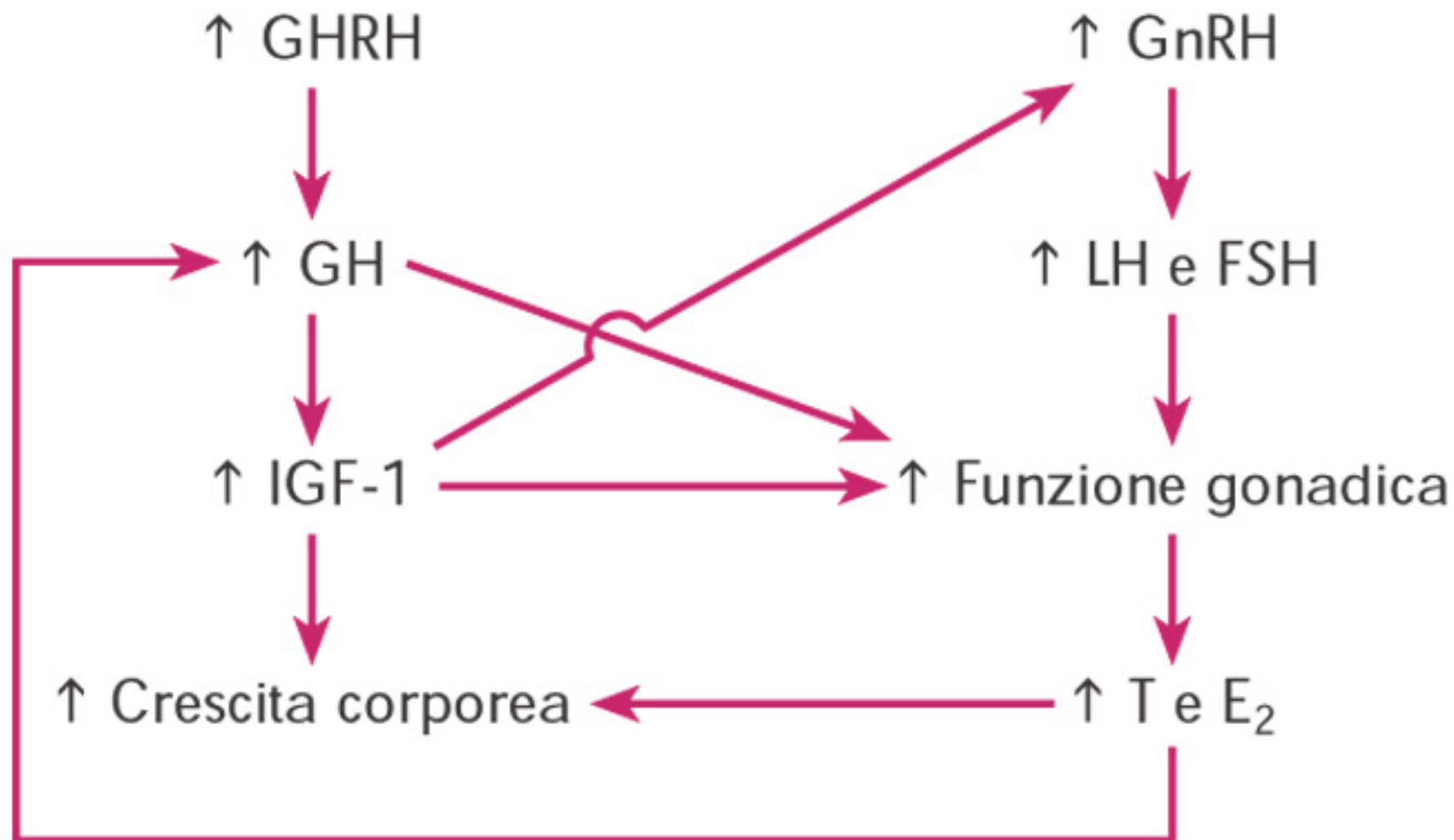
Asse Ipot-Ipof-Test

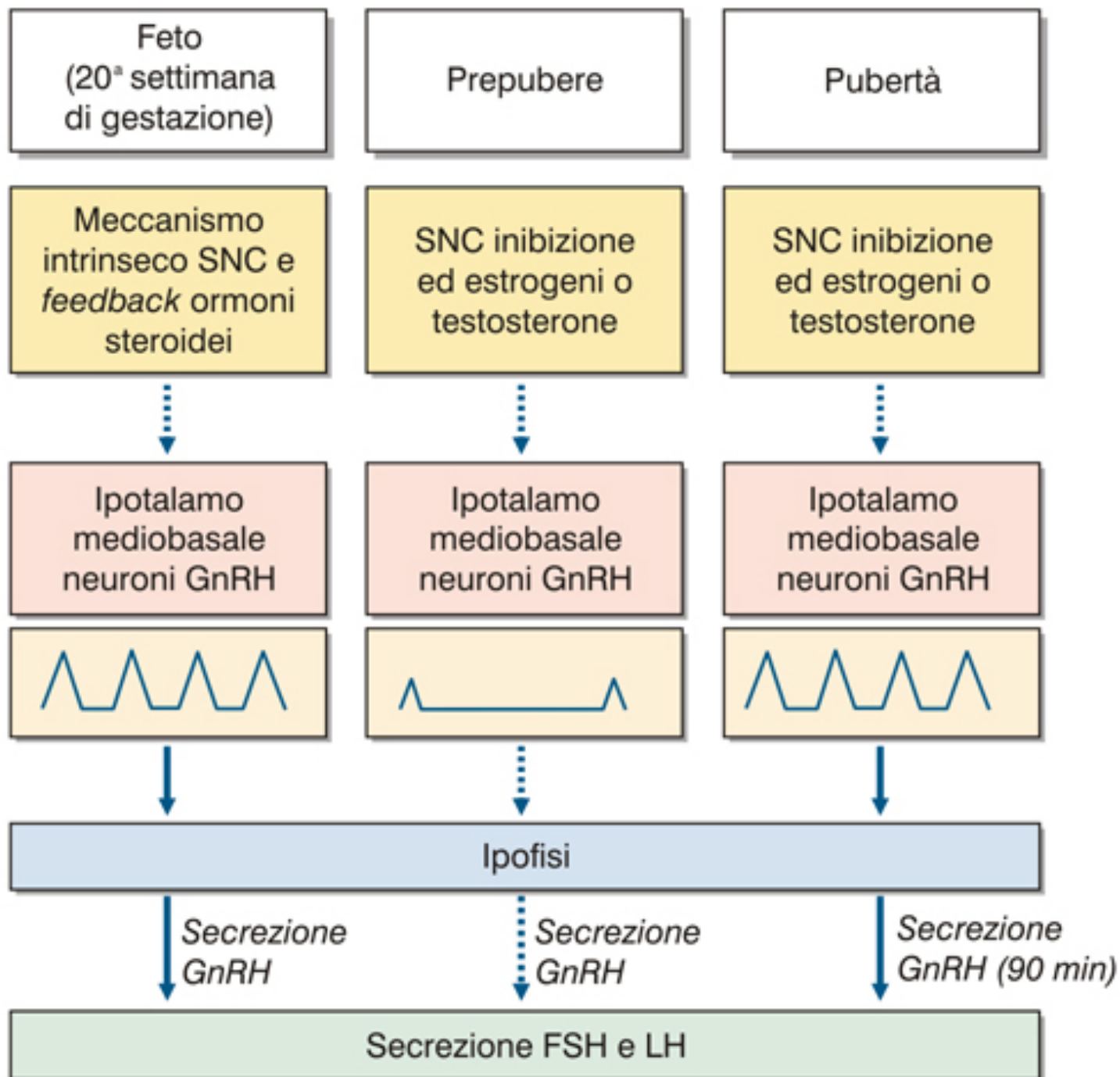


Nucleo arcuato



Sinergismo ormonale





GnRH



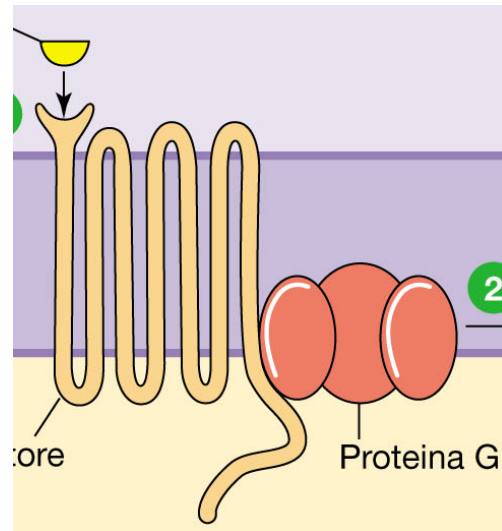
Pyro-Glu-His-Trp-Ser-Tyr-Gly-Leu-Arg-Pro-Gly-CO-NH₂

10 aa

(Chr 8, 4 esoni)

Ipotalamo nucleo arcuato

Gonadi Placenta



Recettore 7DTM Gq PI DAG

Chr 14 diversi esoni

2 splicing alternativi (corta
fungerebbe da inibitore)

GnRHR1
GnRHR2

SNC

Ipofisi

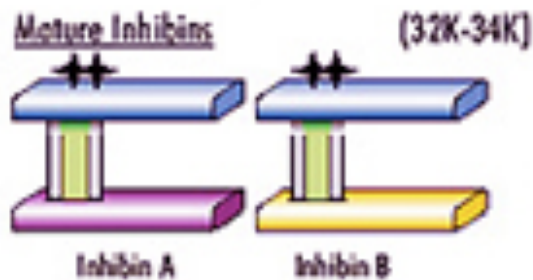
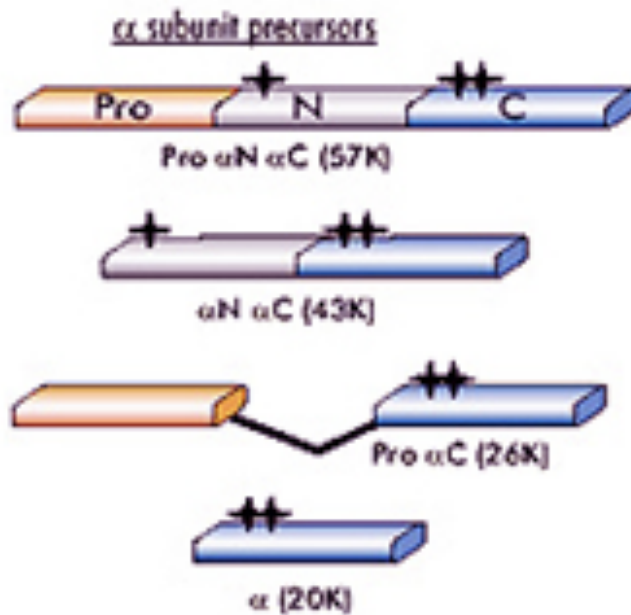
Gonadi Ghiandole mammarie

Intestino

Tumori etc

Various molecular forms of inhibins and activins

Chr2

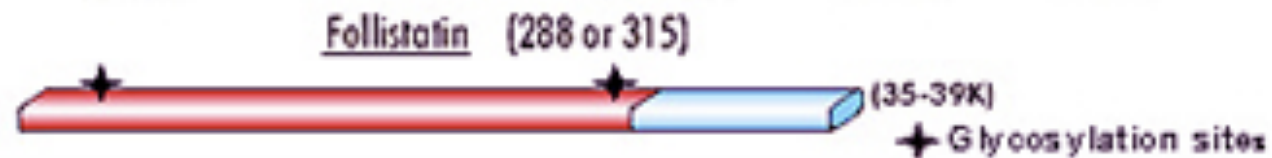
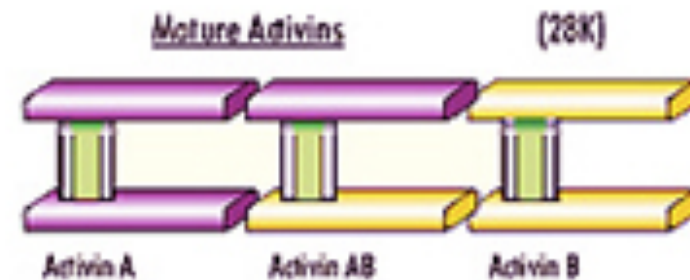


β subunit precursors



Chr7

Chr2



Chr5

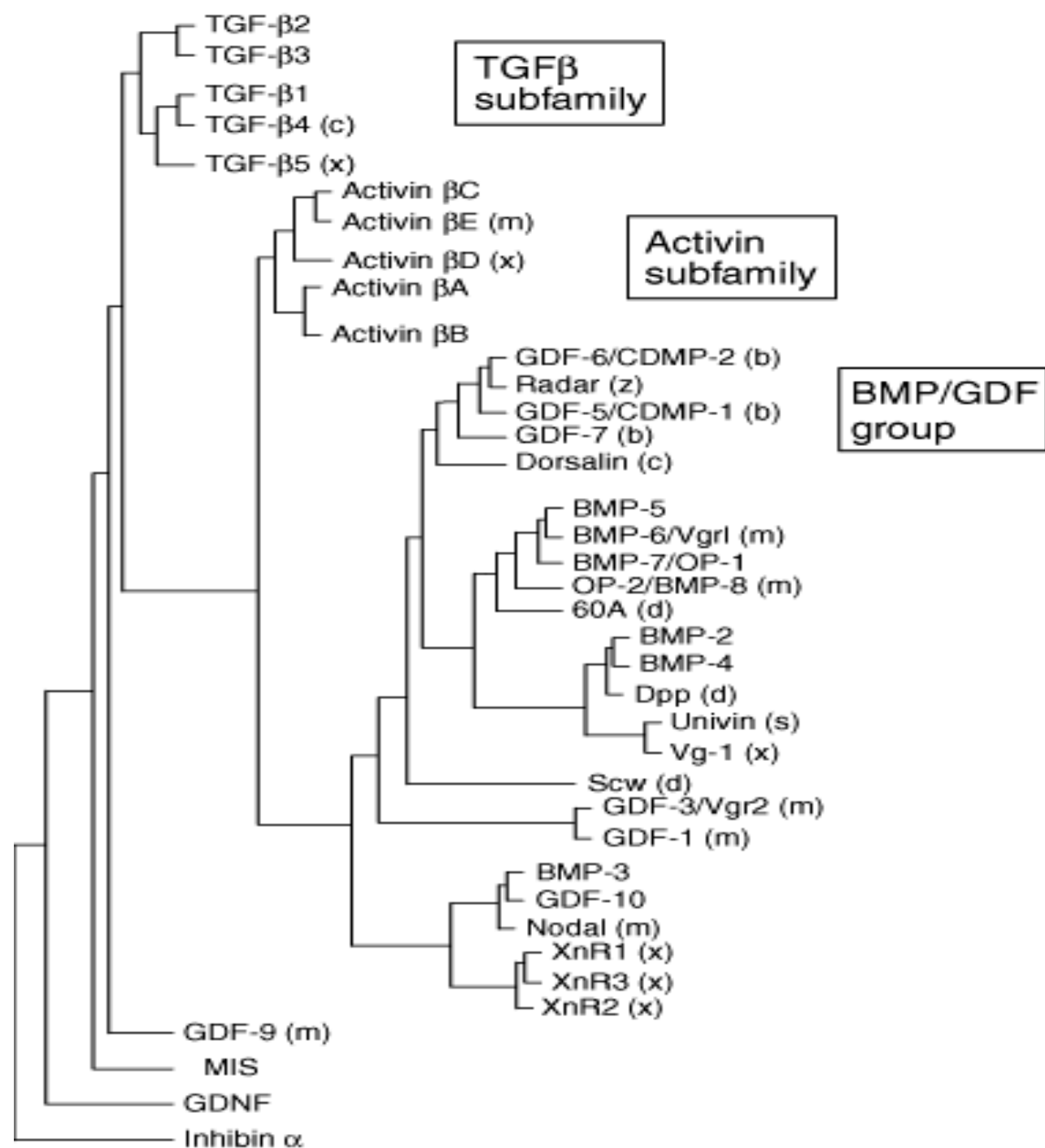
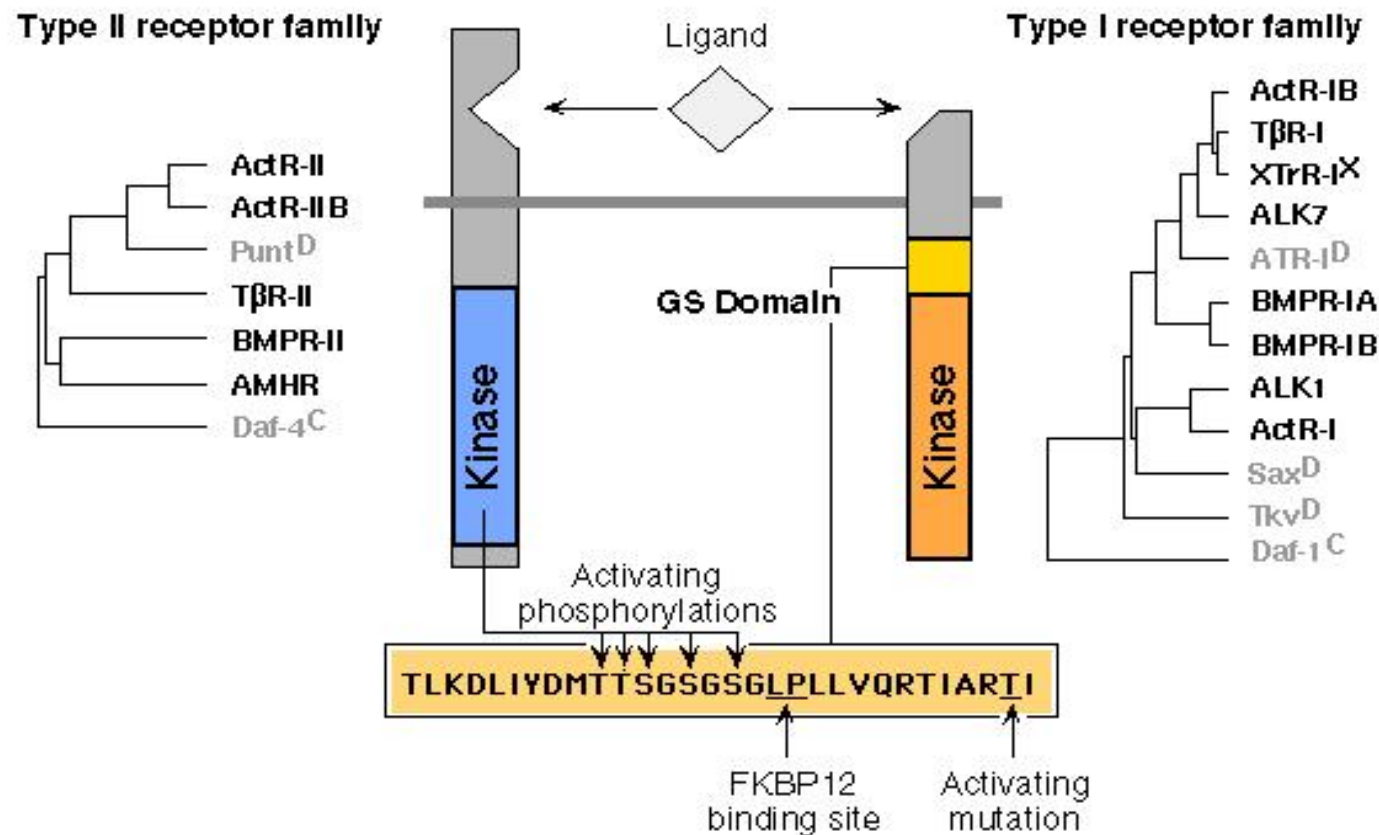
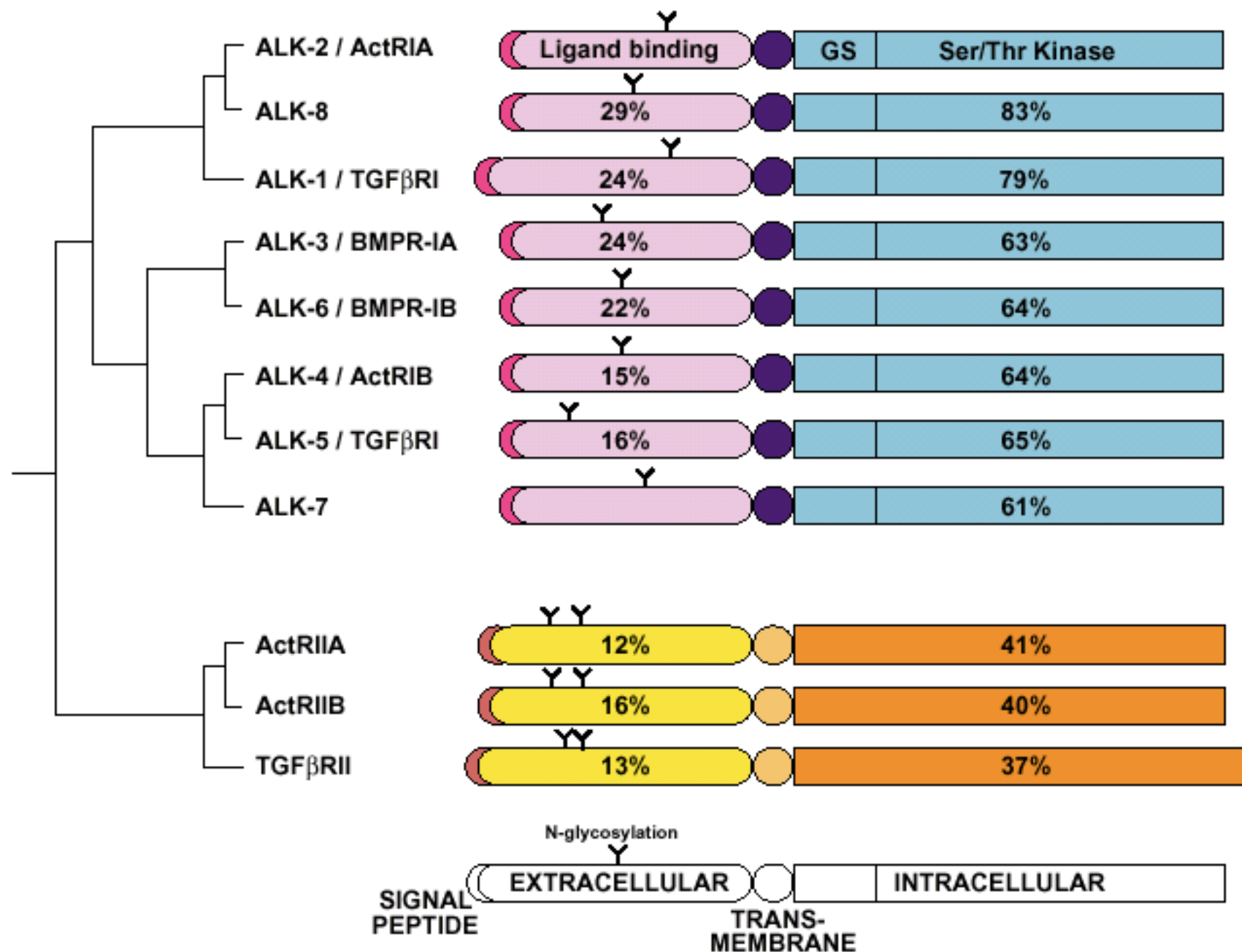


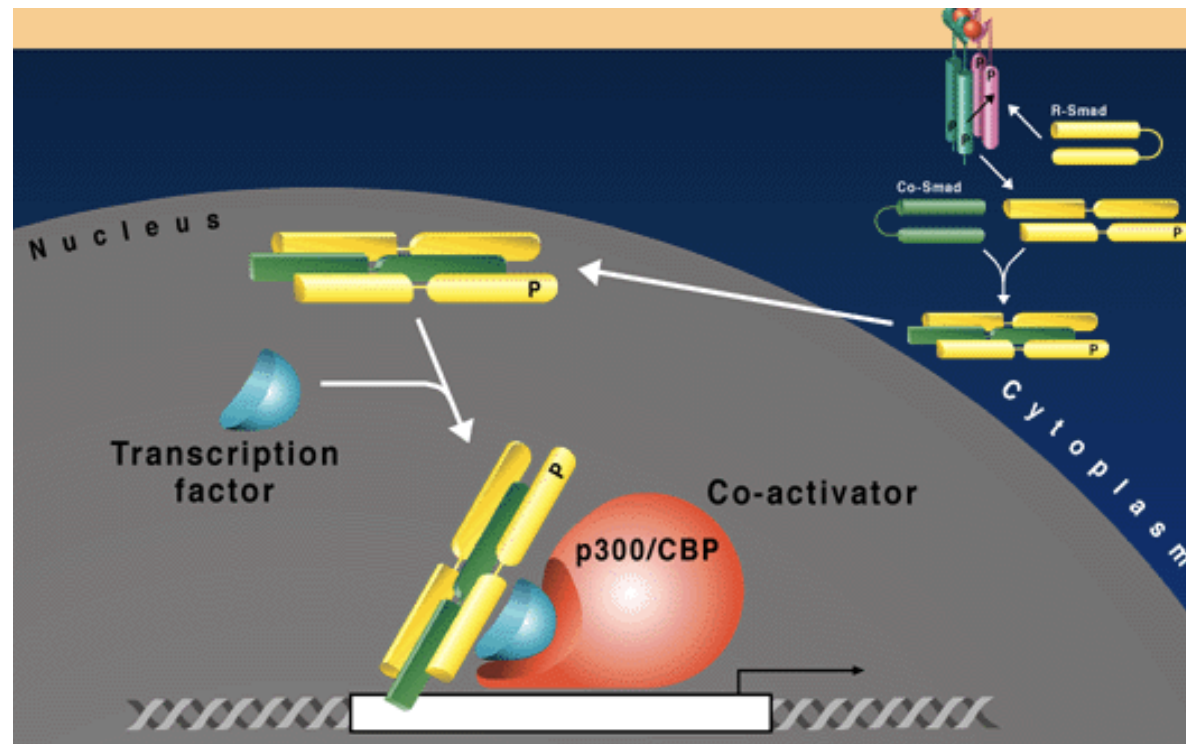
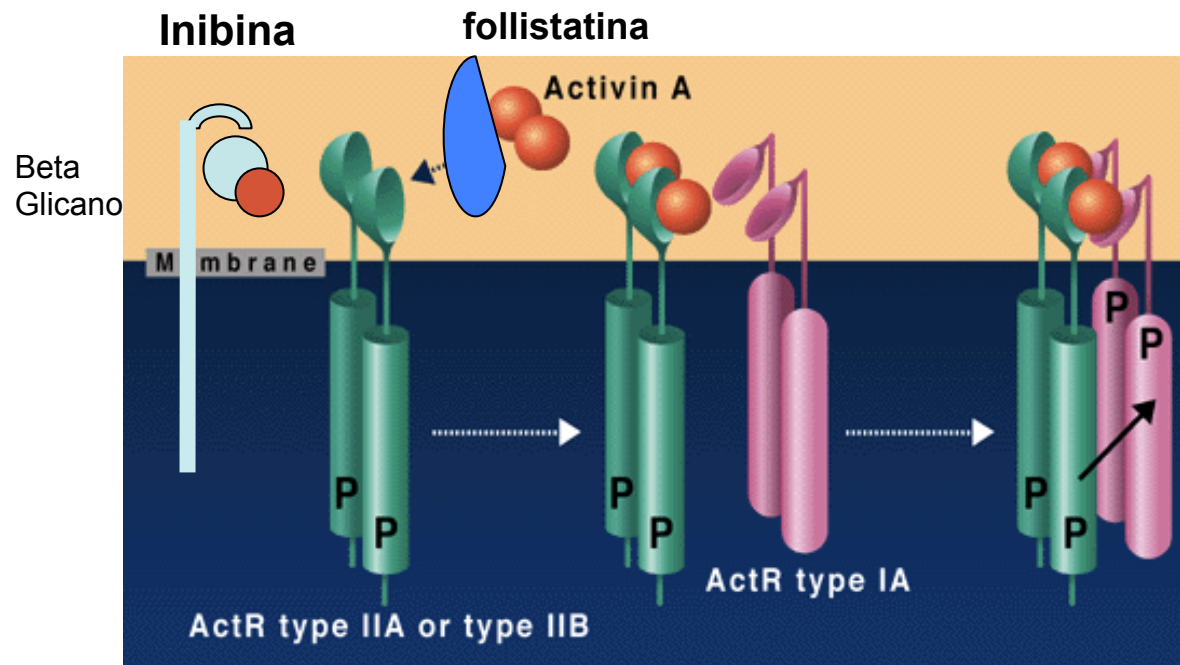
Table 2. Effect of null mutations of TGF- β family members on gonadal development

Family member	Gender affected	Defect	Refs
TGF- β	?	Early death from inflammatory disease	9, 10
Inhibin	Both	Sex cord tumor	18
Activin β A	?	Early death from palatal defects	19
Activin β B	Female	Normal ovaries but litters die	20, 21
Activin RII	Female	No estrous cycles	20, 22
GDF-9	Female	Lack of follicular maturation	50
BMP-8A	Male	Spermatogenesis is not sustained, occasional epididymal degeneration	48
BMP-8B	Male	Defects in spermatogenesis initiation and maintenance	26
AMH and AMHRII	Both	Female infertility owing to ovarian and Müllerian duct regression, Leydig cell hyperplasia and tumors	47, 65

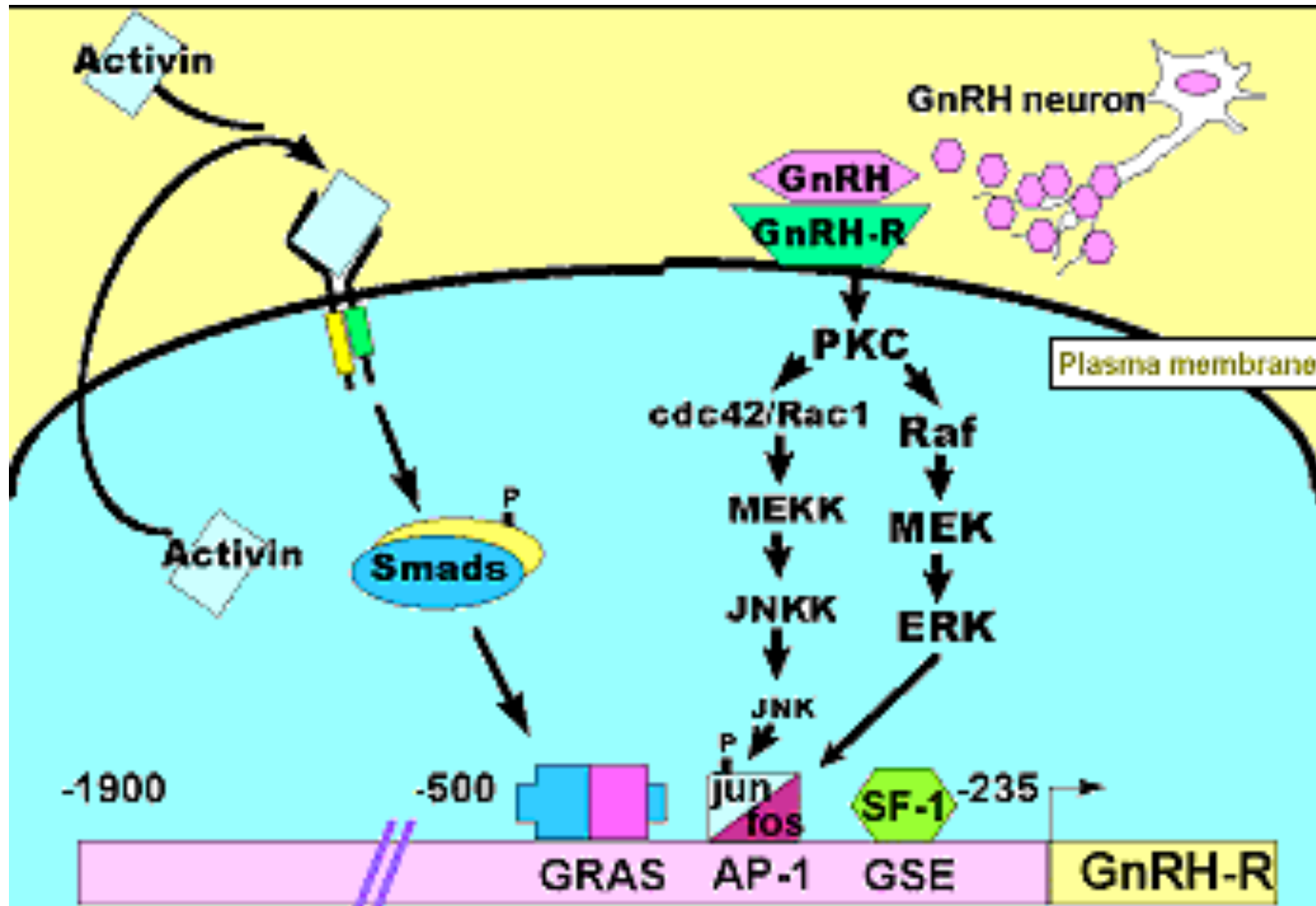
TGF- β Receptors I & II



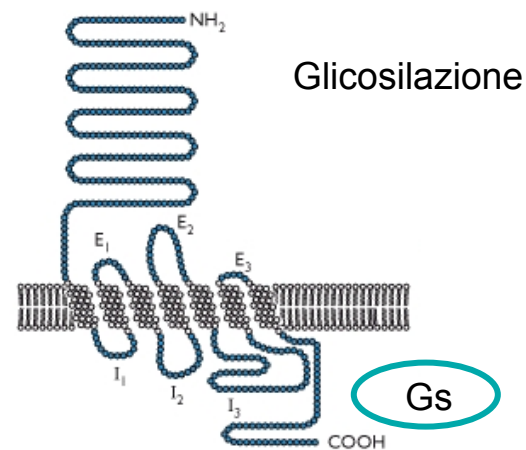
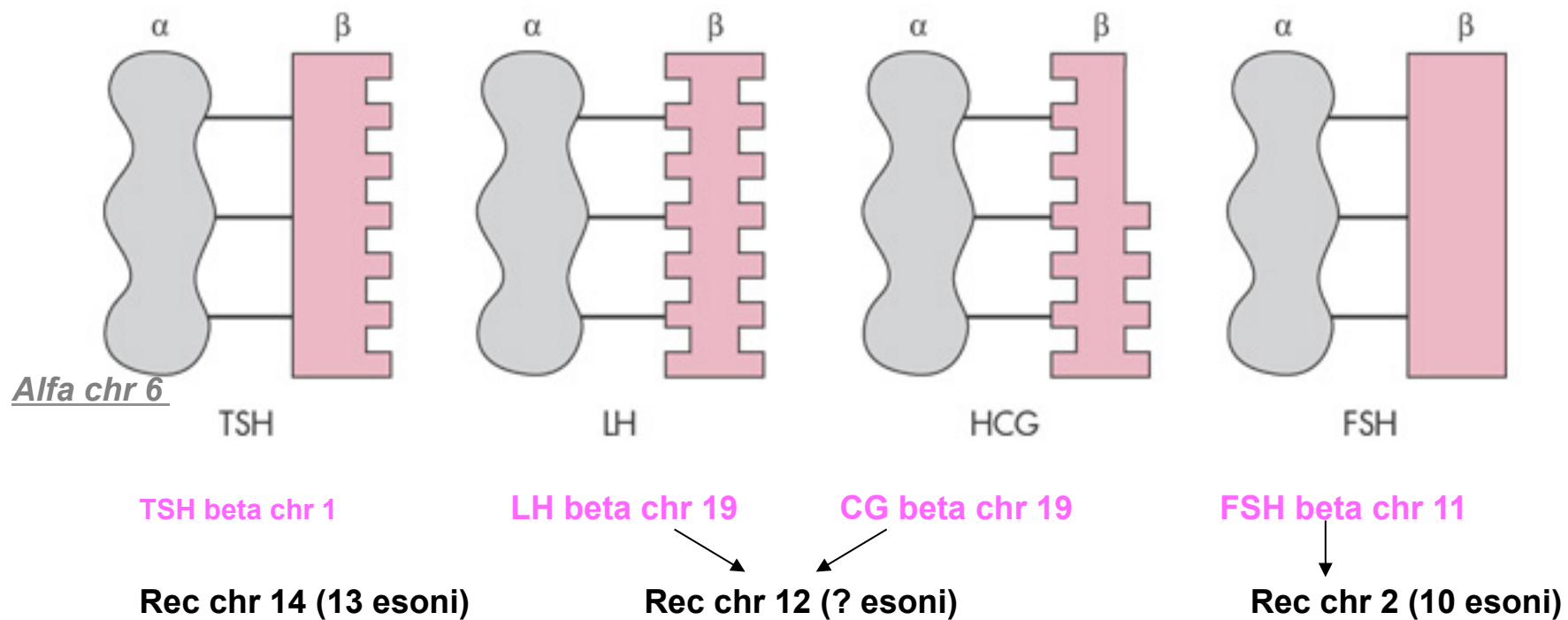


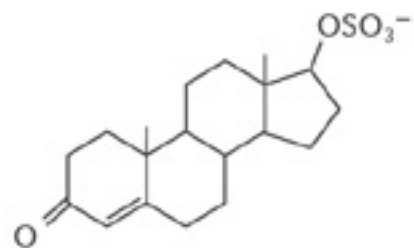


Sinergismo GnRH-Act

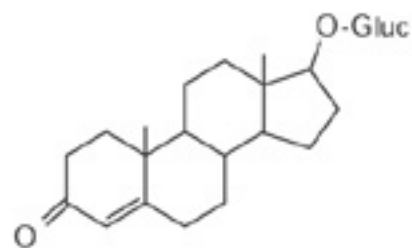


Gonadotropine e recettori

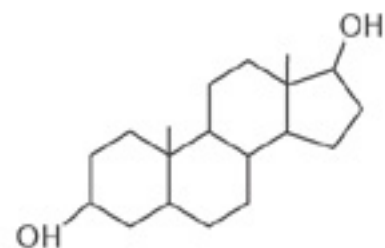




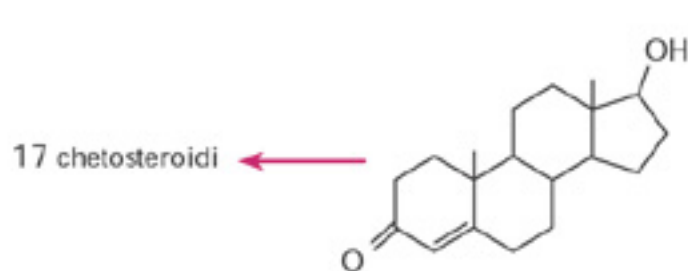
Testosterone solfato



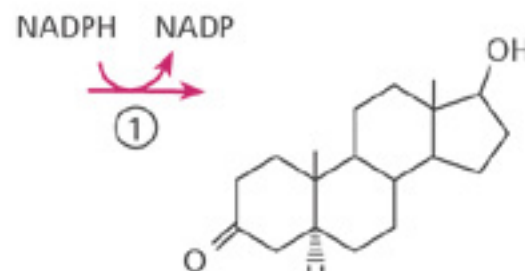
Testosterone glucuronide



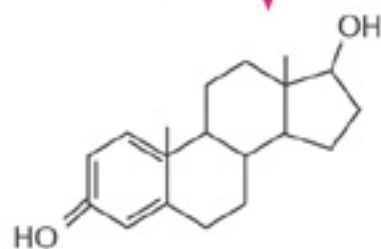
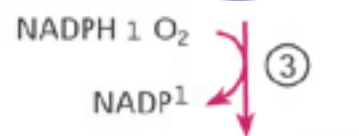
Androstenediolo



Testosterone

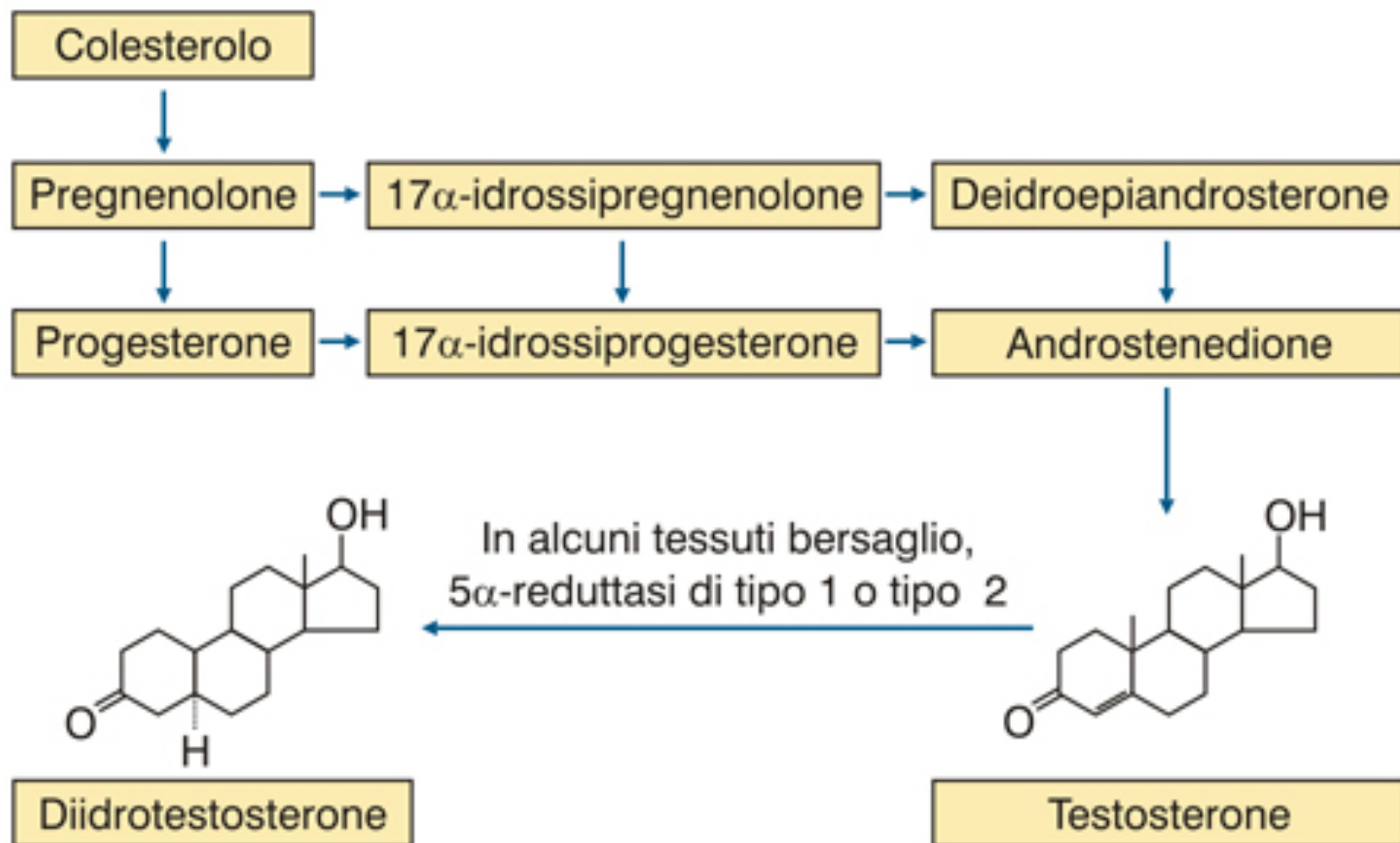


Diidrotestosterone

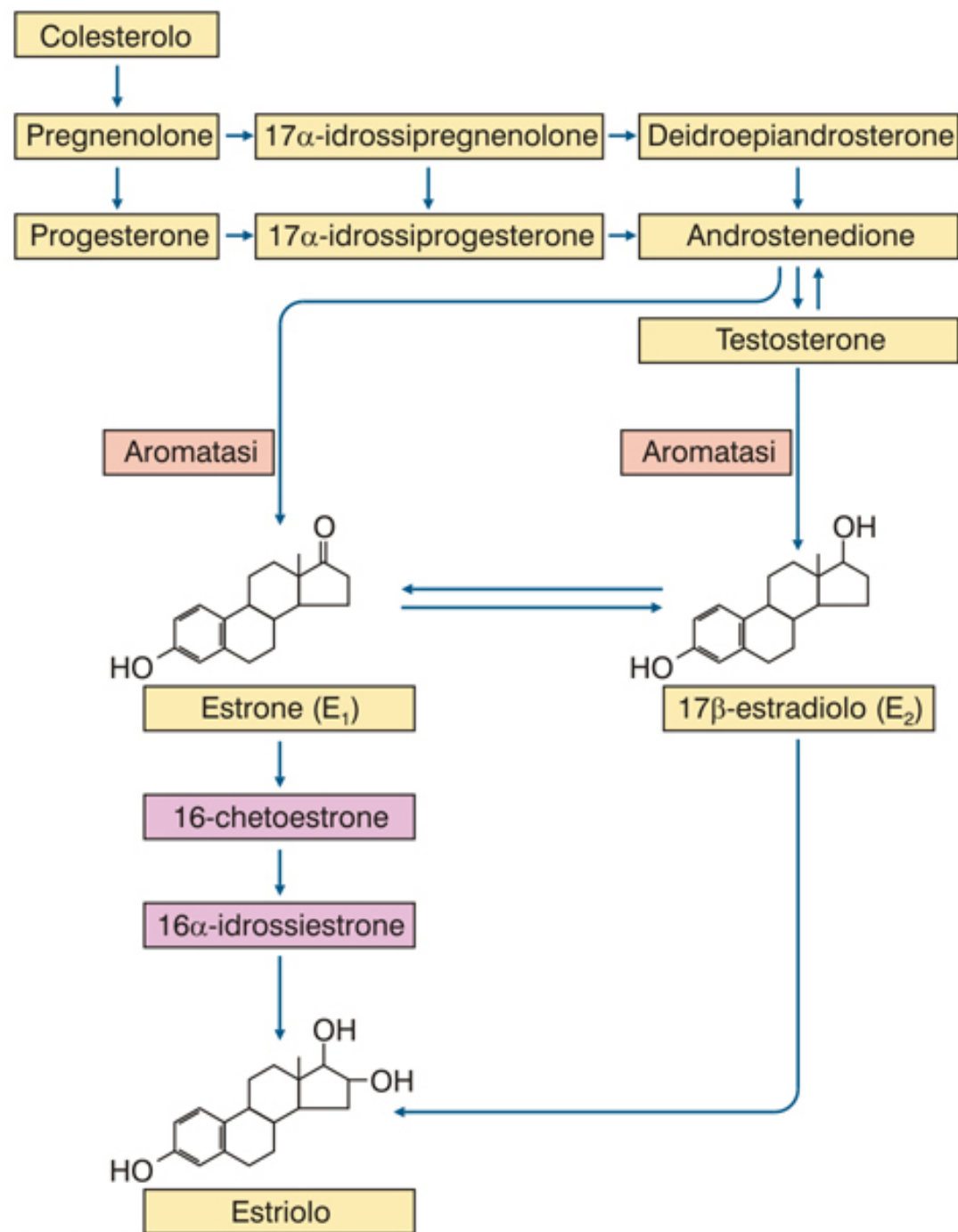


Estradiolo

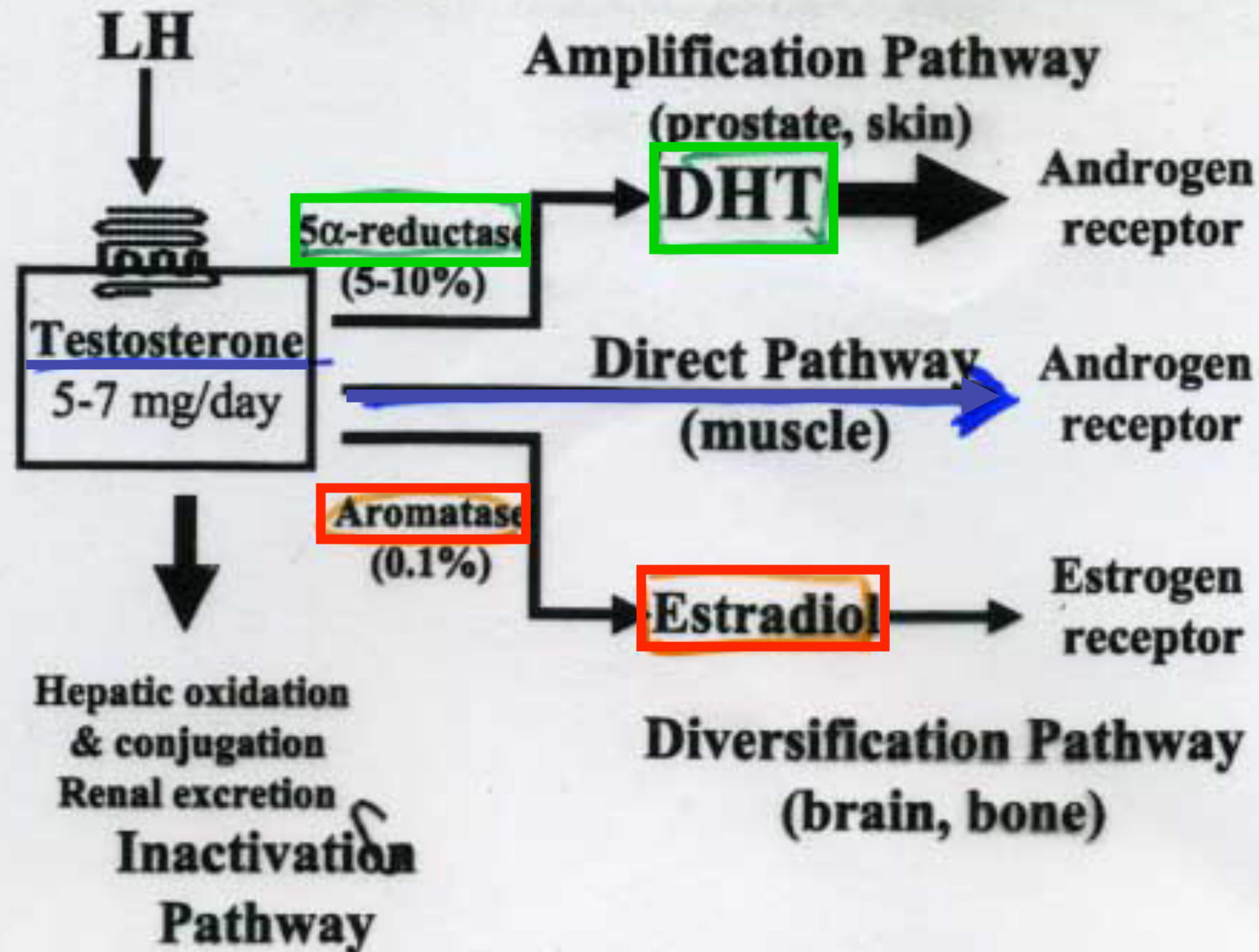
- 1 5 α -riduttasi
- 2 Idrossisteroide deidrogenasi
- 3 Aromatasi
- 4 Androgeno UDP-glucuronosiltransferasi
- 5 Androgeno solfotransferasi



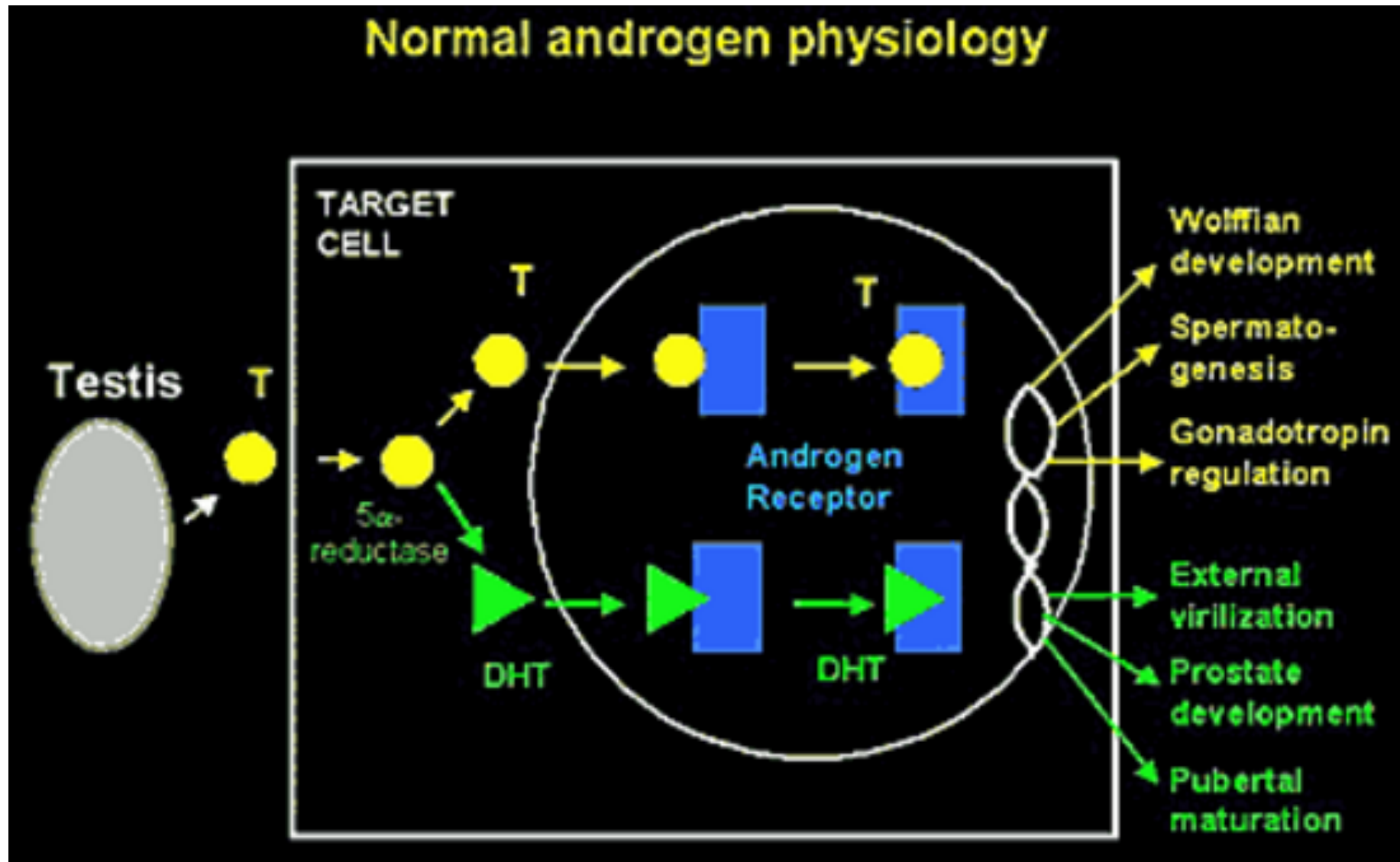
Estrogeni



Pathways of Testosterone Action



AR



Recettore androgeni

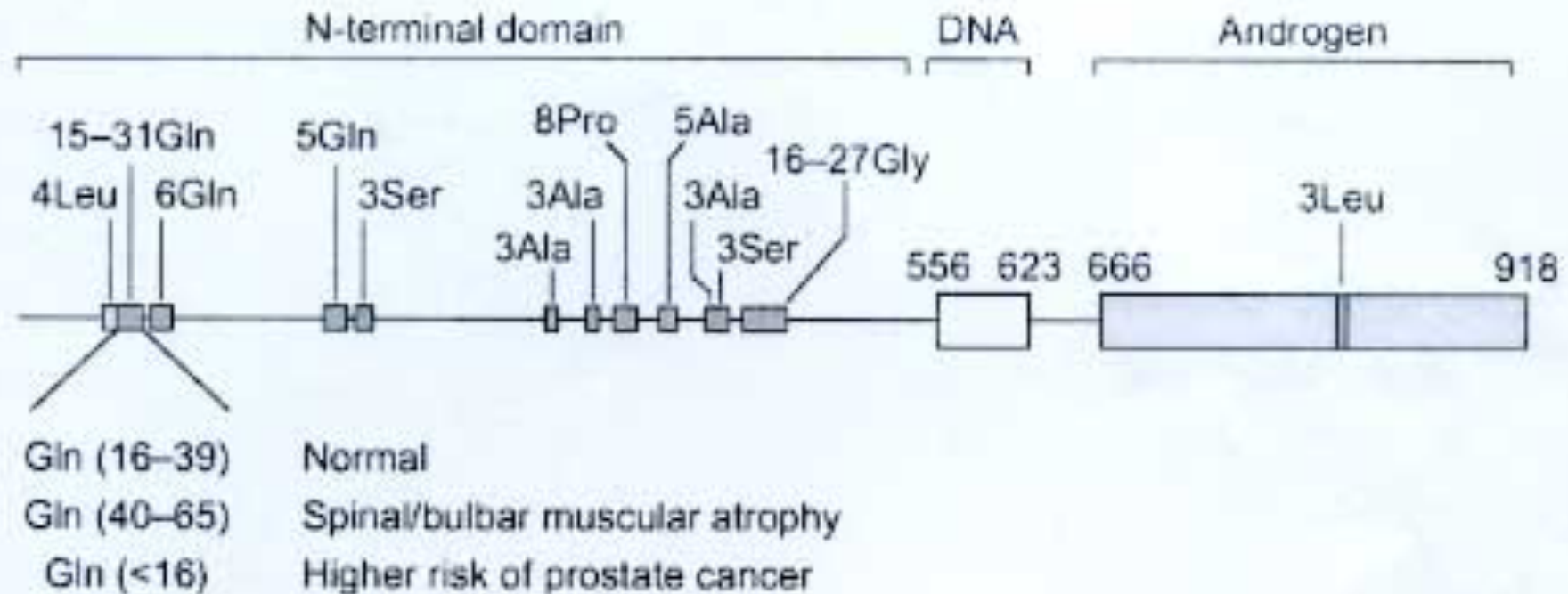


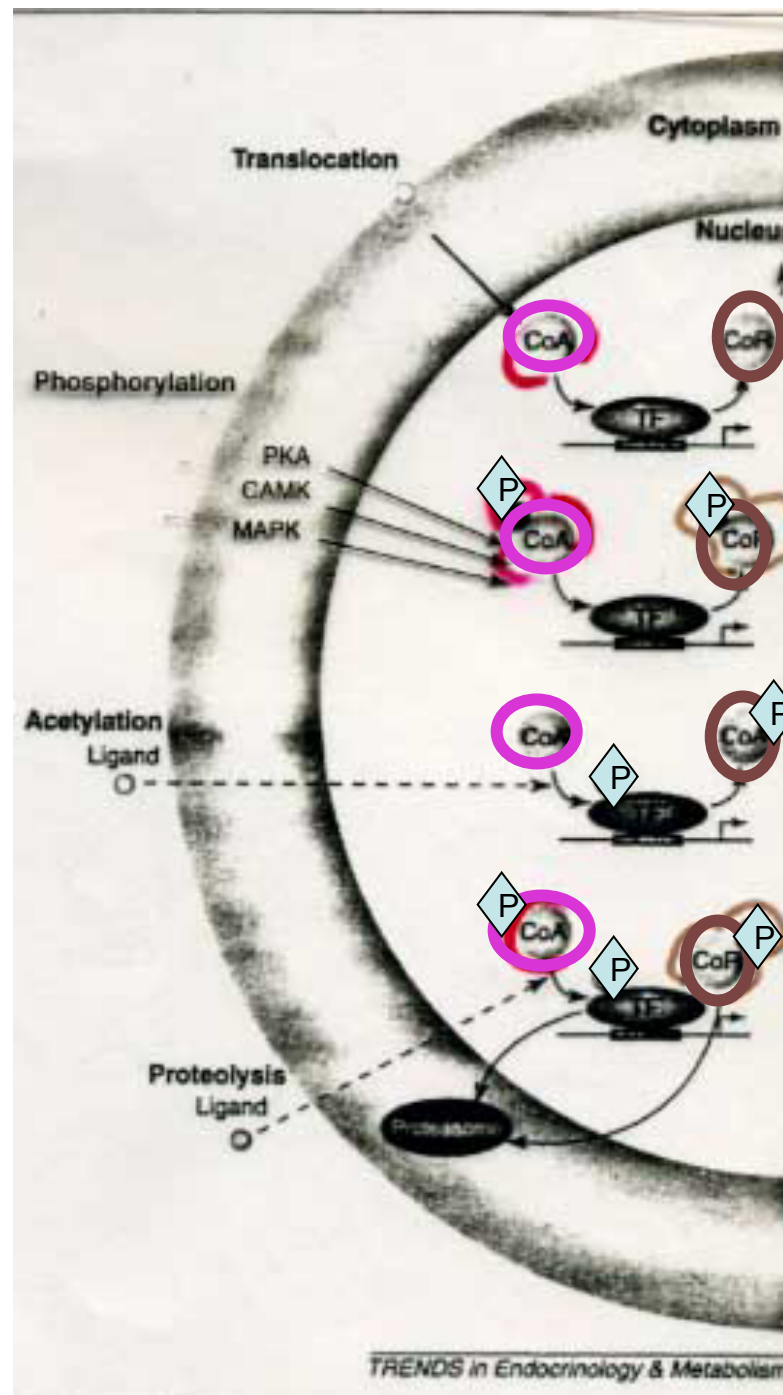
Figure 2. Schematic diagram of the domain structure of the human androgen receptor. N-terminal, DNA-binding and androgen-binding domains, as well as the positions of oligo- and polyamino acid tracts are indicated. Different lengths of the polyglutamine tract have been linked to spinal and bulbar muscular atrophy and prostate cancer.

Chr X

Coattivatori

COATTIVATORI

Phosphorilazione

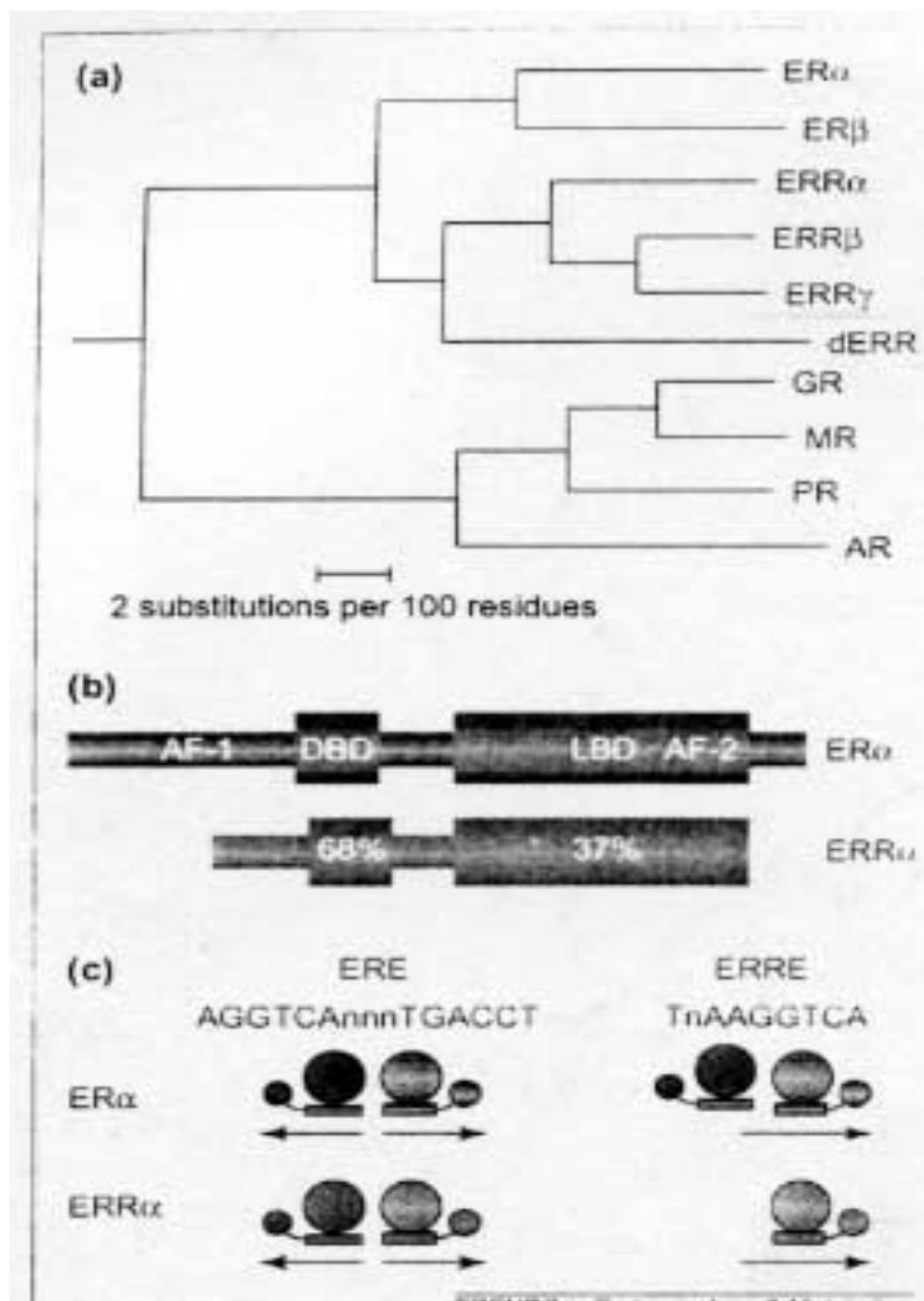


COINIBITORI

Recettori estrogeni

ERα Chr 6

ERβ Chr 14



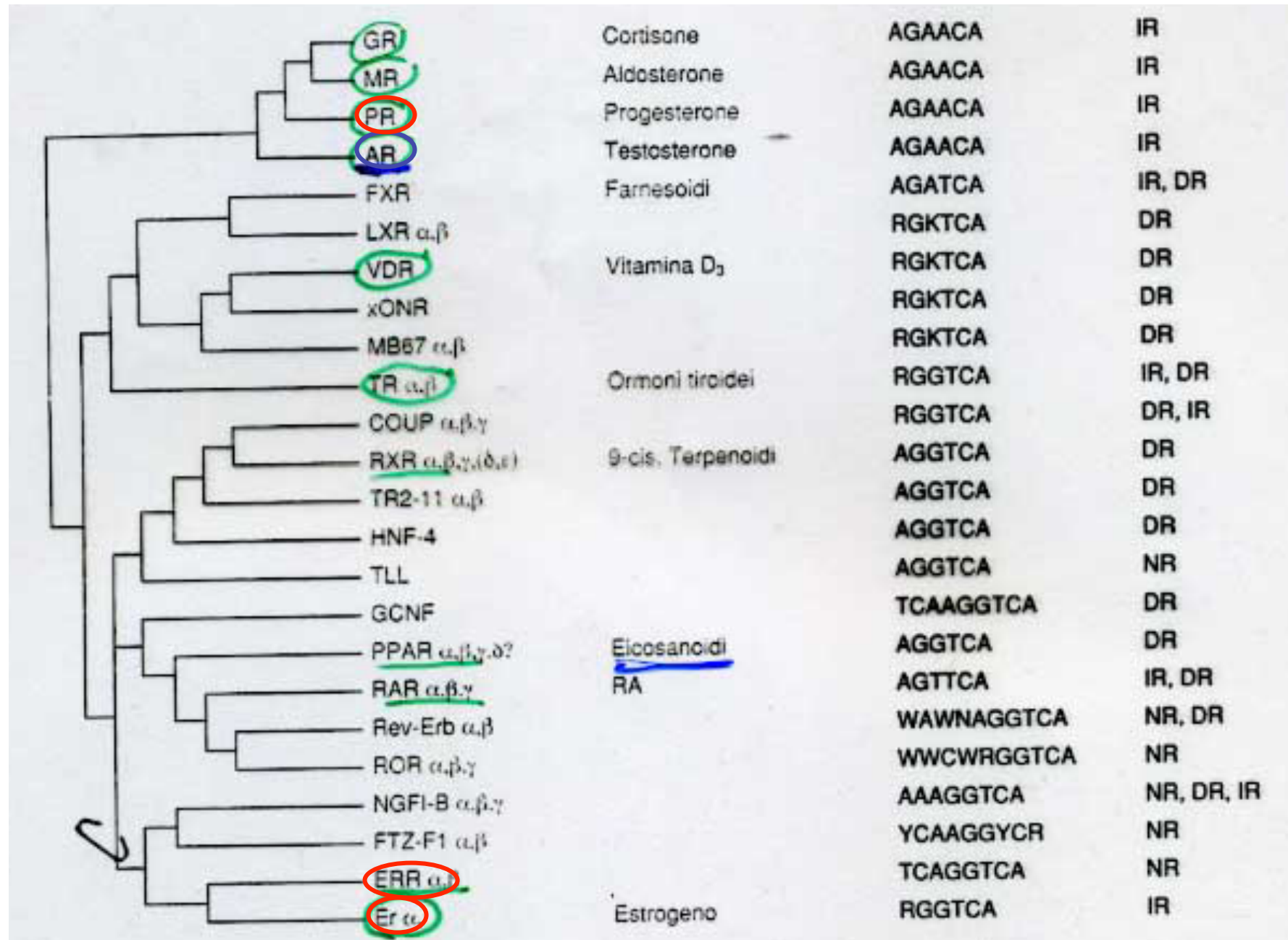
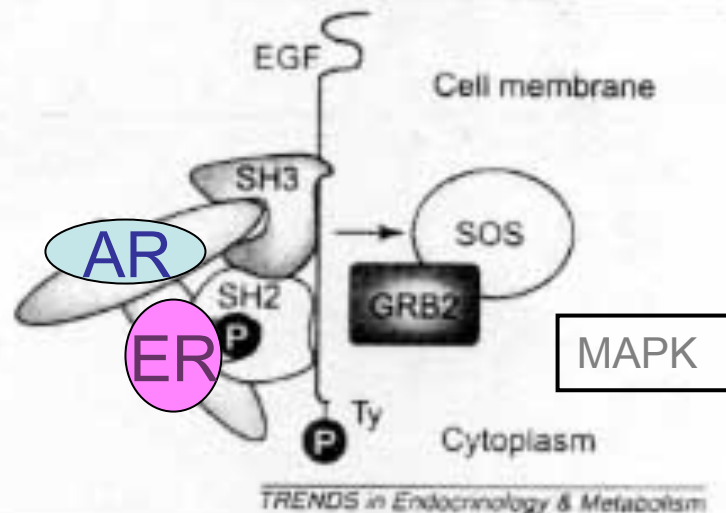


Table 1. Estrogen receptors (ERs) as novel targets for disease

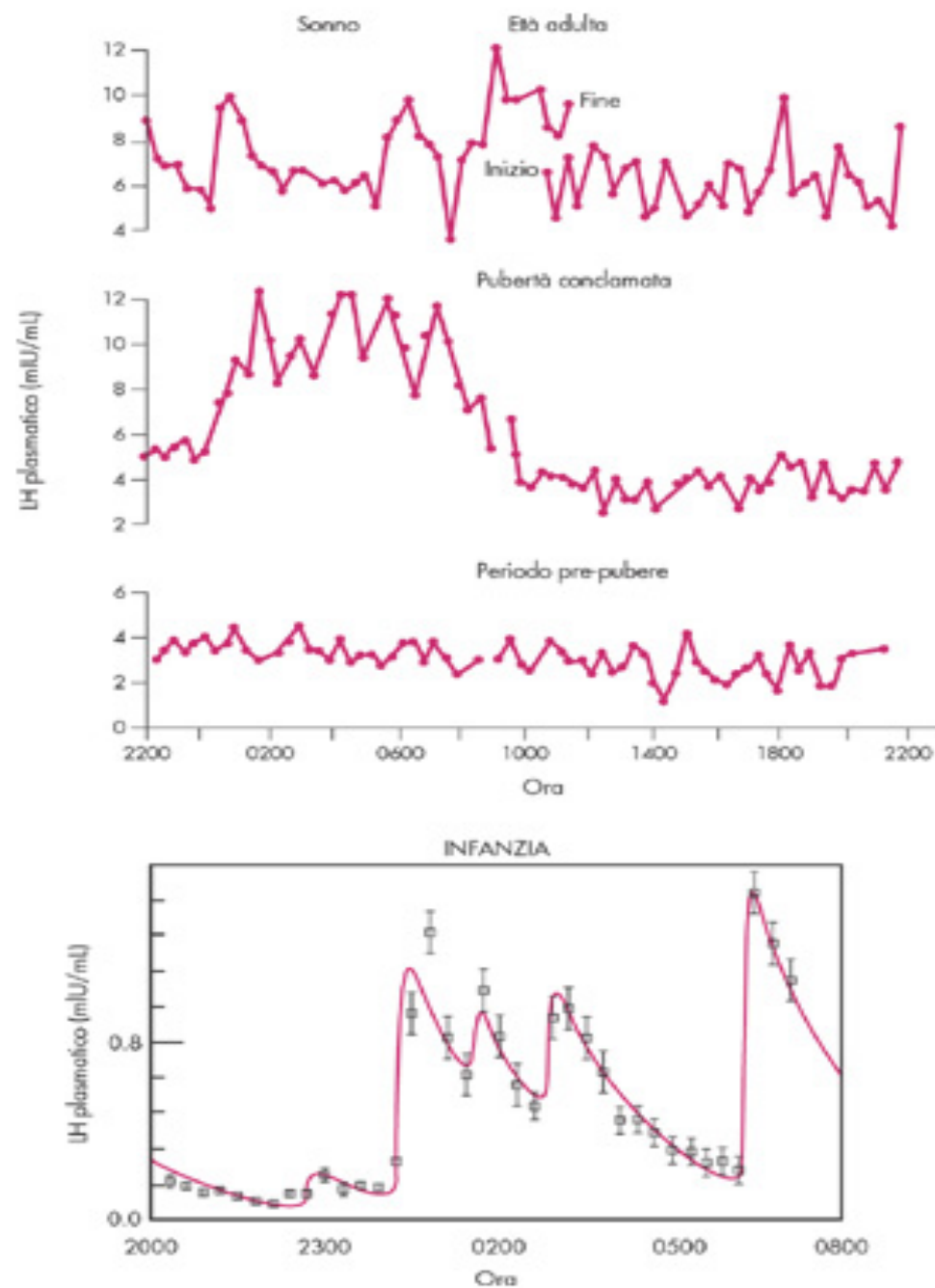
Target tissue	Estrogen receptor present	Disease
Uterus	ER α	Uterine cancer
Prostate stroma	ER α	Benign prostatic hyperplasia
Ovary theca cells	ER α	Polycystic ovary syndrome
Bone	ER α	Osteoporosis
Breast epithelium	ER α , ER β , ER β cx ^a	Breast cancer
Breast stroma	ER β	
Brain	ER α , ER β	Stroke Hypertension Obesity Dementia
Sympathetic ganglia	ER β	Hypertension Bladder control
Colon	ER β	Colon cancer
Prostate epithelium	ER β , ER β cx ^a	Prostate cancer
Ovarian granulosa cells	ER β	Infertility, polycystic ovarian s
Dorsal raphe	ER β	Depression
Bone marrow	ER β	Leukaemia

Table 2. Differential actions of ER α and ER β on different promoters and with different ligands^a

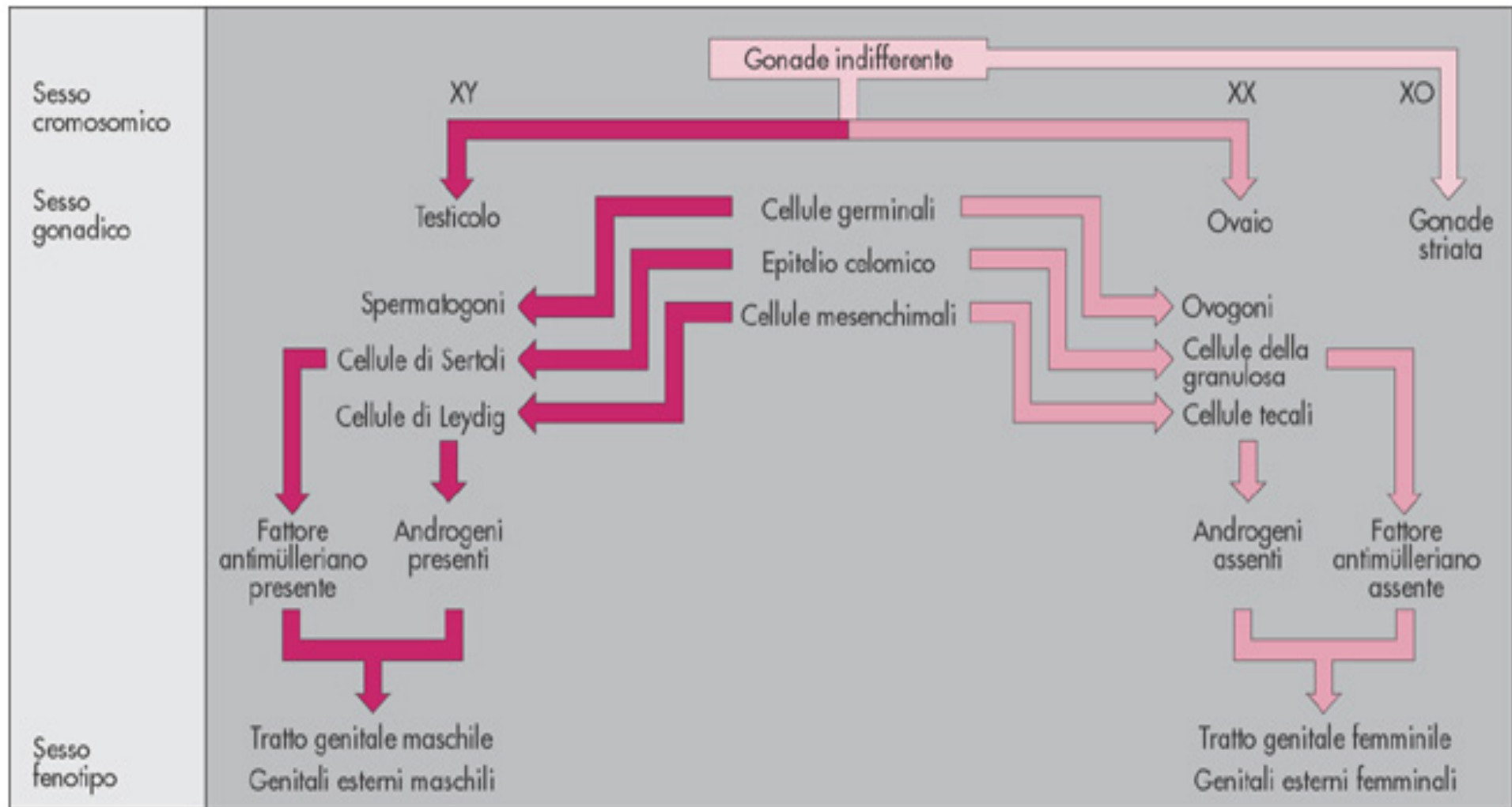
Ligand	ER	Interaction site			NF- κ B promoter ^c
		ERE	AP-1 ^b	Sp1	
E2	ER α	↑	↑	↑ RAR α 1 promoter [24]; ↓ IGF-1 promoter [25]	↓
	ER β	↑	NC	No change in RAR α 1 promoter; ↑ IGF-1 promoter	NC
Tamoxifen	ER α	↓	↓	↓ RAR α 1 promoter	↓
	ER β	↓	↑	↑ RAR α 1 promoter	NC



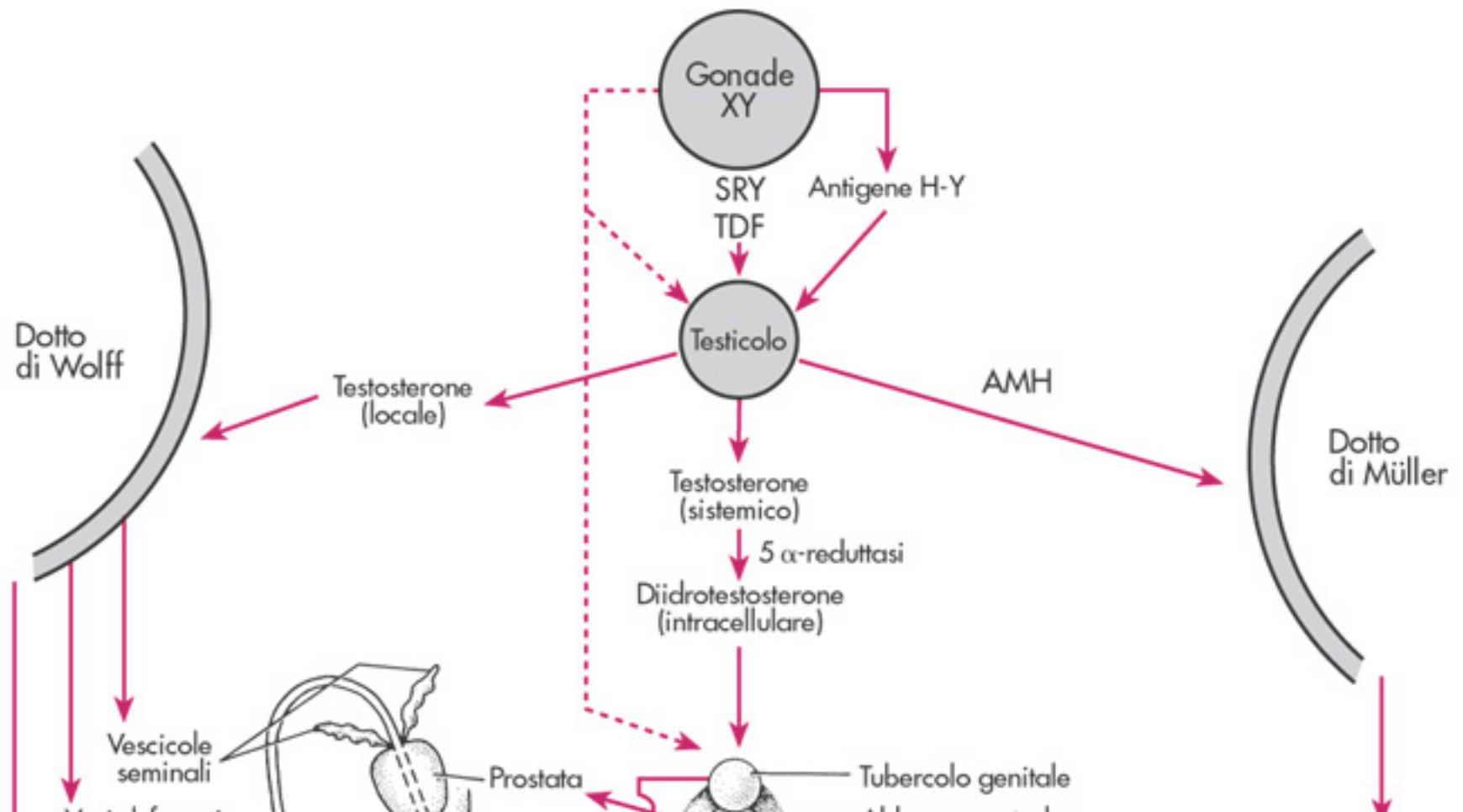
Variazione ormoni pubertà

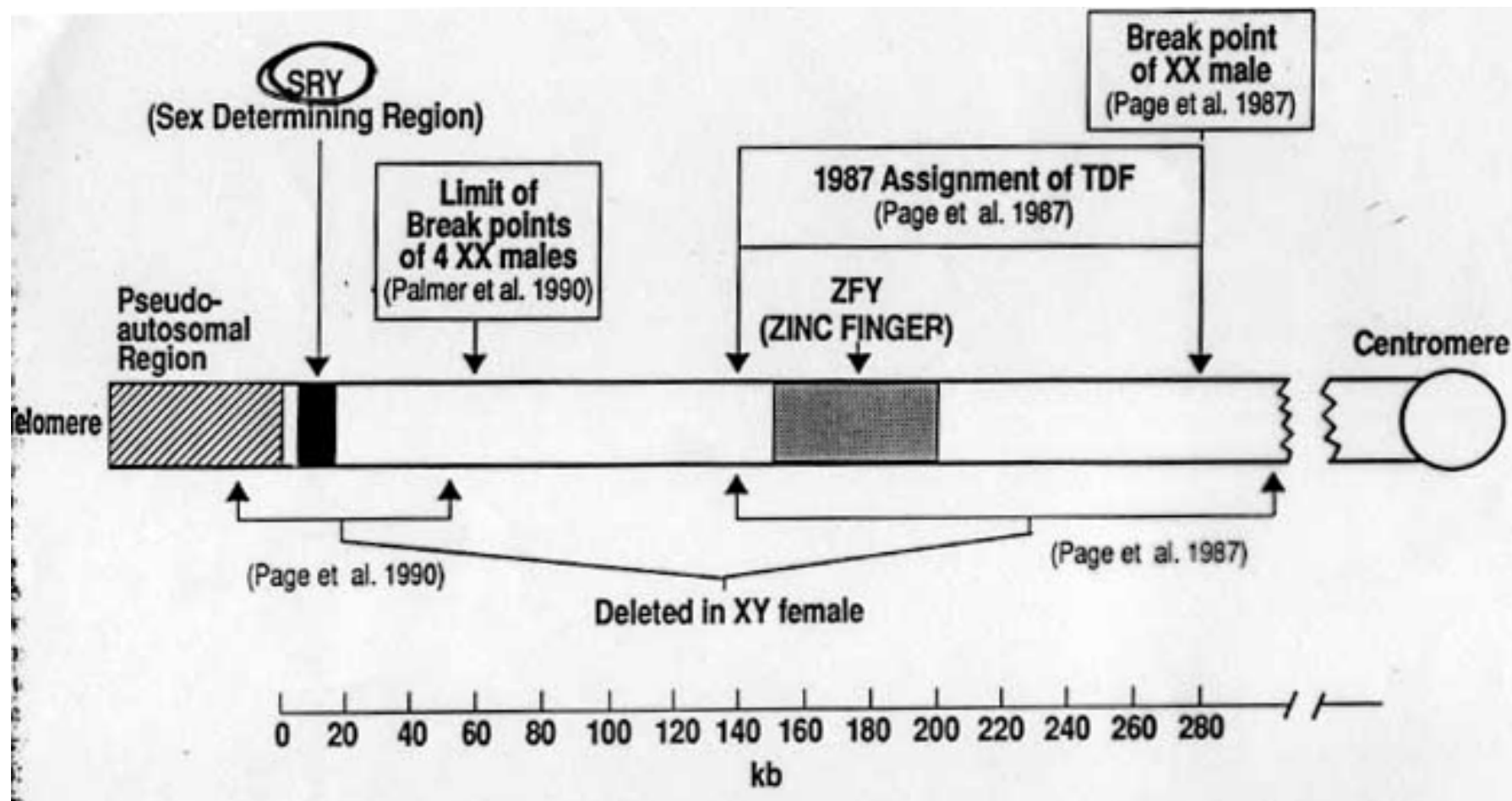


Differenziamento gonadico

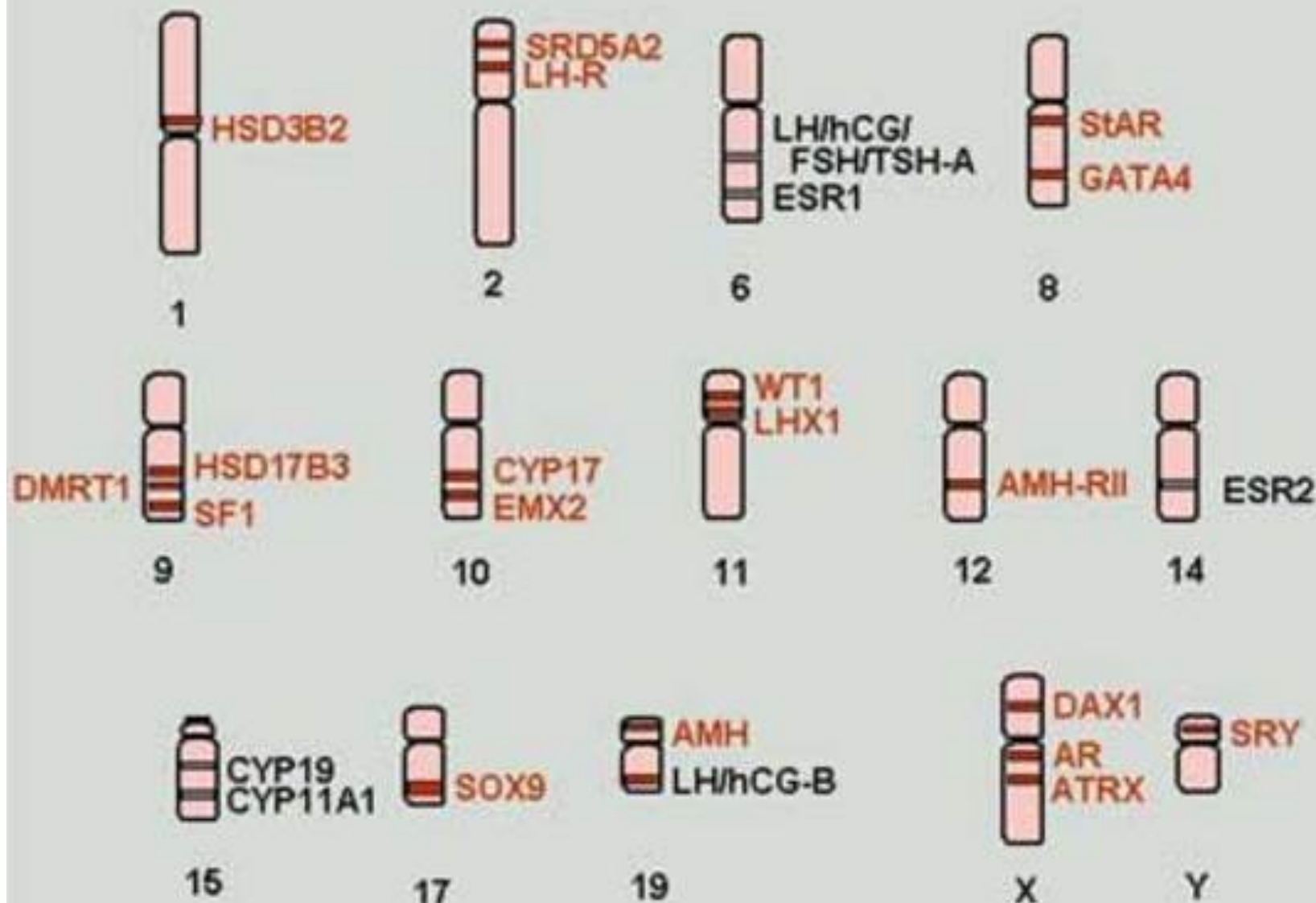


Diff gonadico

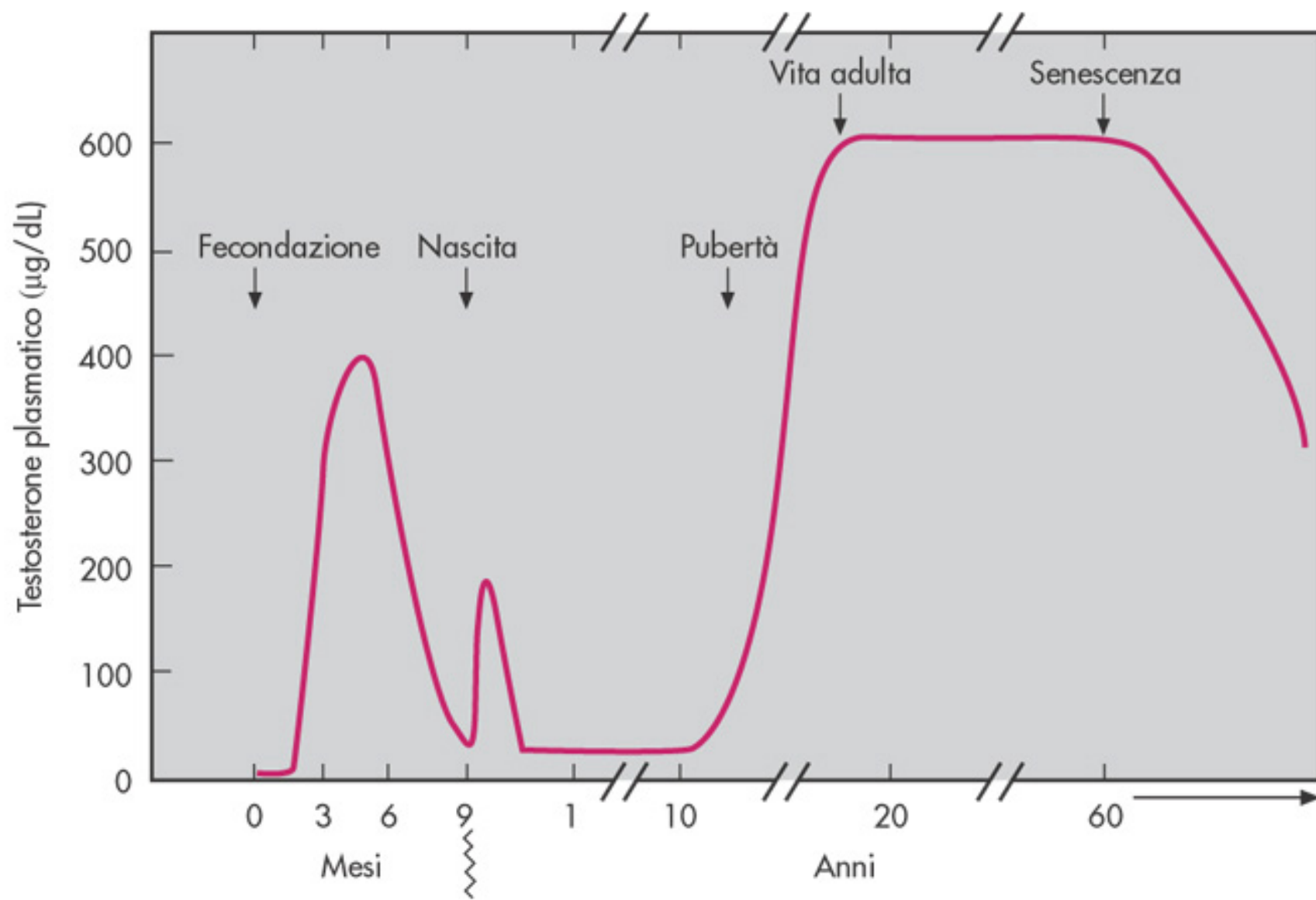


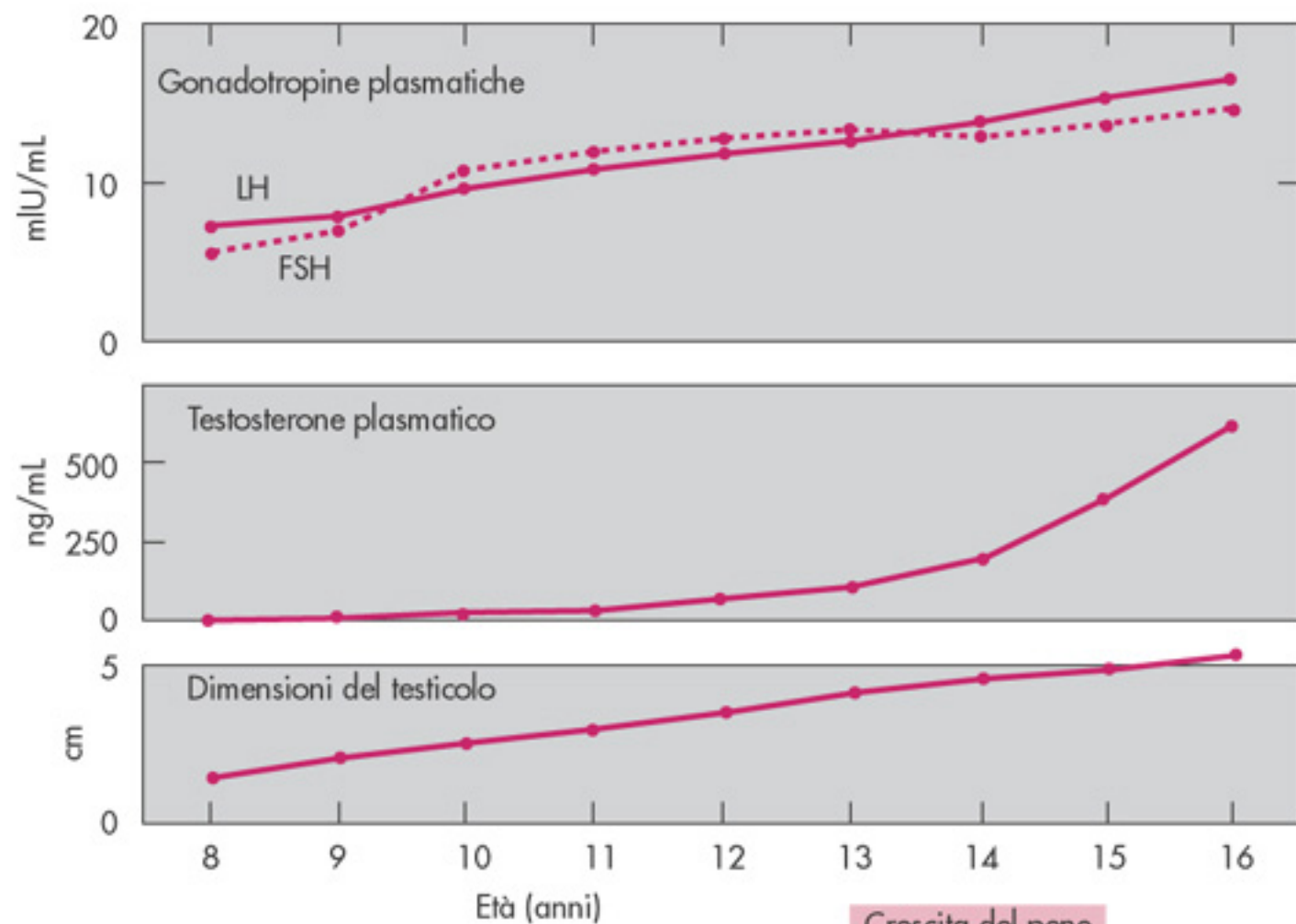


Chromosomal localization of genes involved in sex differentiation



Gene	Locus	Herança*	Fenótipo Predominante
<i>KAL</i>	Xp22.3	X-linked	Hipogonadismo hipogonadotrófico e anosmia/hiposmia
<i>FGFR1</i>	8p11.2	AD	Hipogonadismo hipogonadotrófico e anosmia/hiposmia
<i>SF1</i>	9q33	AR or AD	Sexo reverso XY, agenesia gonadal associada ou não à insuficiência adrenal
<i>DAX1</i>	Xp21.3	Ligada ao X	Hipogonadismo e hipoplasia adrenal congênita; puberdade precoce independente de gonadotrofinas em meninos
<i>Leptina</i>	7q31.3	AR	Hipogonadismo hipogonadotrófico e obesidade
<i>PC1</i>	5q15	AR	Hipogonadismo hipogonadotrófico, hipocortisolismo e obesidade
<i>GnRH</i>	8p21	ND	Provável hipogonadismo hipogonadotrófico isolado
<i>GnRHR</i>	4q21.2	AR	Hipogonadismo hipogonadotrófico isolado
<i>HESX1</i>	3p21.2	AR/AD	Hipopituitarismo, neurohipófise ectópica, displasia septo óptica
<i>LHX3</i>	9q34.3	AR	Hipopituitarismo, mal formações esqueléticas cervicais
<i>PROP1</i>	5q35	AR	Hipopituitarismo
<i>FSHR</i>	2p21	AR	Hipogonadismo hipergonadotrófico, Falência ovariana precoce
<i>LHR</i>	2p21	AR	Hipogonadismo hipergonadotrófico em ambos os sexos; genitália ambígua em homens
<i>LHβ</i>	19q13.32	AR	Hipogonadismo hipergonadotrófico
<i>FSHβ</i>	11p13	AR	Hipogonadismo hipergonadotrófico





Crescita del pene

Peli pubici

Accrescimento rapido

↑
Picco di velocità

Differenziamento aree cerebrali

Secrezione pulsatile GnRH ritmi circadiani

Amigdala più sviluppata

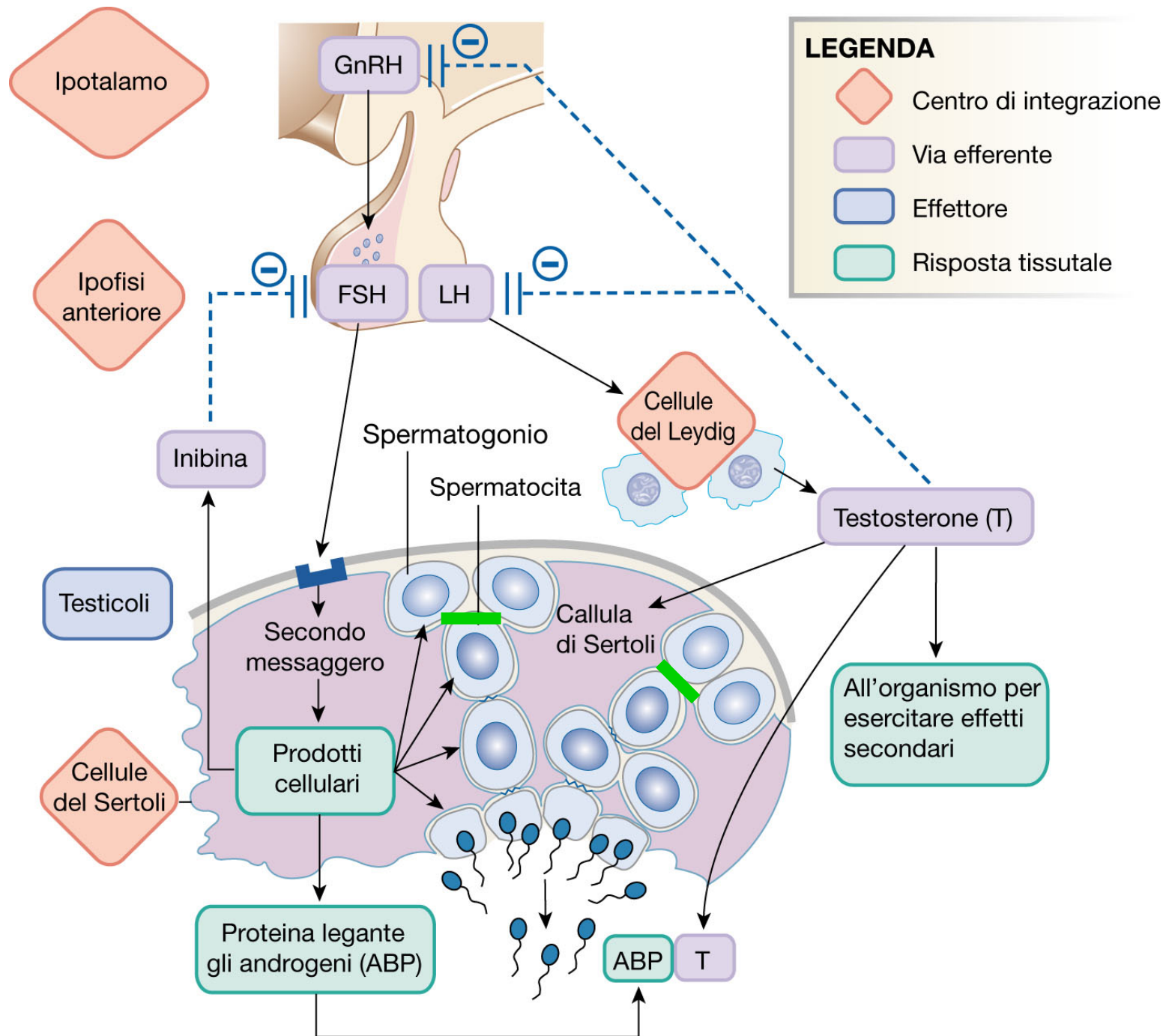
Centri ipotalamici area preottica aggressività +

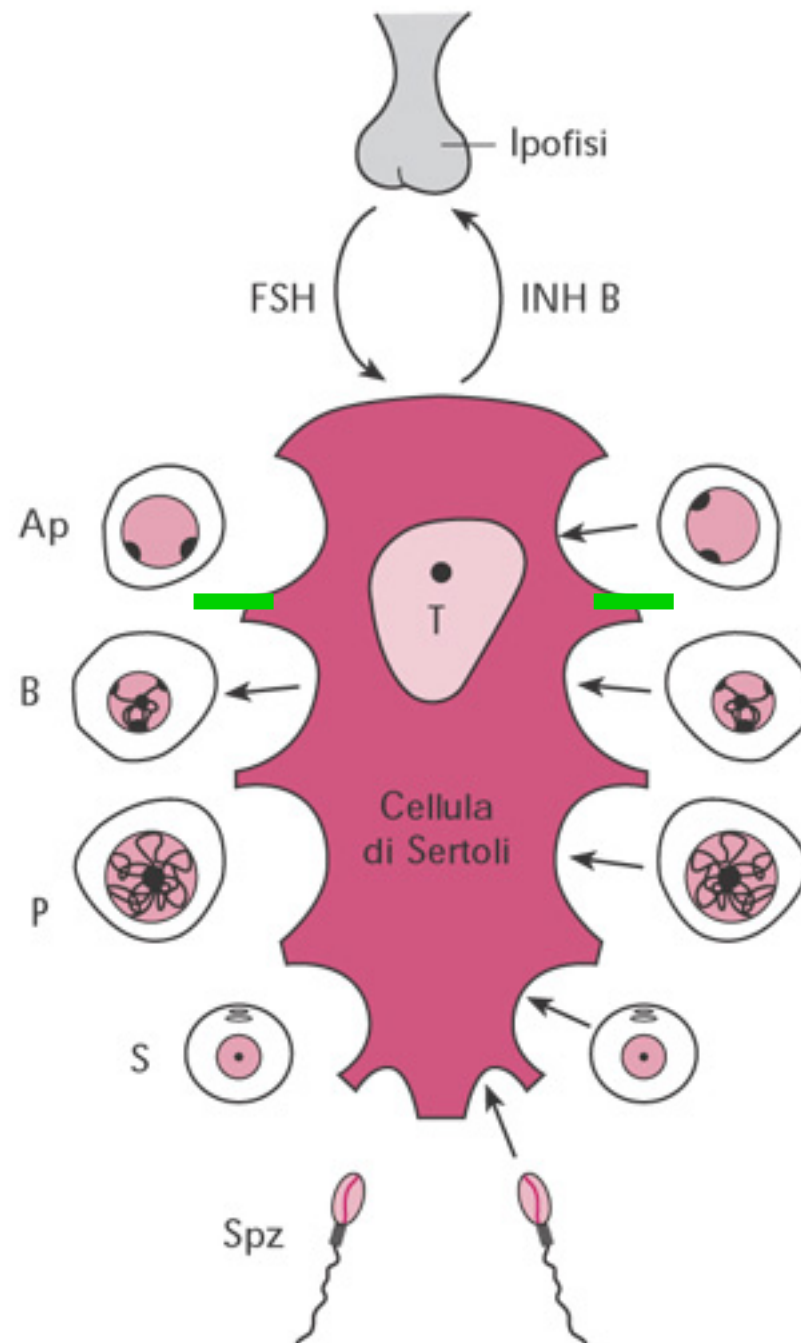
Sistema limbico - corpo calloso - area del linguaggio -

Aree corticali.....aree prefrontali...

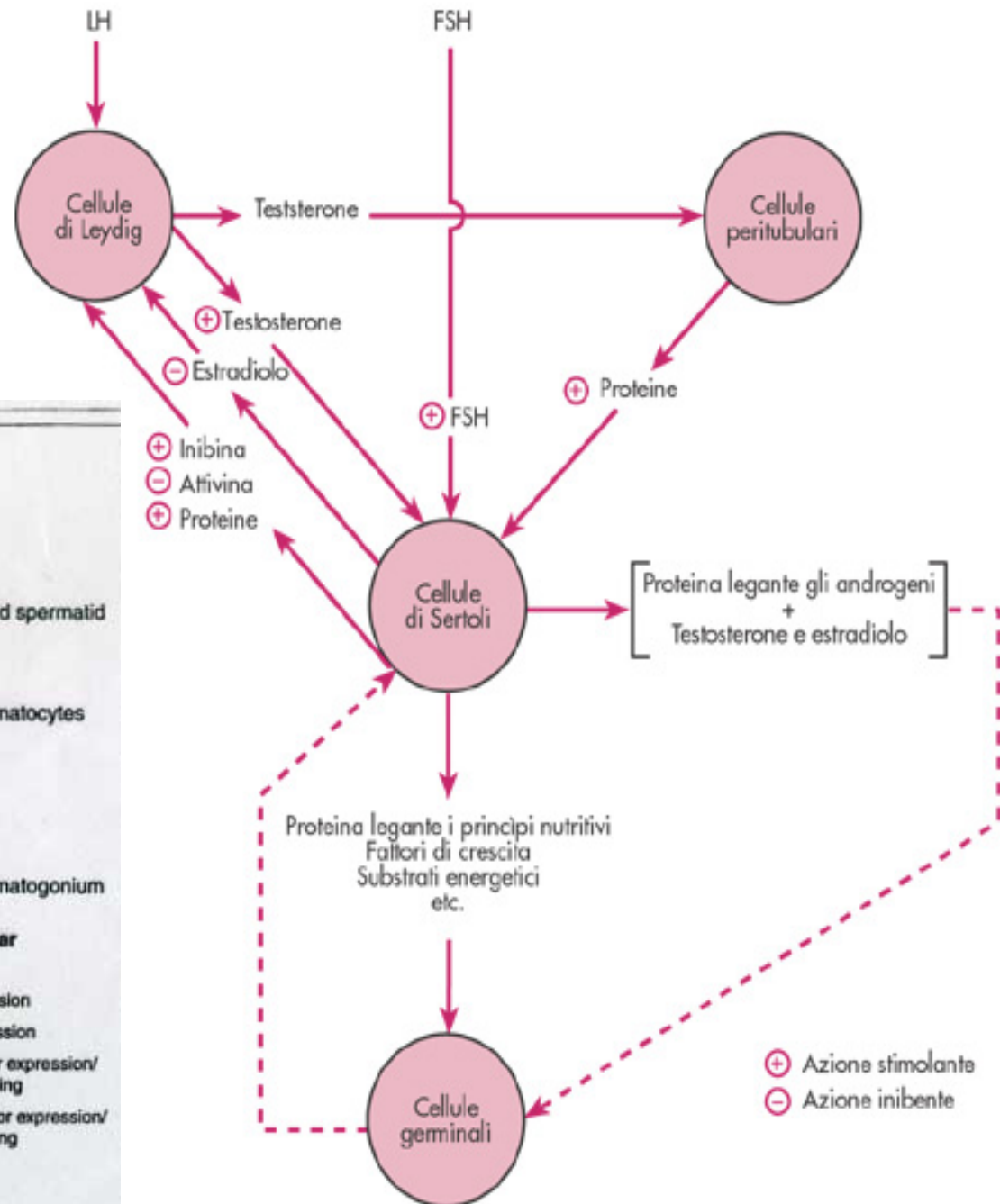
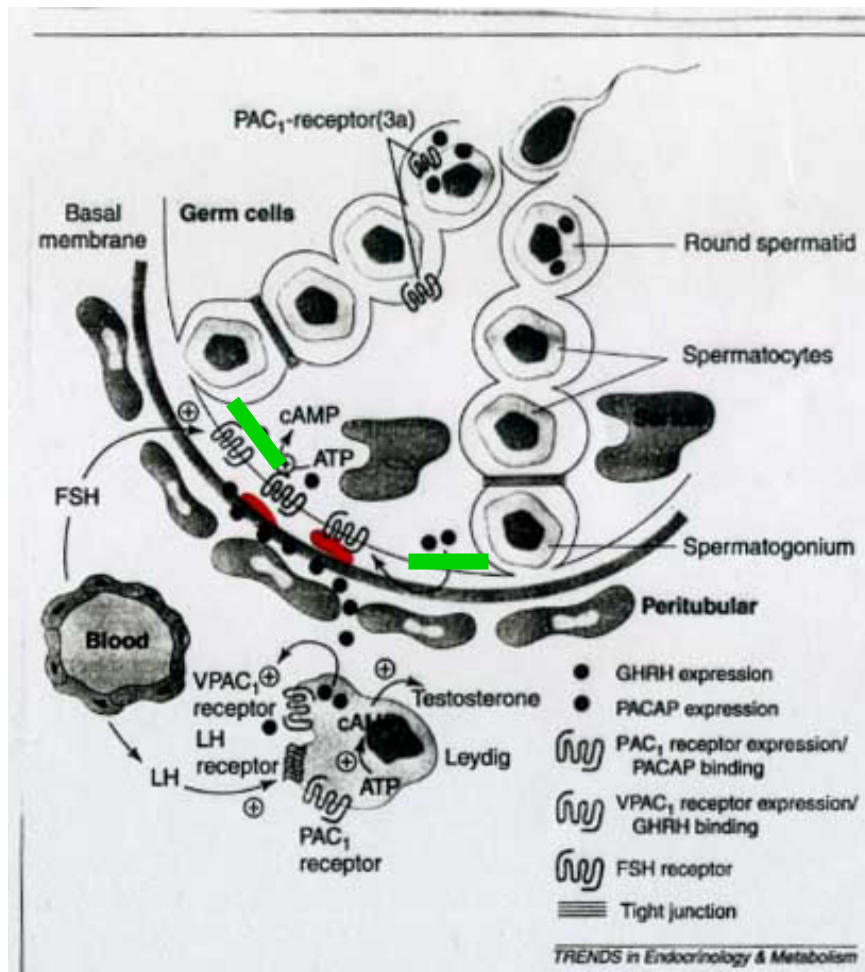
Il testosterone fetale passa la barriera ematoencefalica e viene trasformato in alcune aree in estrogeni.

Gli estrogeni placentari non passano la barriera ematoencefalica perché legati a proteine placentari ad alta affinità

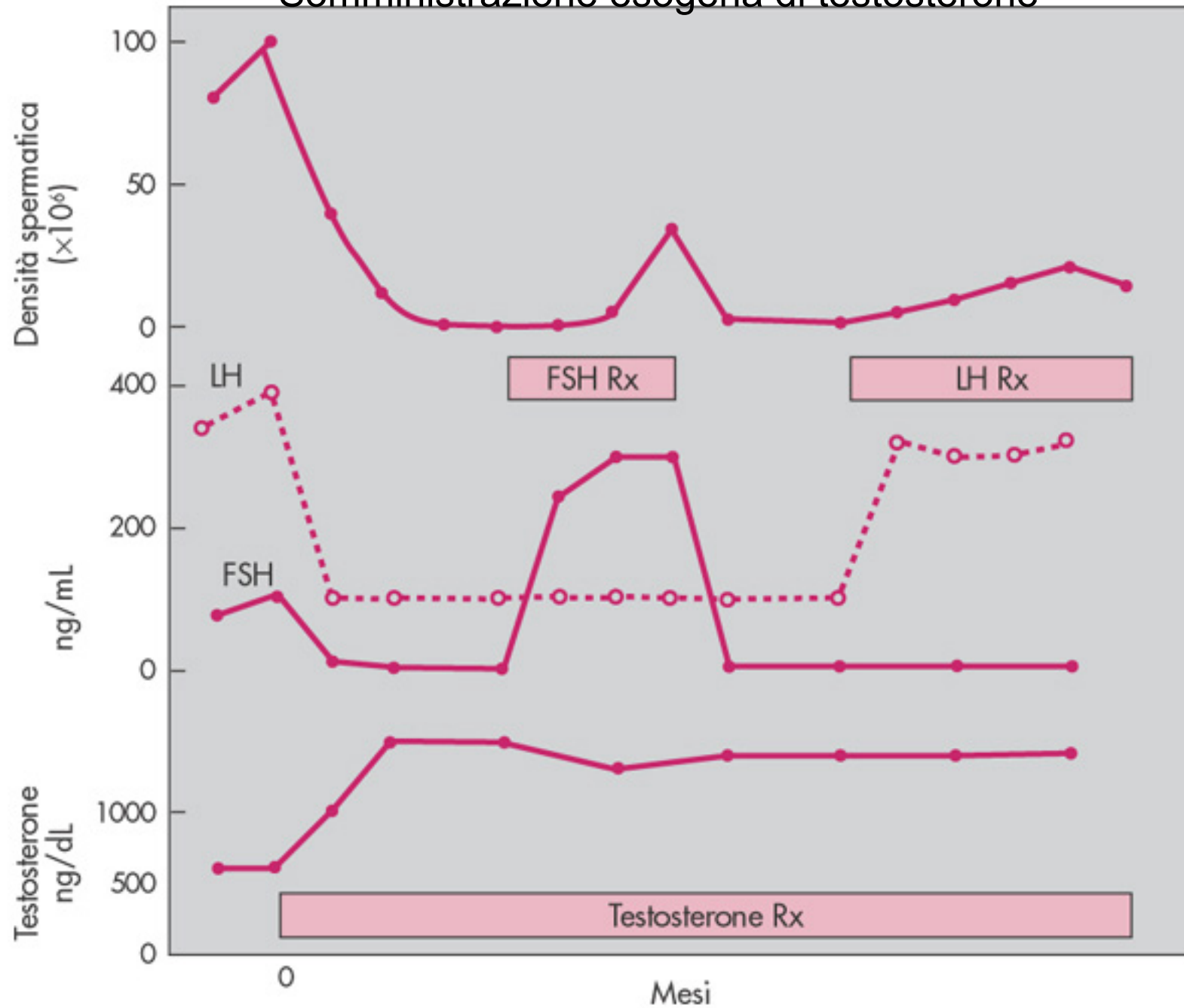




Arrività
endocrina e
paracrina
intra- e extragonadica



Somministrazione esogena di testosterone



5alfa reduttasi

Azioni principali degli ormoni androgeni.	
Testosterone	Diidrotestosterone
<u>Sviluppo fetale di</u> Epididimo Vasi deferenti Vescicole seminali	Sviluppo fetale di Pene Uretra del pene Scroto Prostata
Crescita puberale di Pene Vescicole seminali Muscoli Scheletro Laringe	Crescita puberale di Scroto Prostata Peli (distribuzione maschile) Ghiandole sebacee
Spermatogenesi	Secrezione prostatica

Prostata, vescicole seminali,
epididimo, cute SNC

5 α Reduttasi 2
FINASTERIDE

5 α R-1

DUTASTERIDE
entrambe

