http://aris.gusc.lv/06Daugavpils/Research/NuclearReceptor.pdf

NUCLEAR RECEPTORS NR 2019 Member

Subfamily		Group NRNC	Symbol[6]	Abbreviation	Name	Gene	lipophilic Ligand(s)
1 Thyroid Hormone Receptor-like	A	Thyroid hormone receptor	NR1A1	TRα	receptor-α	*THRA*	thyroid hormone
			NR1A2	TRβ	receptor-β	*THRB*	
	B	Retinoic acid receptor	NR1B1	RARα	receptor-α	*RARA*	vitamin A and related compounds
			NR1B2	RARβ	receptor-β	*RARB*	
			NR1B3	RARγ	receptor-γ	*RARG*	
	C	**Peroxisome proliferator-activated receptor**	NR1C1	PPARα	receptor-α	*PPARA*	**fatty acids, prostaglandins**
			NR1C2	PPAR-β/δ	receptor-β/δ	*PPARD*	
			NR1C3	**PPARγ**	**receptor-γ**	***PPARG***	
	D	Rev-ErbA	NR1D1	Rev-ErbAα	Rev-ErbAα	*NR1D1*	heme
			NR1D2	Rev-ErbAβ	Rev-ErbAα	*NR1D2*	
	F	RAR-related orphan receptor	NR1F1	RORα	orphan receptor-α	*RORA*	**cholesterol**, ATRA
			NR1F2	RORβ	orphan receptor-β	*RORB*	
			NR1F3	RORγ	orphan receptor-γ	*RORC*	
	H	Liver X receptor-like	NR1H3	LXRα	Liver X receptor-α	*NR1H3*	oxysterols
			NR1H2	LXRβ	Liver X receptor-β	*NR1H2*	
			NR1H4	FXR	Farnesoid X receptor	*NR1H4*	
	I	Vitamin D receptor-like	NR1I1	VDR	D receptor	*VDR*	vitamin D
			NR1I2	PXR	Pregnane X receptor	*NR1I2*	xenobiotics
			NR1I3	CAR	receptor	*NR1I3*	androstane
	X	NRs with two DNA binding domains[35][36]	NR1X1	2DBD-NRα			
			NR1X2	2DBD-NRβ			
			NR1X3	2DBD-NRγ			

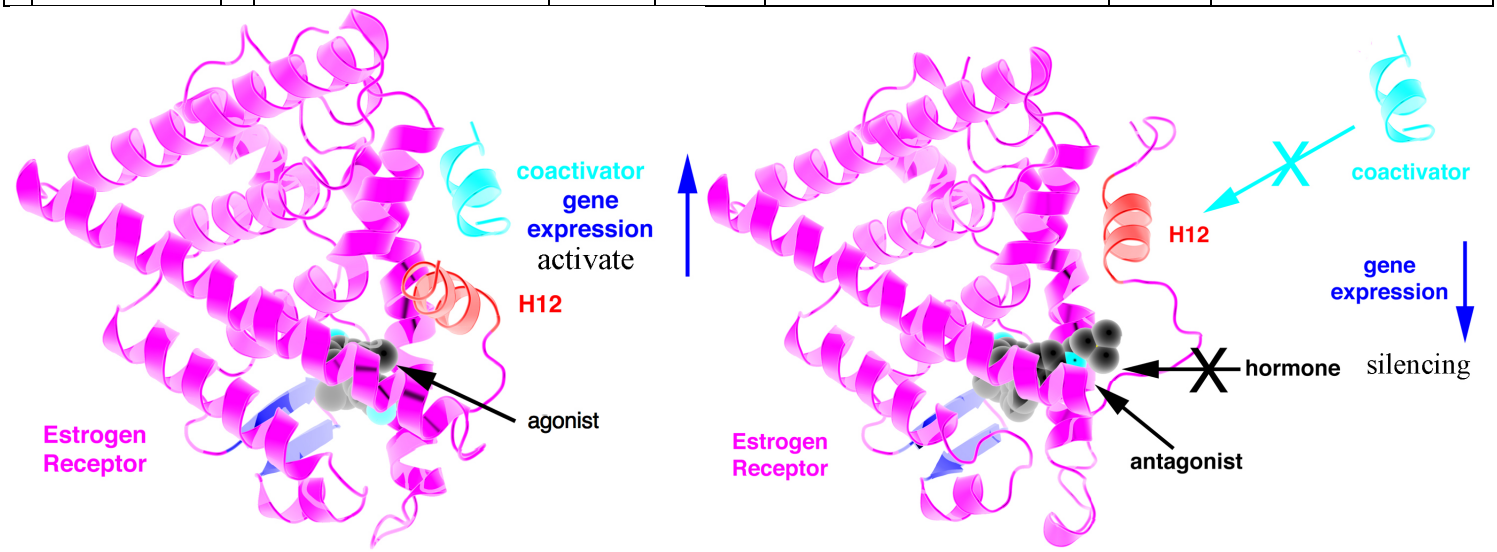
Nuclear receptors NRs are a major transcription factor family whose members selectively bind small-molecule **lipophilic ligands** and transduce those signals into specific changes in **gene programs**. **HETERO-DIMER RXRα + PPARγ** ; each MONOMER have 1)Ligand-Binding Domains **LBD**s;2) DNA-Binding Domains **DBD**

2 Retinoid X Receptor-like	A	Hepatocyte nuclear factor-4	NR2A1	HNF4α	nuclear factor-4-α	*HNF4A*	fatty acids
			NR2A2	HNF4γ	nuclear factor-4-γ	*HNF4G*	
	B	**Retinoid X receptor**	**NR2B1**	**RXRα**	**receptor-α**	***RXRA***	**retinoids**
			NR2B2	RXRβ	receptor-β	*RXRB*	
			NR2B3	RXRγ	receptor-γ	*RXRG*	
	C	Testicular receptor	NR2C1	TR2	receptor 2	*NR2C1*	
			NR2C2	TR4	receptor 4	*NR2C2*	
	E	TLX/PNR	NR2E1	TLX	Drosophila tailless gene	*NR2E1*	Homologue of the
			NR2E3	PNR	nuclear receptor	*NR2E3*	Photoreceptor cell-specific
	F	COUP/EAR	NR2F1	COUP-TFI	transcription factor I	*NR2F1*	Chicken ovalbumin upstream promoter-
			NR2F2	COUP-TFII	transcription factor II	*NR2F2*	Chicken ovalbumin upstream promoter-
			NR2F6	EAR-2	V-erbA-related	*NR2F6*	

A/B regions poorly conserved that in some cases act as potent transcriptional activators, provide sites of protein **phosphorylation** or form direct interactions with other receptor domains or regulatory proteins. Highly conserved **DBD** contains two zinc-binding sites capable of sequence-specific binding to **DNA**. **Hydrophobic** molecules bind to the **LBD**, repositioning **helix 12** into an active conformation recruits **co-regulators**. **Coactivators** members of the **steroid receptor coactivator SRC** contain LXXLL motifs that dock to **LBD**. **PPARγ** **LBD+DBD** **RXRα** enhance binding response-element **A**, **T**, **G**, **C** on DNA sequence. The **androgen receptor** (**AR**), also known as **NR3C4** (**nuclear receptor** subfamily 3, group C, member 4), is a type of **nuclear receptor**that is activated by binding of either of the androgenic hormones **testosterone** or**dihydrotestosterone** in the cytoplasm and then translocating into the nucleus.

3 Estrogen	A	Estrogen receptor	NR3A1	ERα	Estrogen receptor-α	*ESR1*	estrogens

	Receptor-like			NR3A2	ERβ	Estrogen receptor-β		
		B	Estrogen related receptor	NR3B1	ERRα	receptor-α	*ESR2*	Estrogen-related
				NR3B2	ERRβ	receptor-β	*ESRRA*	Estrogen-related
				NR3B3	ERRγ	receptor-γ	*ESRRB*	Estrogen-related
		C	3-Ketosteroid receptors	NR3C1	GR	receptor	*ESRRG*	Glucocorticoid
				NR3C2	MR	Mineralocorticoid receptor	*NR3C1*	cortisol
				NR3C3	PR	Progesterone receptor	*NR3C2*	aldosterone
				NR3C4	AR	Androgen receptor	*PGR*	progesterone, testosterone
4	Nerve Growth Factor IB-like	**A**	NGFIB/NURR1/NOR1	NR4A1	NGFIB	Nerve Growth factor IB	*AR*	testosterone
				NR4A2	NURR1	Nuclear receptor related 1	*NR4A1*	
				NR4A3	NOR1	Neuron-derived orphan receptor 1	*NR4A2*	
5	Steroidogenic Factor-like	**A**	SF1/LRH1	NR5A1	SF1	Steroidogenic factor 1	*NR4A3*	
				NR5A2	LRH-1	Liver receptor homolog-1	*NR5A1*	phosphatidylinositols
6	Germ Cell Nuclear Factor-like	**A**	GCNF	NR6A1	GCNF	Germ cell nuclear factor	*NR5A2*	phosphatidylinositols
0	Miscellaneous	**B**	DAX/SHP	NR0B1	DAX1	Dosage-sensitive sex reversal, adrenal hypoplasia critical region, on chromosome X, gene 1	*NR6A1*	
				NR0B2	SHP	Small heterodimer partner	*NR0B1*	*NR0B2*



Ligand bind **LBD** change conformation with **coactivator** helix **H12 NR** DNA binding domain :

1) for **agonist** activate **gene** expression. Receptor+Hormone works.

2)for **antagonists gene** expression silencing no **coactivation** of **gene** expression.

Receptor is +busy + not working (silencing).

The **androgen receptor** (**AR**), also known as **NR3C4** (**nuclear receptor** subfamily 3, group C, member 4), is a type of **nuclear receptor**that is activated by binding of either of the androgenic hormones **testosterone** or**dihydrotestosterone** in the cytoplasm and then translocating into the nucleus. The **androgen receptor** is most closely related to the progesterone receptor, and progestins in higher dosages can block the **androgen receptor**. The main function of the **androgen receptor** is as a DNA-binding transcription factor that regulates gene expression; however, the **androgen receptor** has other functions as well. **Androgen** regulated genes are critical for the development and maintenance of the male sexual phenotype.