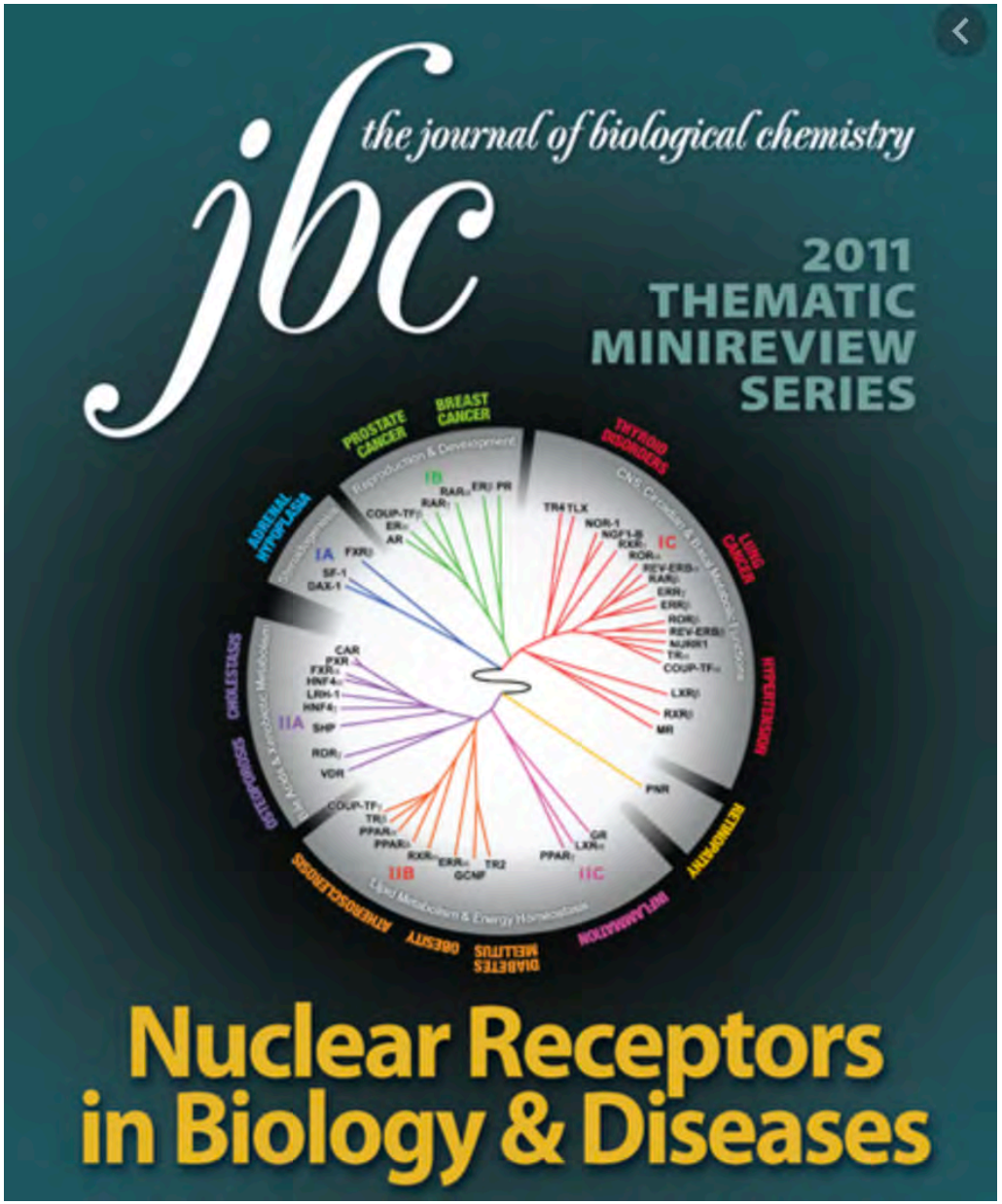
nanoRx
FROM HEALTH SCARE TO HEALTH CARE



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A unique property of nuclear receptors that differentiates them from other classes of receptors is their ability to directly interact with and control the expression of genomic DNA. As a consequence, nuclear receptors play key roles in homeostasis.

Nuclear receptors (NRs) are a family of highly conserved transcription factors that regulate transcription in response to small lipophilic compounds. They play a role in every aspect of development, physiology and disease in humans.

In contrast to the classical endocrine receptors that originally defined the family, recent studies suggest that the first NRs might have been sensors of their environment, binding ligands that were external to the host organism

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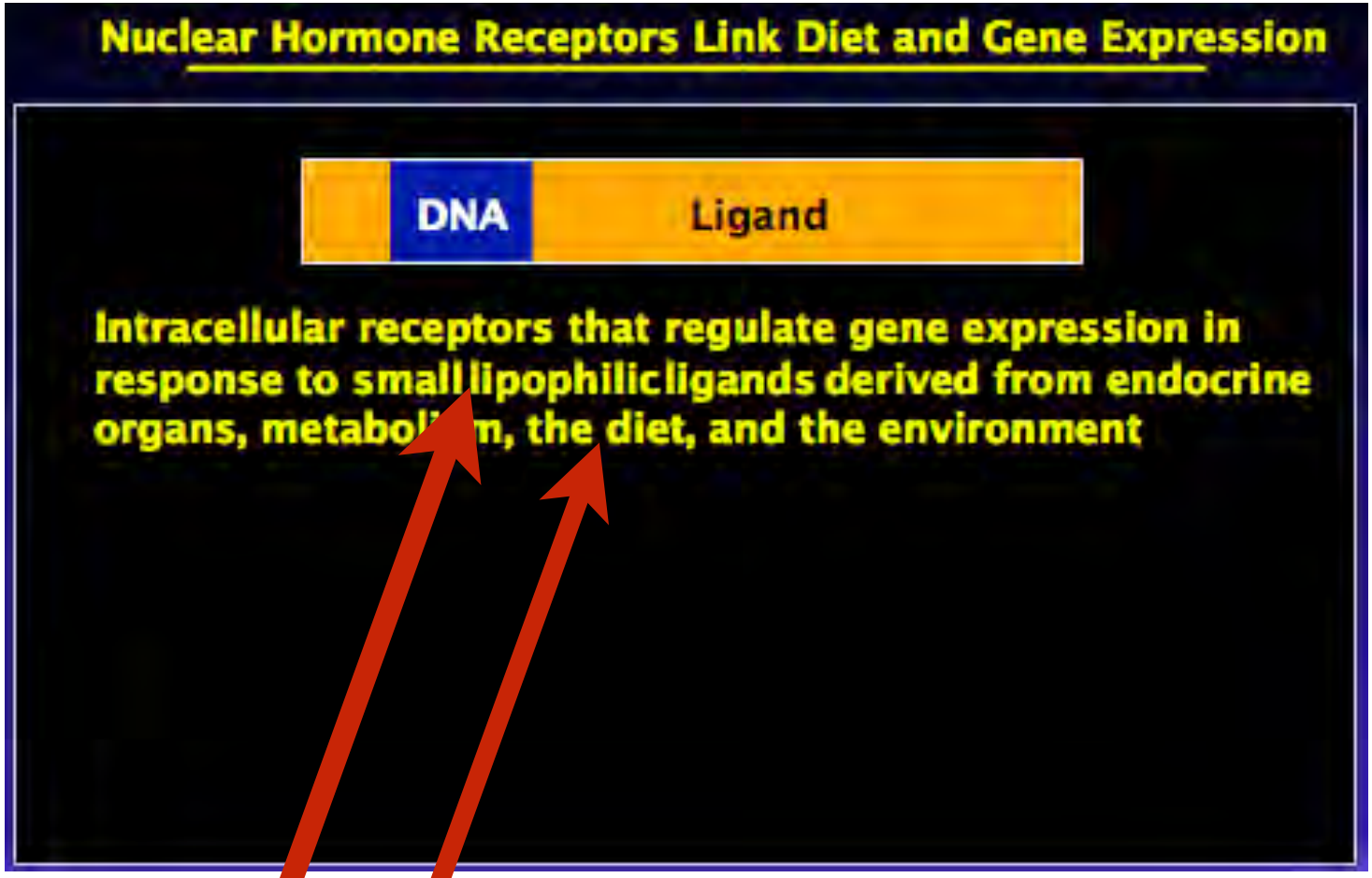
The popularity of NRs as drug targets is due to the fact that, in addition to playing a key role in these physiological processes, the receptors naturally contain a hydrophobic pocket that binds small hydrophobic molecules, and the most effective drugs are typically small hydrophobic compounds (METADICHOL) can cross the plasma membrane



METADICHOL

Nuclear Hormone receptors differ fundamentally from cell surface receptors in that the complex of ligand and receptor is directly responsible for the physiological regulatory action, with no intervening chain of events involving other mediator molecules.

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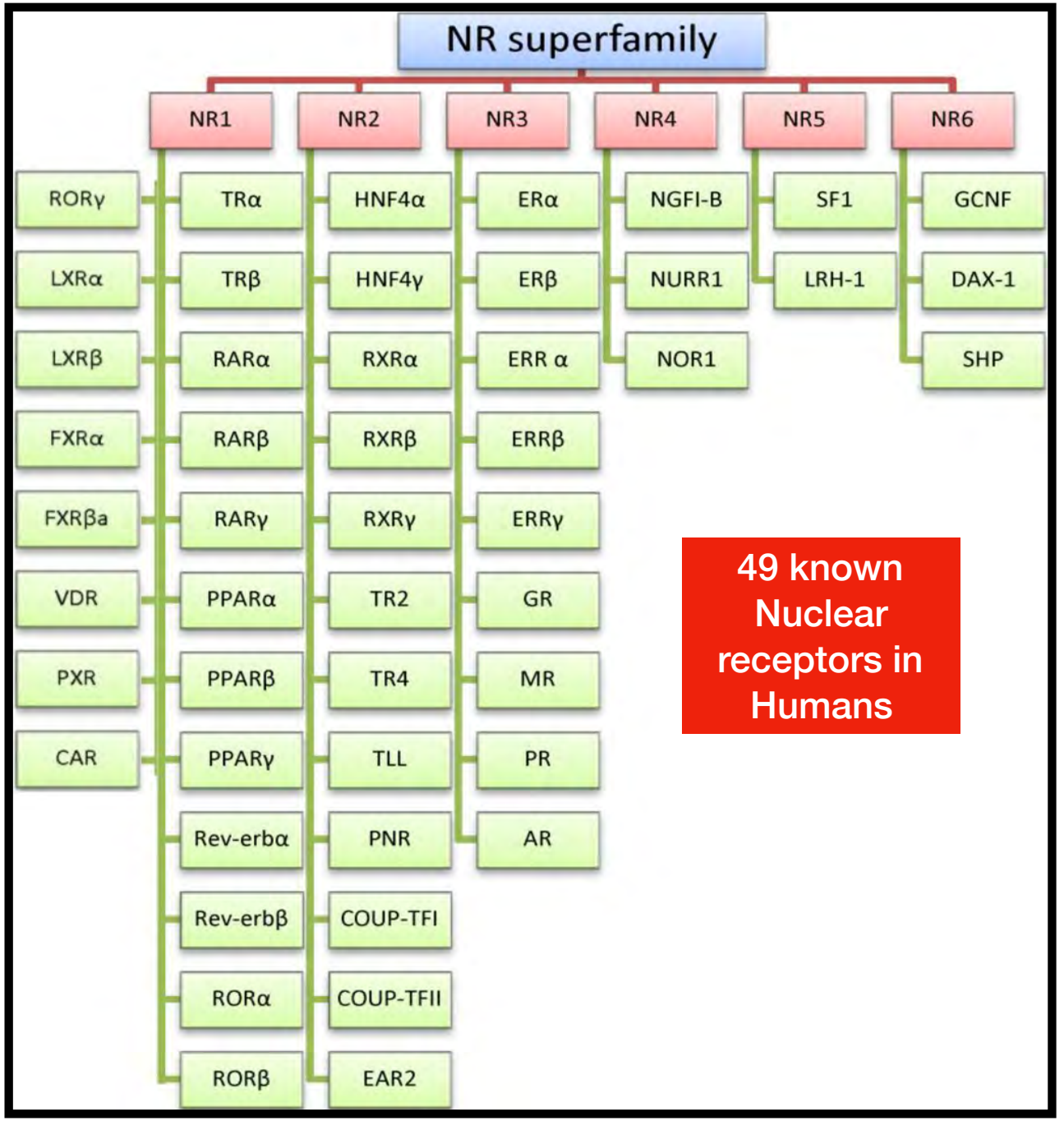

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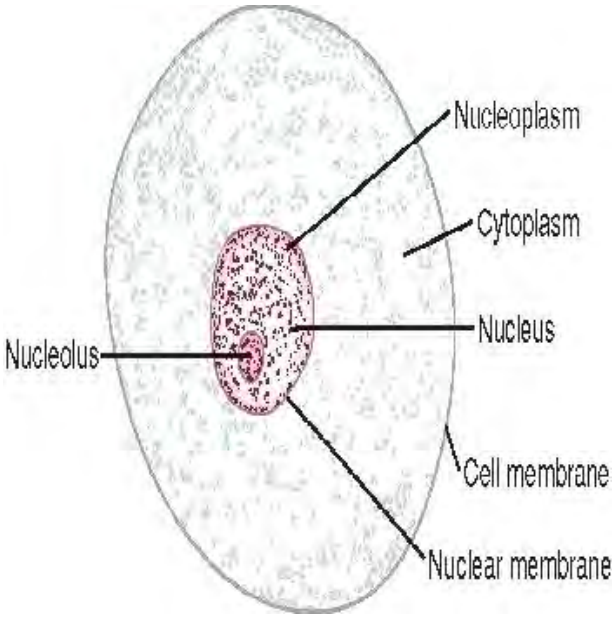
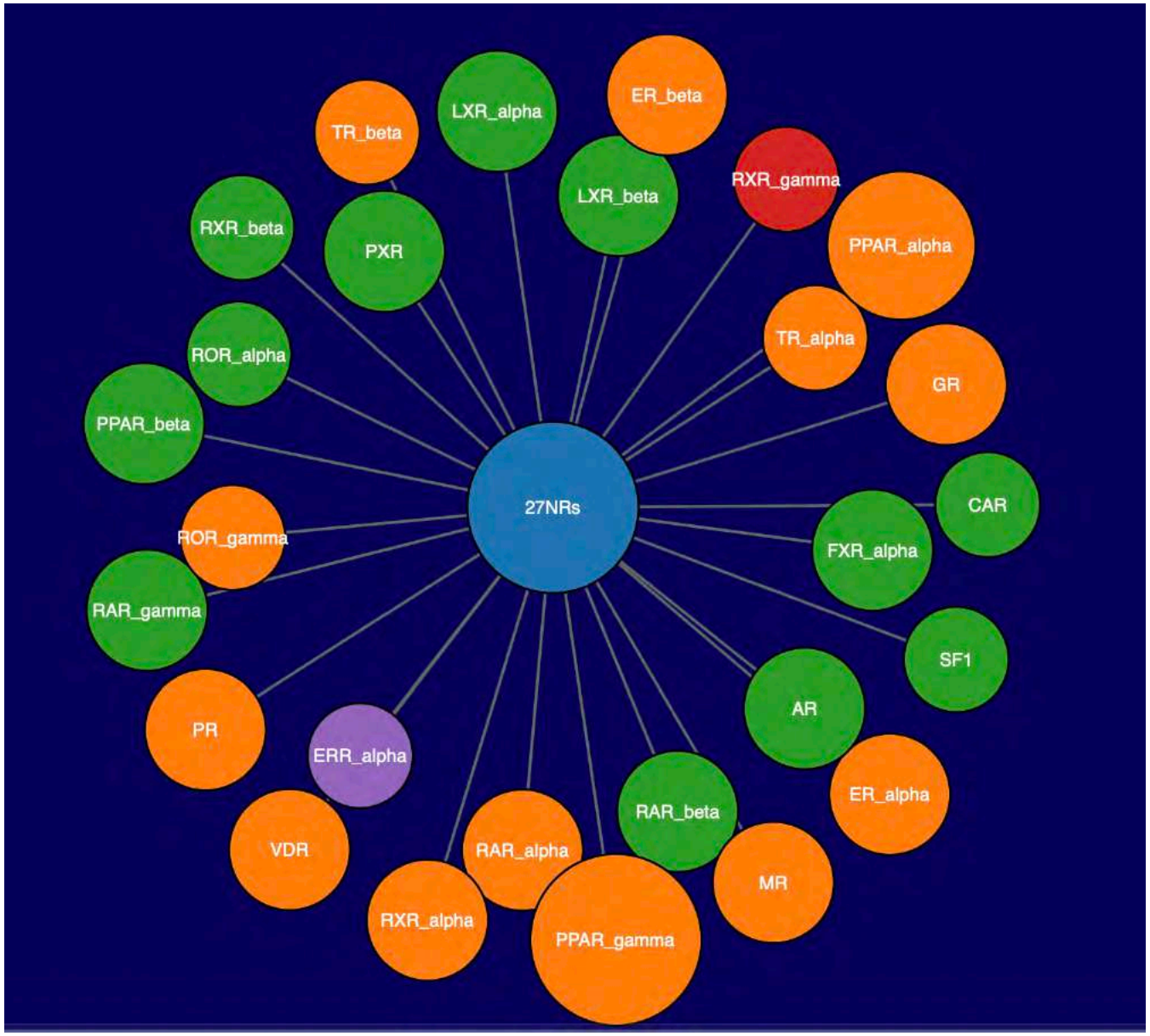
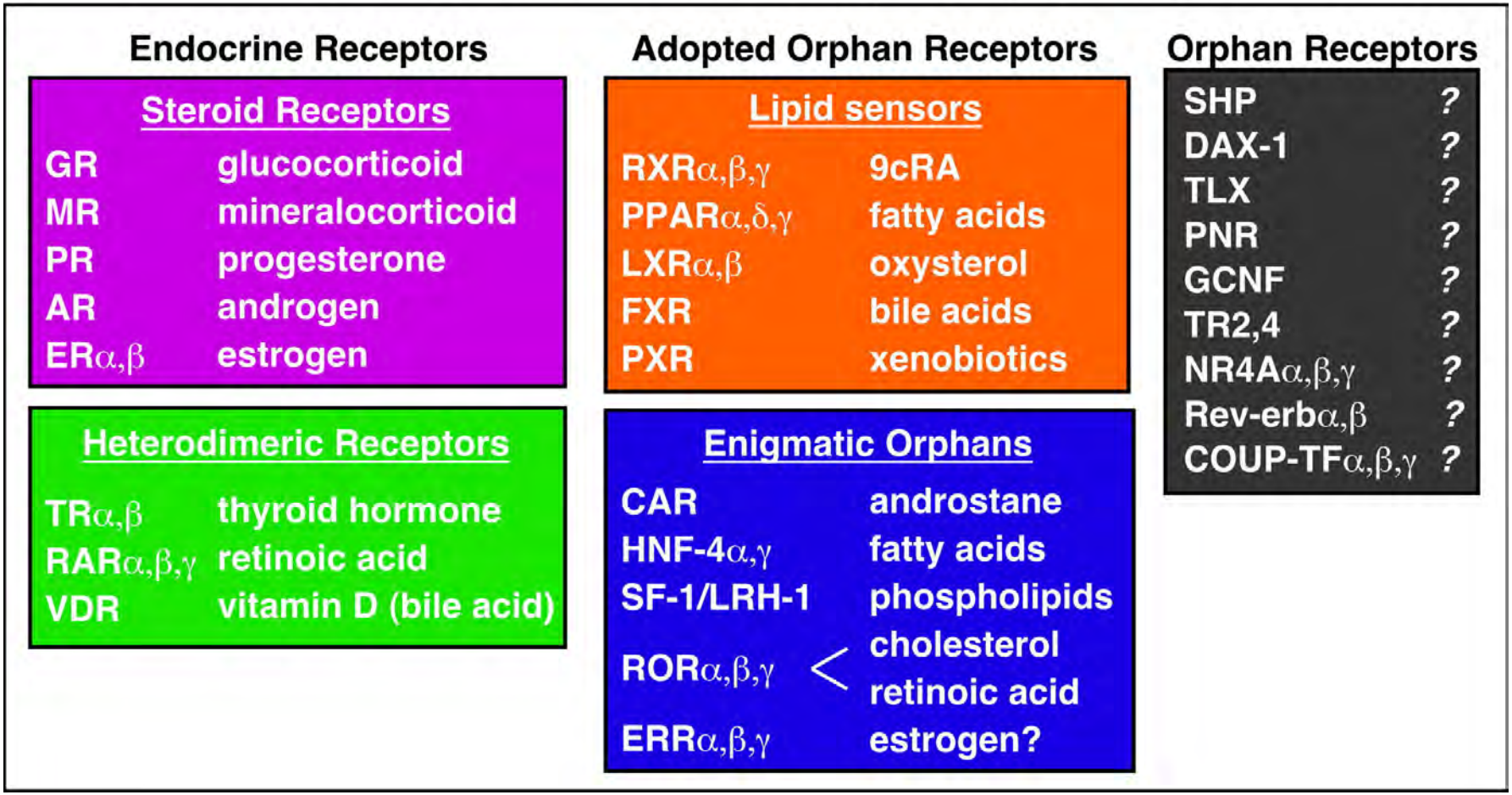




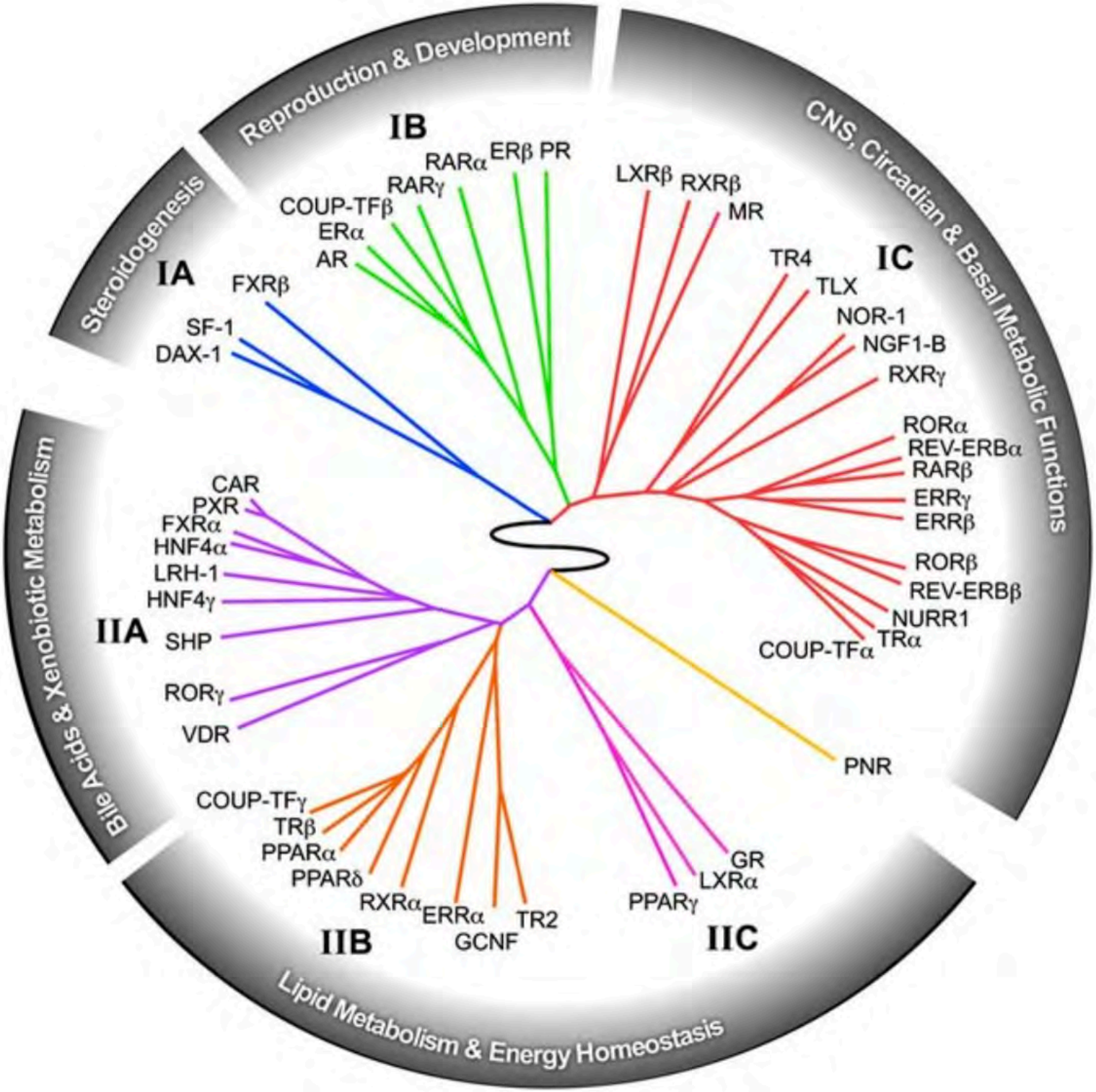
There are 49 Nuclear receptors in Humans shows here are those that are well known . Metadichol binds to these for which have ligands and in vitro tests are available

Human Nuclear Hormone Receptor Super Family



These 27 human receptors have available assay where we tested against Metadichol and it binds to all of them

Nr's and their role in maintaining homeostasis



NR current therapeutics

Current and Potential Therapeutic Indications

TRβ	Obesity, dyslipidemia, hypothryroidism
PPARα	Dyslipidemia, atherosclerosis, inflammation
PPARγ	Diabetes, obesity, cancer, inflammation, osteoporosis
LXRα/β	Dyslipidemia, atherosclerosis, diabetes
VDR	Osteoporosis, psoriasis, cancer, inflammation
GR	Arthritis, asthma, immunosuppression, obesity, diabetes
MR	Hypertension, CHF
PR	Contraception, cancer, osteoporosis
AR	Frailty, prostate cancer, sexual dysfunction, osteoporosis
ERα	Breast cancer, osteoporosis, cardiovascular disease, gynecological disorders, Alzheimer's
ERβ	Prostate cancer, osteoporosis, obesity, cardiovascular disease, Alzheimer's
HNF4α	Diabetes, dyslipidemia
RAR(α,β,γ)	Cancer, psoriasis
RXR(α,β,γ)	Diabetes, cancer

NR possible therapeutics

Possible Therapeutic Indications

Rev-Erb (α,β)	Circadian rhythym atherosclerosis
RORα	Atherosclerosis, dyslipidemia, inflammation, rheumatoid arthritis, osteoporosis, neurodegeneration
RORγ	Osteoporosis, immunosuppression
FXR	Dyslipidemia, liver disease
PXR, CAR	Xenobiotic metabolism
TR2, TR4	Cancer, male fertility
TLX	Neurodegeneration
PNR	Retinal degeneration
COUP-TFI	Breast cancer, neural development
COUP-TFII	Cancer, angiogenesis
EAR2	Uterine/gynecological disorders

•NGFI-B	Drug abuse, cancer, schizophrenia, manic-depression, psychoses, neurodegeneration, immunomodulation
•NURR1	Parkinson's, schizophrenia, manic-depression, cancer
•NOR1	Drug abuse, cancer, immunomodulation
•SF-1	Adrenal disease, disorders of steroid metabolism
•LRH	Breast cancer, fertility, dyslipidemia
•GCNF	Fertility/contraception
•DAX-1	Adrenal disease, fertility, gynecologic disorders
•SHP	Obesity, dyslipidemia, diabetes, liver disease, cancer
•ERRα	Osteoporosis, dyslipidemia
•ERRβ	Fertility

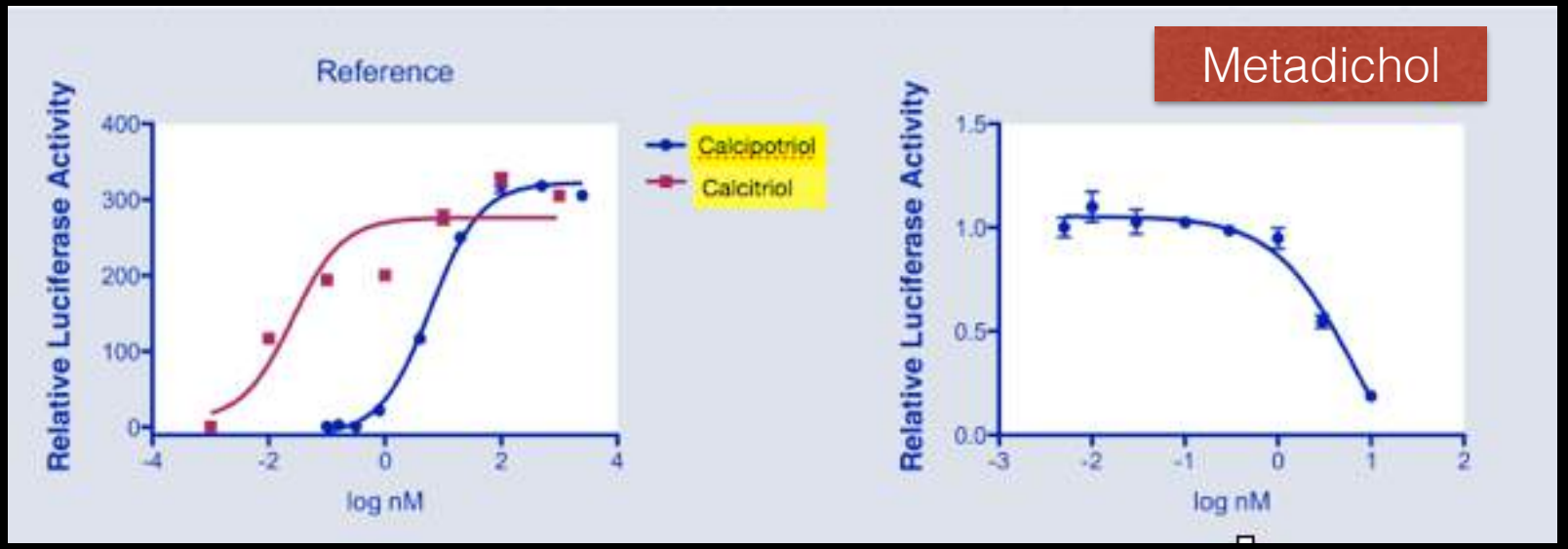
NRR

Sources: Lifespan Database
Giguere, V. *Endocrine Rev.* 1999, *20*, 689-725
Willson, T. M.; Moore, J. T. *Mol. Endocrinology* 2002, *16*, 1135-1144

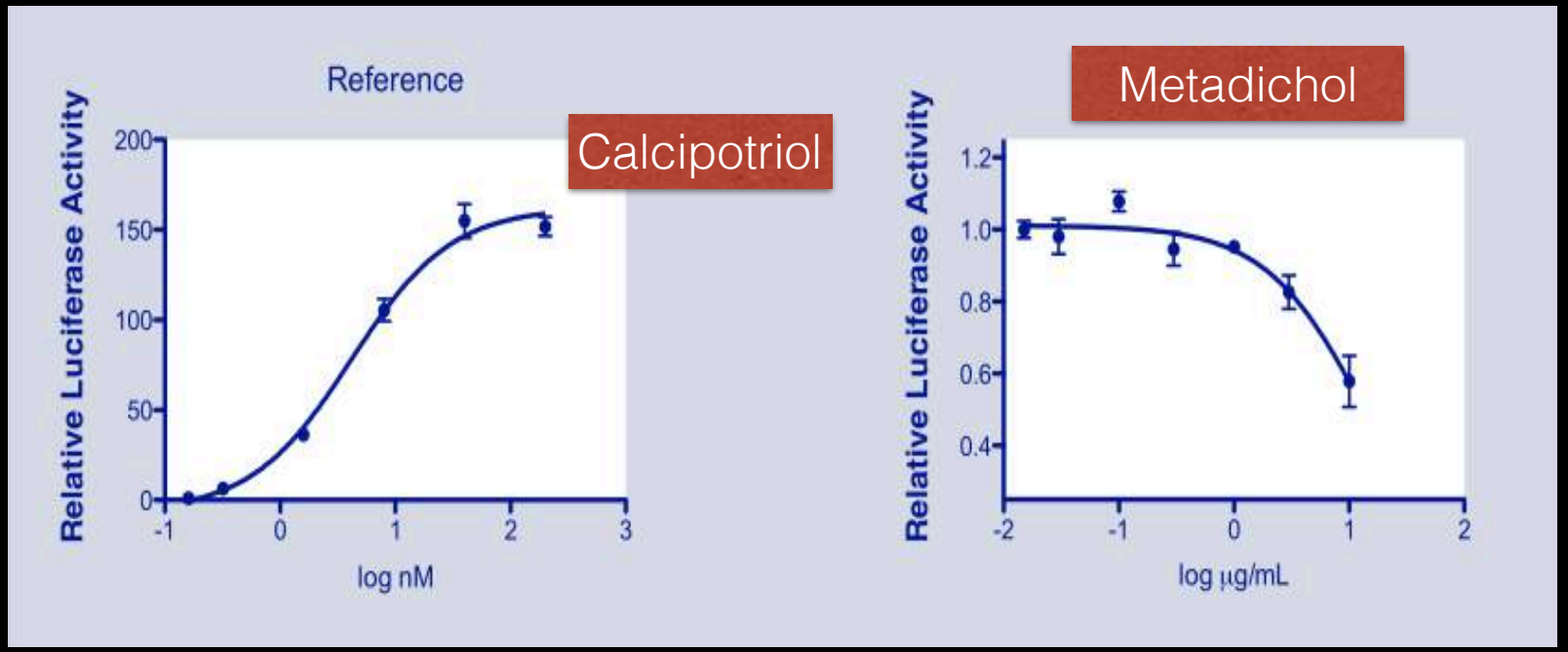
Cell transactivation assay on human VDR

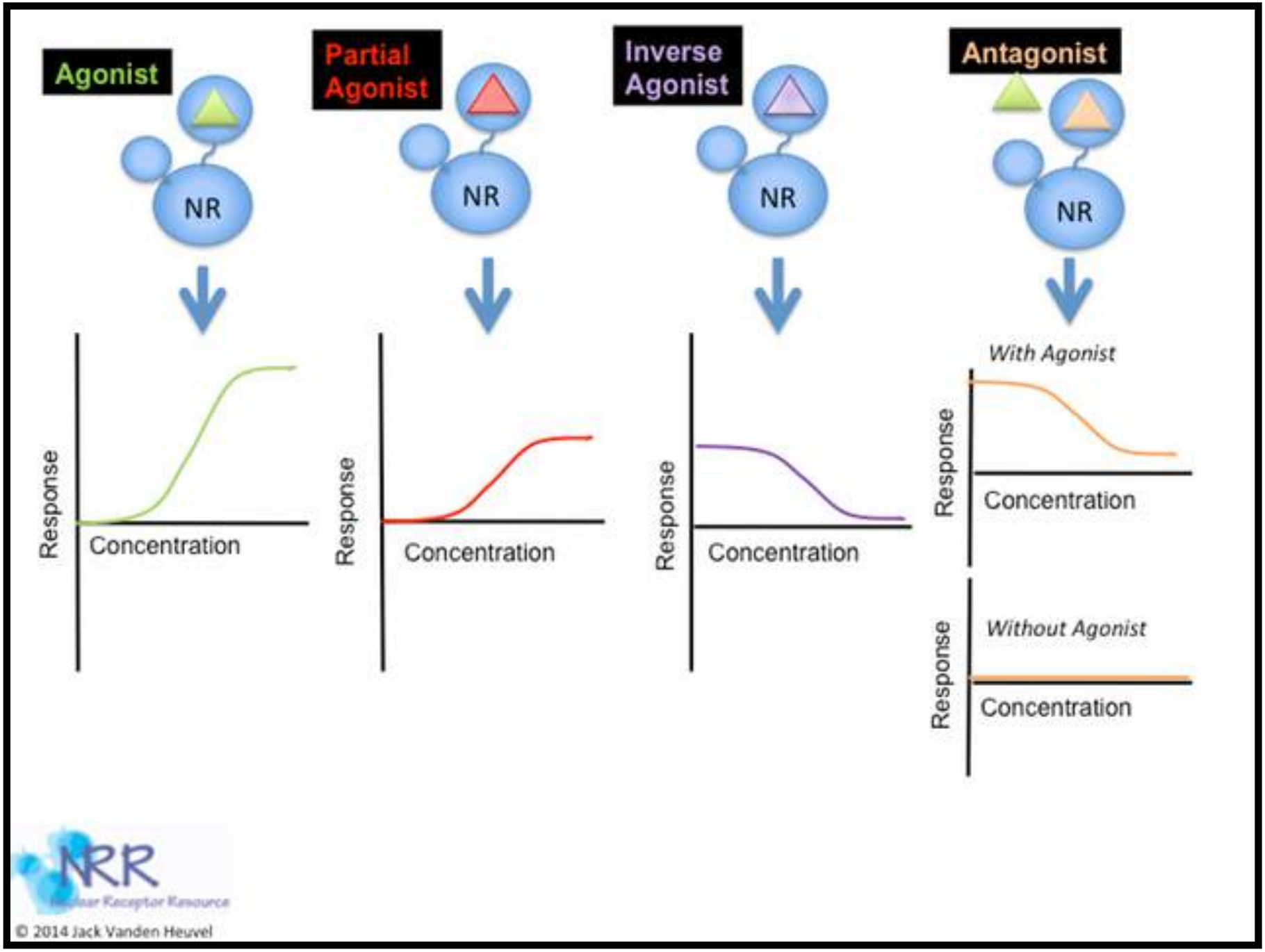
Work done by Indigo Biosciences PA, USA

Agonist Assay



Antagonist Assay




Agonist
NR
Response
Concentration
Partial Agonist
NR
Response
Concentration
Inverse Agonist
NR
Response
Concentration
Antagonist
NR
With Agonist
Response
Concentration
Without Agonist
Response
Concentration
NRR
Nuclear Receptor Resource
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Inverse agonists block constitutive response

Metadichol exhibits dual properties
for e.g Increasing Insulin Secretion (type 1) and reducing Insulin (type 2)

It behaves more like a Protean agonist.

Protean agonists act as both positive and negative agonists on the same receptor, depending on the degree of constitutive activity that is present.

If there is no constitutive activity, the agonist would be a positive agonist.

When constitutive activity is present, the Protean agonist would be an inverse agonist.

Neubig. R.R., Missing Links: Mechanisms of Protean Agonism, Mol. Pharmaco: 2007; l71:200–1202.

Metadichol and Central Control System of the Human Machine

UNIQUE DNA CODE

10 TRILLION CELLS

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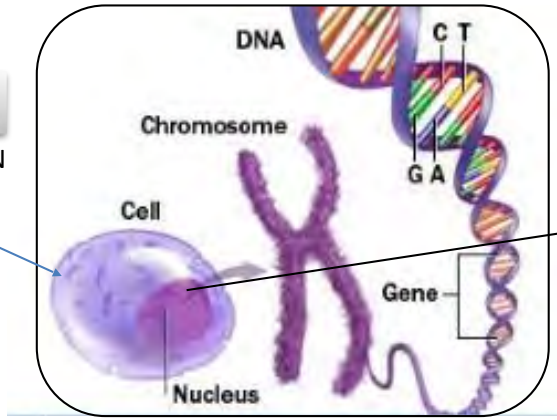
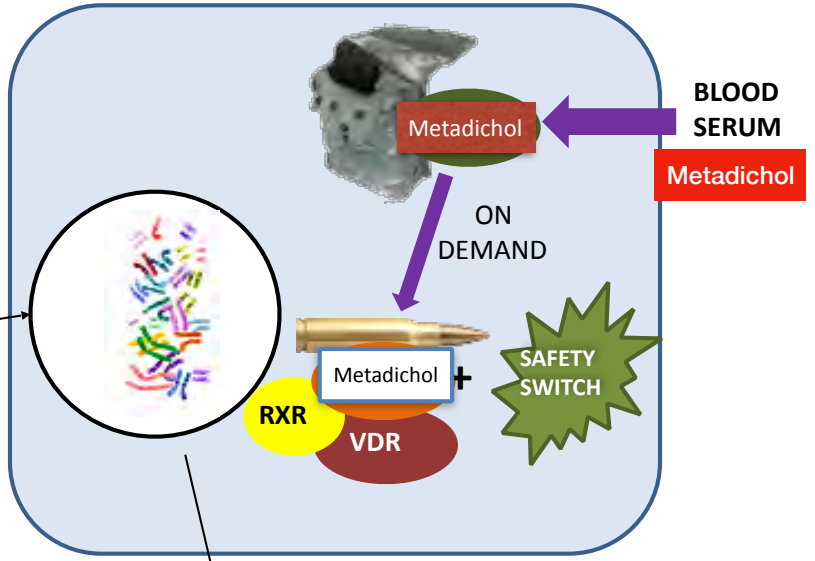
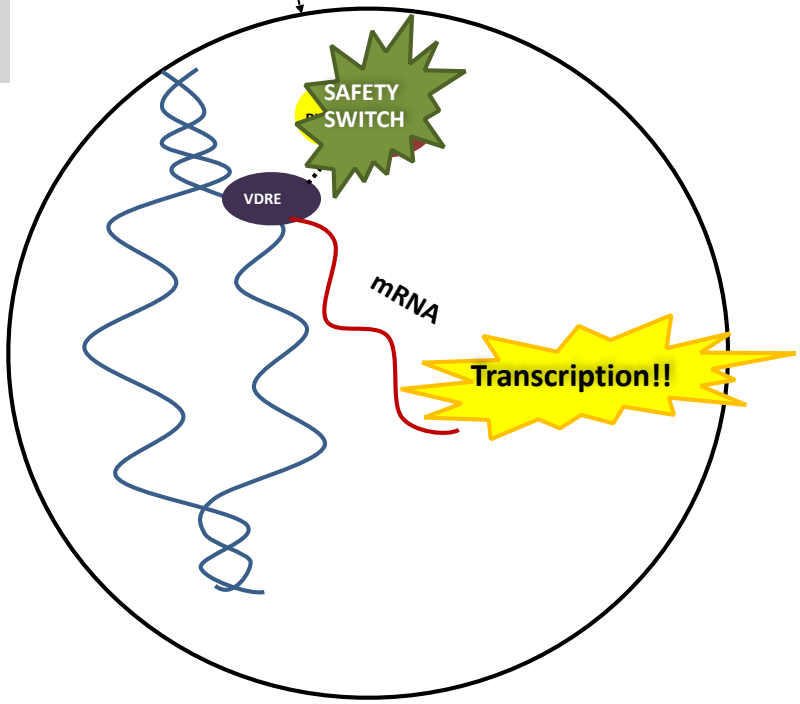
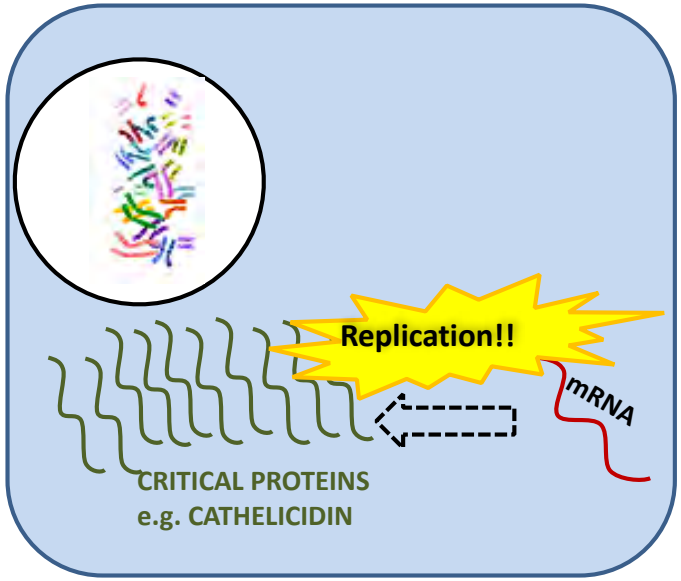




This process is repeated when Metadichol interacts with other Nuclear receptors.
Shown here is with VDR





- Blood Pressure
- Cancer
- Heart Disease
- MS, TB, Flu
- Asthma
- T1 Diabetes
- T2 Diabetes
- Obesity
- Met Syndrome
- Alzheimers

Reference and adapted from
2014 Ivor Cummins BE(Chem) CEng MIEI