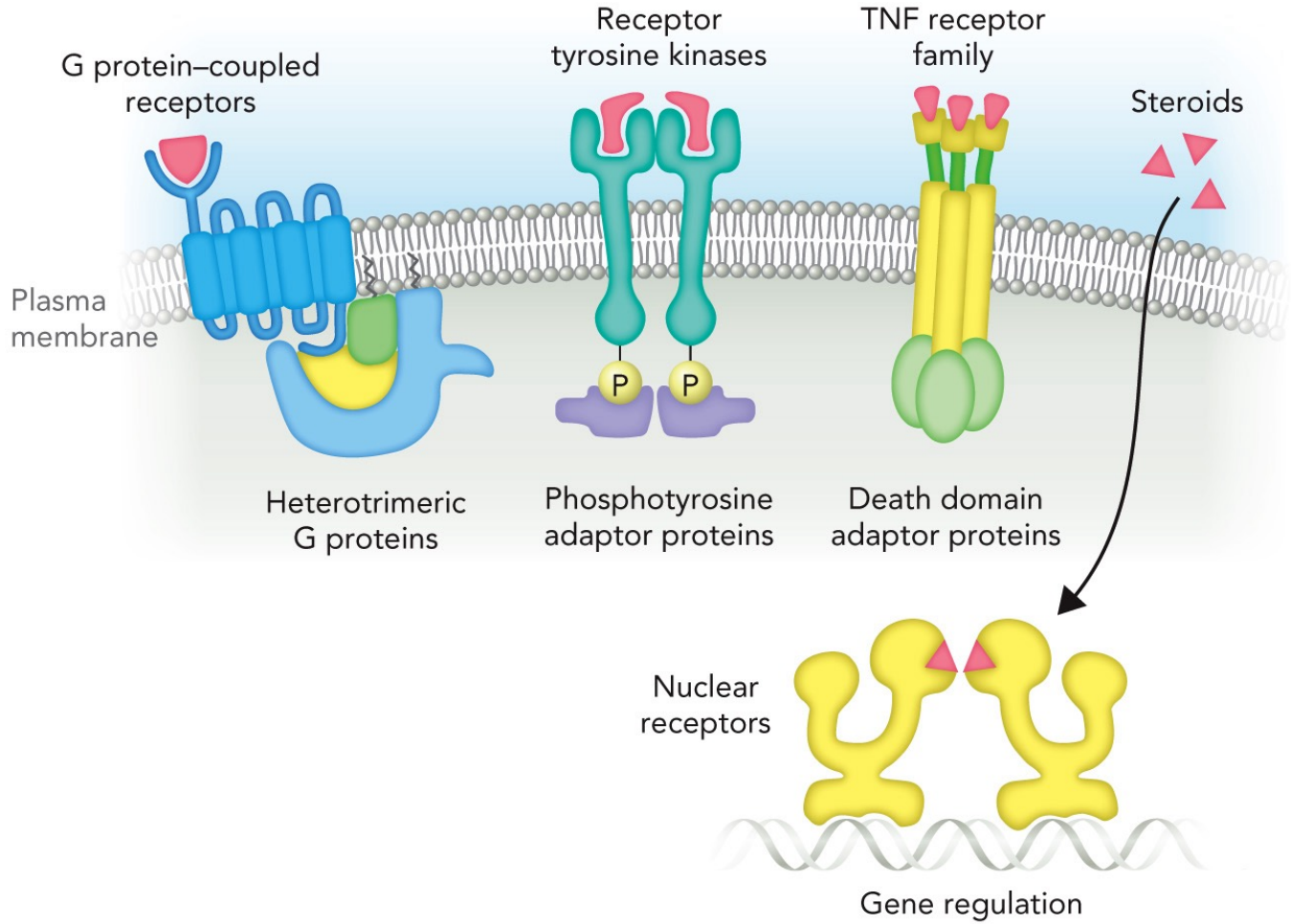
Classes of Receptor Proteins in Eukaryotes,



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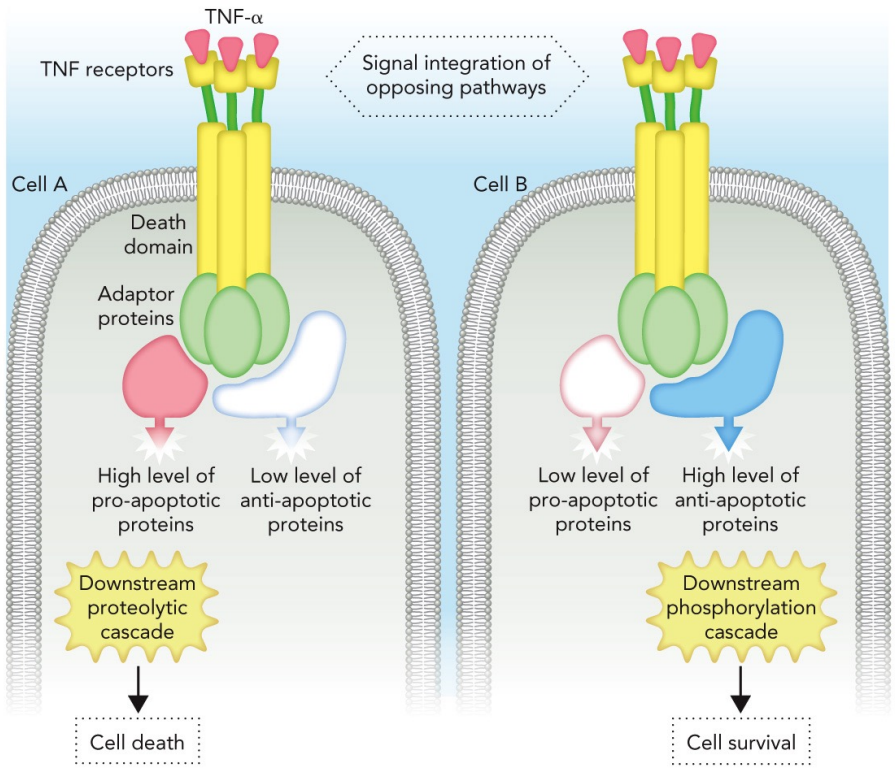
8.4 Tumor Necrosis Factor Receptor Signaling

- A single receptor stimulates intracellular pathways with opposing cellular responses.



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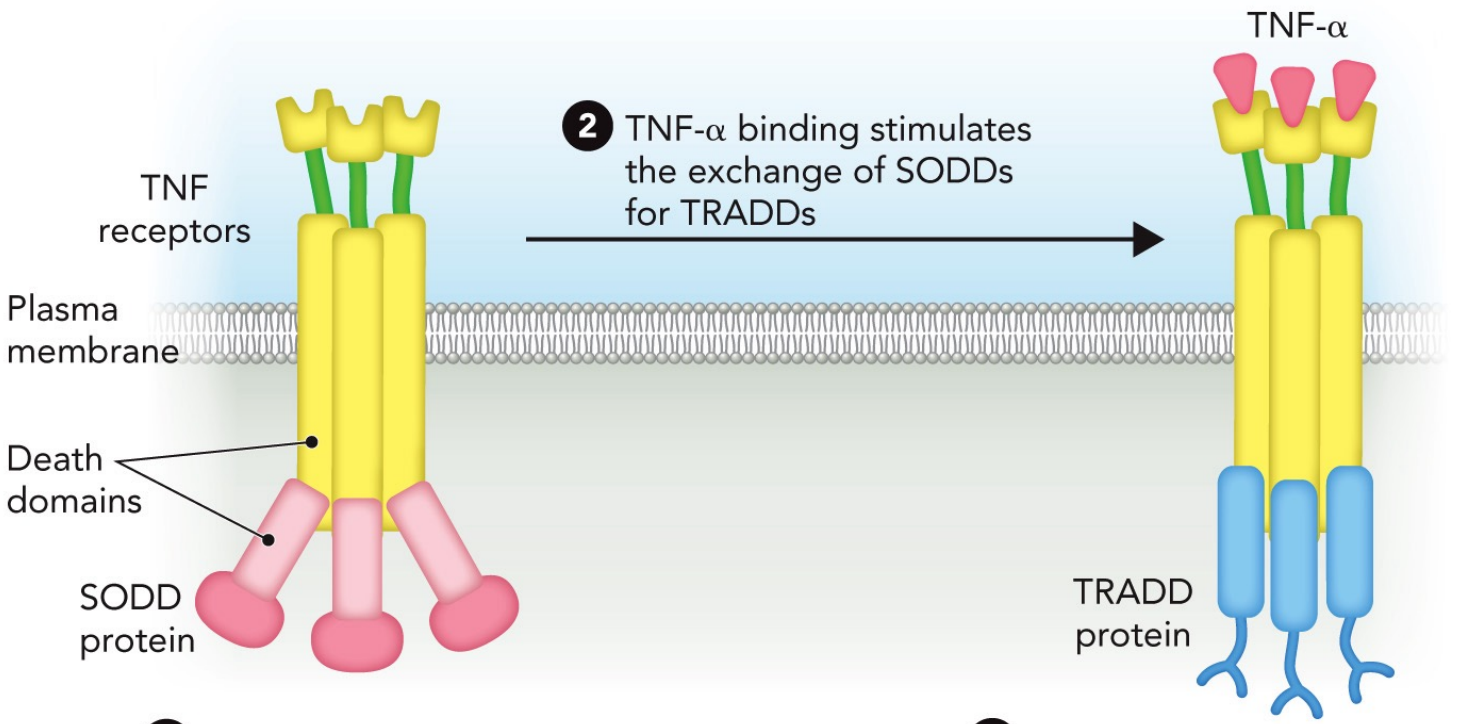
Activation of TNF Receptor Complexes

- TNF is a homotrimer.
- Binding of TNF-α induces a conformational change in the TNF receptor at the death domain (DD).
- This causes a silencing of the death domain (SODD).

TNF Receptor Associated Death Domain (TRADD)

- TRADD binds to the TNF receptor.



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Apoptosis

- Procaspase 8 is cleaved into caspase 8.
- Caspase 8 cleaves procaspase 3 and generates caspase 3, the “executioner” caspase.
- Key regulatory molecules are degraded and the cell dies.

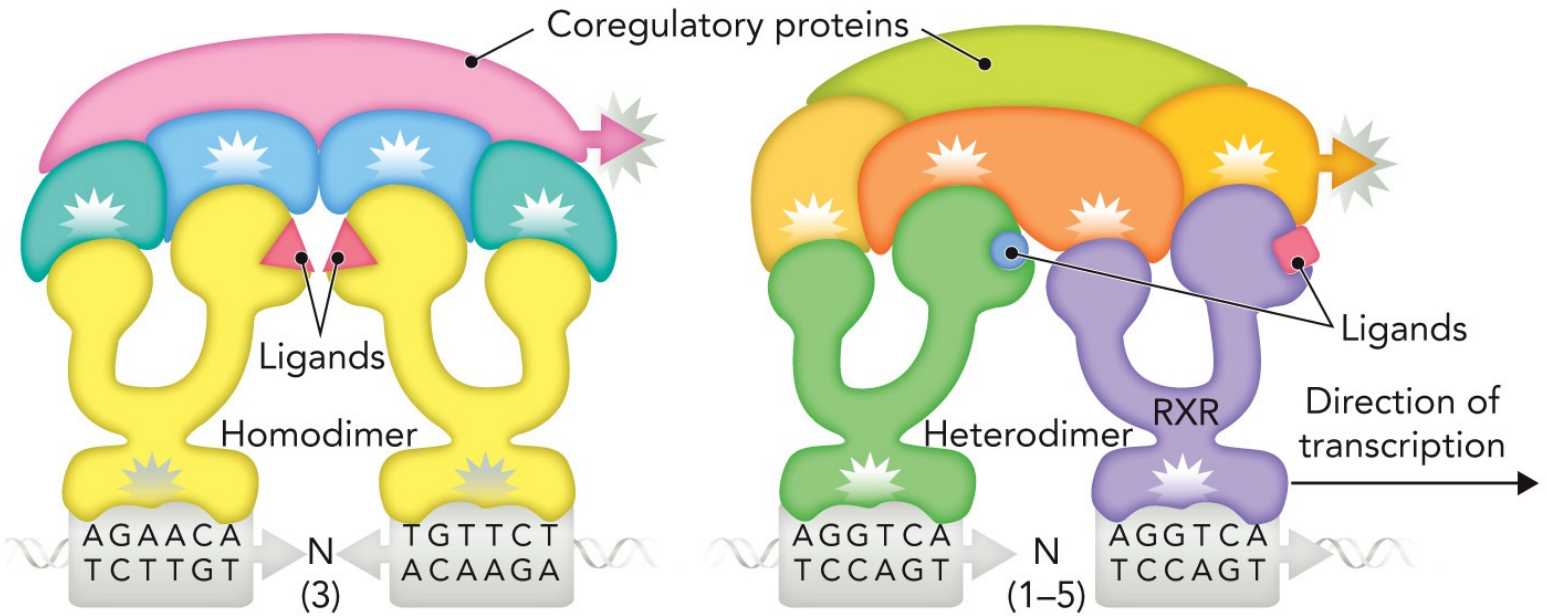
8.5 Nuclear Receptor Signaling, Part 1

- Also known as intracellular receptors
- Not bound to membrane
- Serves as transcription factors that regulate gene expression

8.5 Nuclear Receptor Signaling, Part 2

- Examples include:
  - Steroid receptors
  - Metabolite receptors
- Governed by three parameters:
  - Cell-specific expression of nuclear receptors
  - Localized bioavailability of ligands
  - Differential accessibility of target gene DNA sequences in chromatin to nuclear receptor binding

Steroid and Metabolite Receptors



Steroid Receptors
Glucocorticoid receptor
Estrogen receptor
Androgen receptor
Progesterone receptor
Aldosterone receptor

Metabolite Receptors
Retinoid X receptor (RXR)
Vitamin D receptor
Retinoic acid receptor
Thyroid hormone receptor
Peroxisome proliferator–activated receptor

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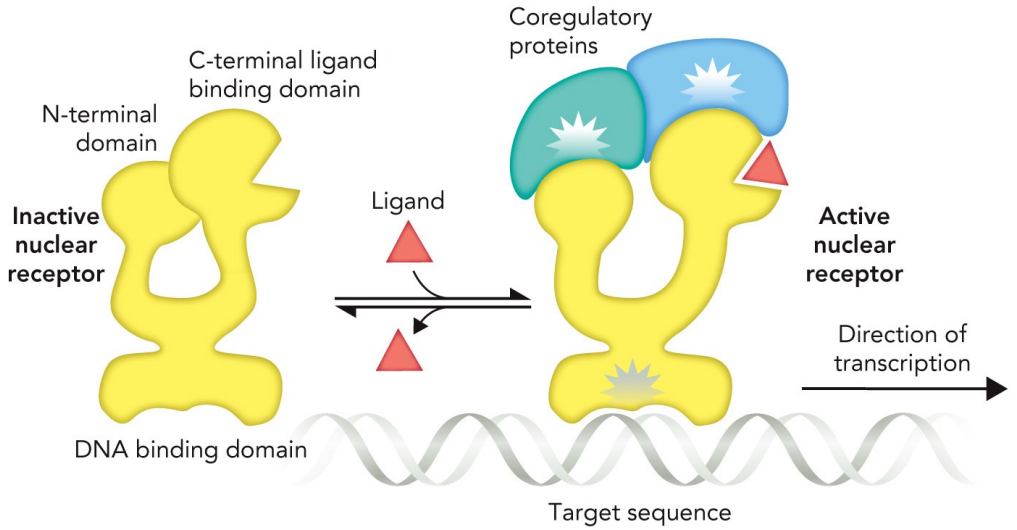
Nuclear Receptor Signaling Synopsis

- Binding of lipophilic first messengers to binding domain
  - Can occur with or without DNA present
- Ligand activated nuclear receptors recruit co-regulatory proteins which alter transcription rates through acetylation or deacetylation



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Steroid Receptors

- Head-to-head homodimers that can bind to inverted repeat DNA sequences
  - That is, 5’-AGAACA-3’
- Ligands are cholesterol derivatives.

Metabolite Receptors

- Form head-to-tail heterodimer
- Bind to direct DNA sequences
  - That is, 5′-AGGTCA-3′
- Ligands are derived from:
  - Vitamins
  - Unsaturated fatty acids
  - Essential amino acids

Glucocorticoid Signaling

- Glucocorticoids are important for lung development, carbohydrate metabolism, and the inflammatory response.

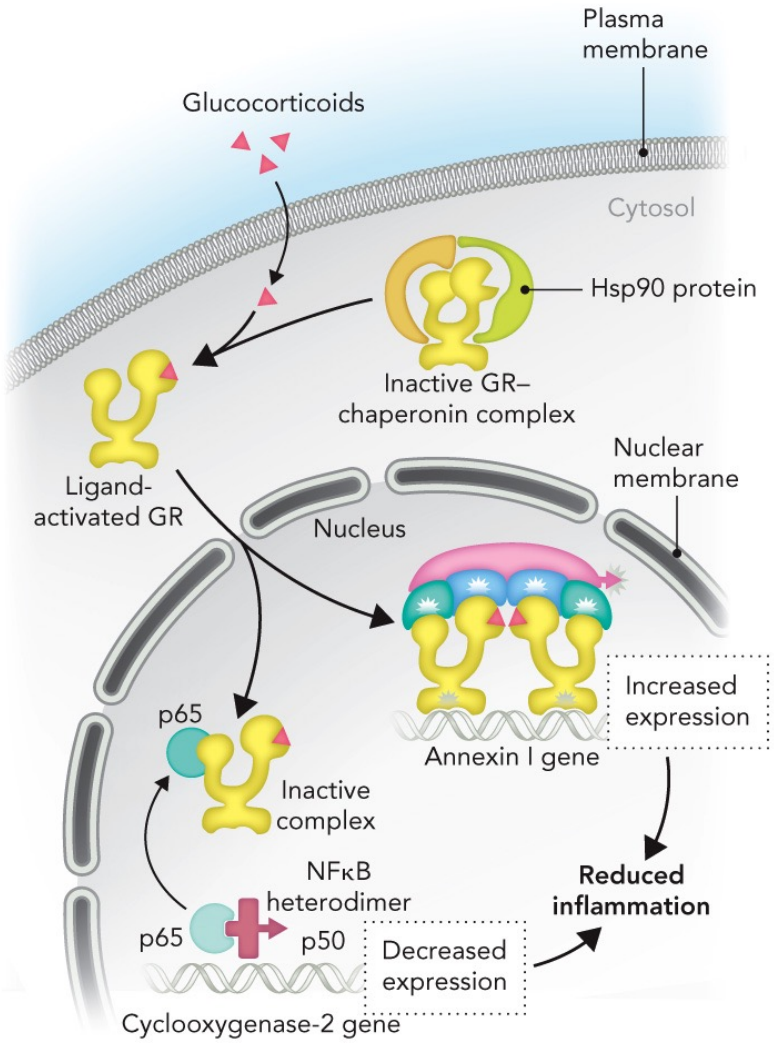

Figure 8.66

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