

Evolution & the Steroid Hormone Response System



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Environmental Hormones

**Nothing in Biology Makes
Sense Except in the Light of
Evolution**

Theodosius Dobzhansky

Evolution: Two Components

- **Variation in a population**
 - **Most mutations reduce fitness**
- **Natural Selection**
 - **Conditions favor certain mutations**
 - **Being in the right place, right time**

Evolutionary Landmarks



Sequences: multicellular animals 0.7 to 1 billion yrs ago

Vendian: soft bodied animals

Cambrian: ~35 phyla, invertebrates, chordates

Evolutionary Landmarks



RNA World?: Genes, enzymes constructed of RNA

Cyanobacteria: DNA, proteins, oxygen enters atmosphere

Oxygen catastrophe: symbionts with mitochondria

Environment & Evolution

- **Cambrian**
 - **Sufficient oxygen ~550 myrs ago**
 - **Support large animal metabolism?**
- **Post Cambrian**
 - **Sufficient ozone ~ 400 myrs ago**
 - **Protect animals & land plants?**

Hormone Binding Domain Comparison

<u>Human</u>	<u>Xenopus</u>
Androgen	88%
Estrogen-alpha	79%
Glucocorticoid	76%
Mineralocorticoid	85%

Hormone Binding Domain Comparison

<u>Human</u>	<u>Progesterone</u>	<u>Estrogen</u>
Androgen	54%	20%
Estrogen-alpha	23%	-
Glucocorticoid	54%	26%
Mineralocorticoid	55%	23%

Steroid Receptor Evolution

- **Slow change from fish to humans**
- **Sequence analysis predicts fish ER- β**
- **Receptor Phylogeny: two duplications**
- **During genome-size duplications?**

Steroid Receptor Evolution

- ER is ancestral to AR, PR, GR, MR
- No close relative in *C. elegans* or Fly
 - Discontinuity in BLAST analysis
- Origin during early Cambrian?
 - Amphioxus?
 - Hagfish?

Ancestral Receptor: Adrenal & Sex Steroids

Questions:

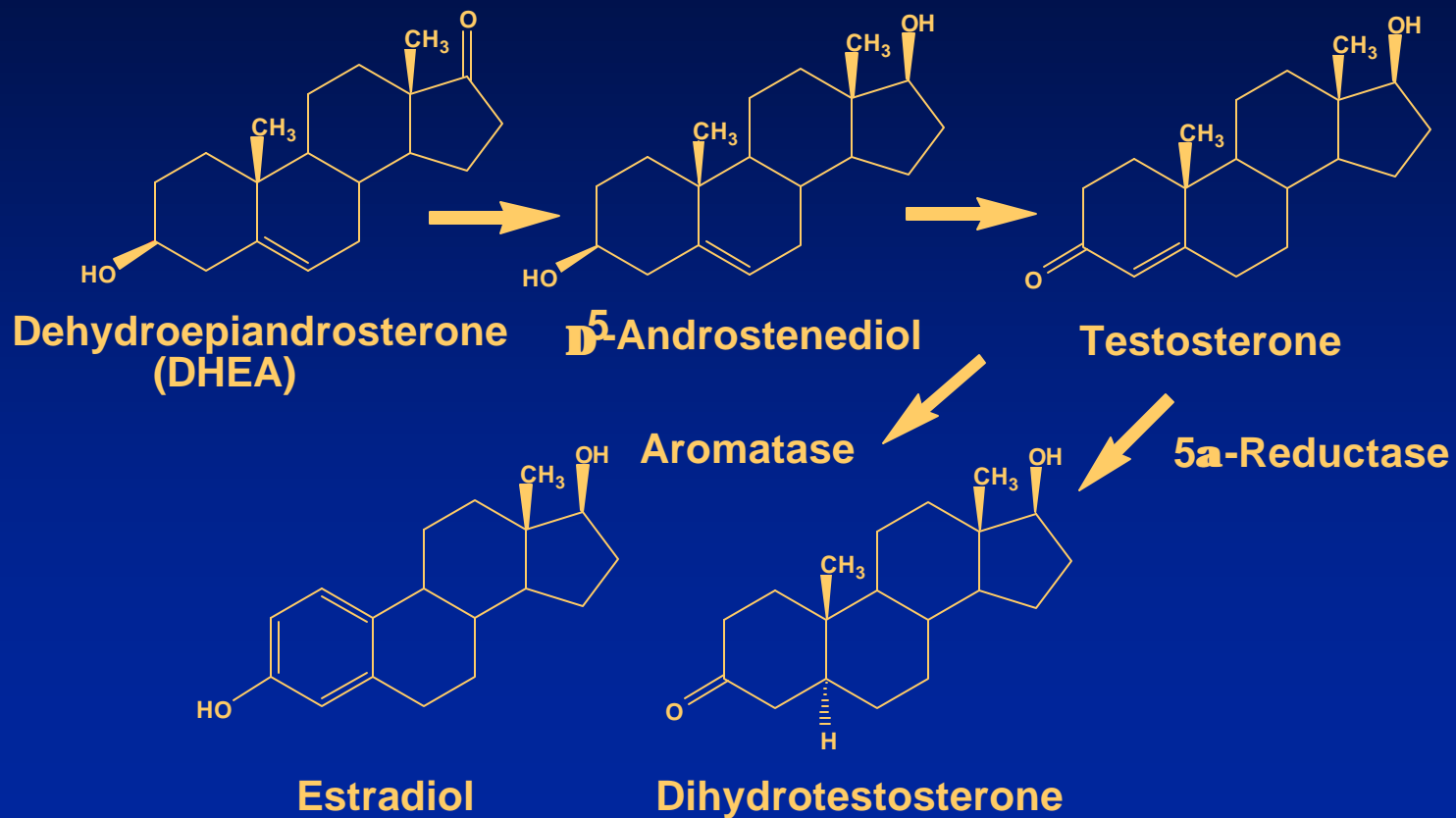
What steroid(s) did it recognize?

Other ligands?

Functions of receptor/ligands?

Ancestral functions: modern organisms?

D⁵-Androstenediol: Ancestral Androgen/Estrogen?



Environmental Hormones