



Centrum pro výzkum
toxických látek
v prostředí

BIOMARKERS AND TOXICITY MECHANISMS

09 – Intercellular communication & regulation

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Tento projekt je spolufinancován Evropským sociálním fondem a státním rozpočtem České republiky.



INVESTICE DO ROZVOJE VZDĚLÁVÁNÍ

Cell communication & regulation: a target for toxicants

... especially sensitively regulated processes are highly susceptible to toxicants

→ toxicity to REGULATIONS & SIGNALLING

Hierarchy in signalling

- **systems**: neuronal \leftrightarrow endocrine
- **cell-to-cell**
 - hormonal & neuronal signal transmission
 - contact channels
- **intracellular** signal transduction

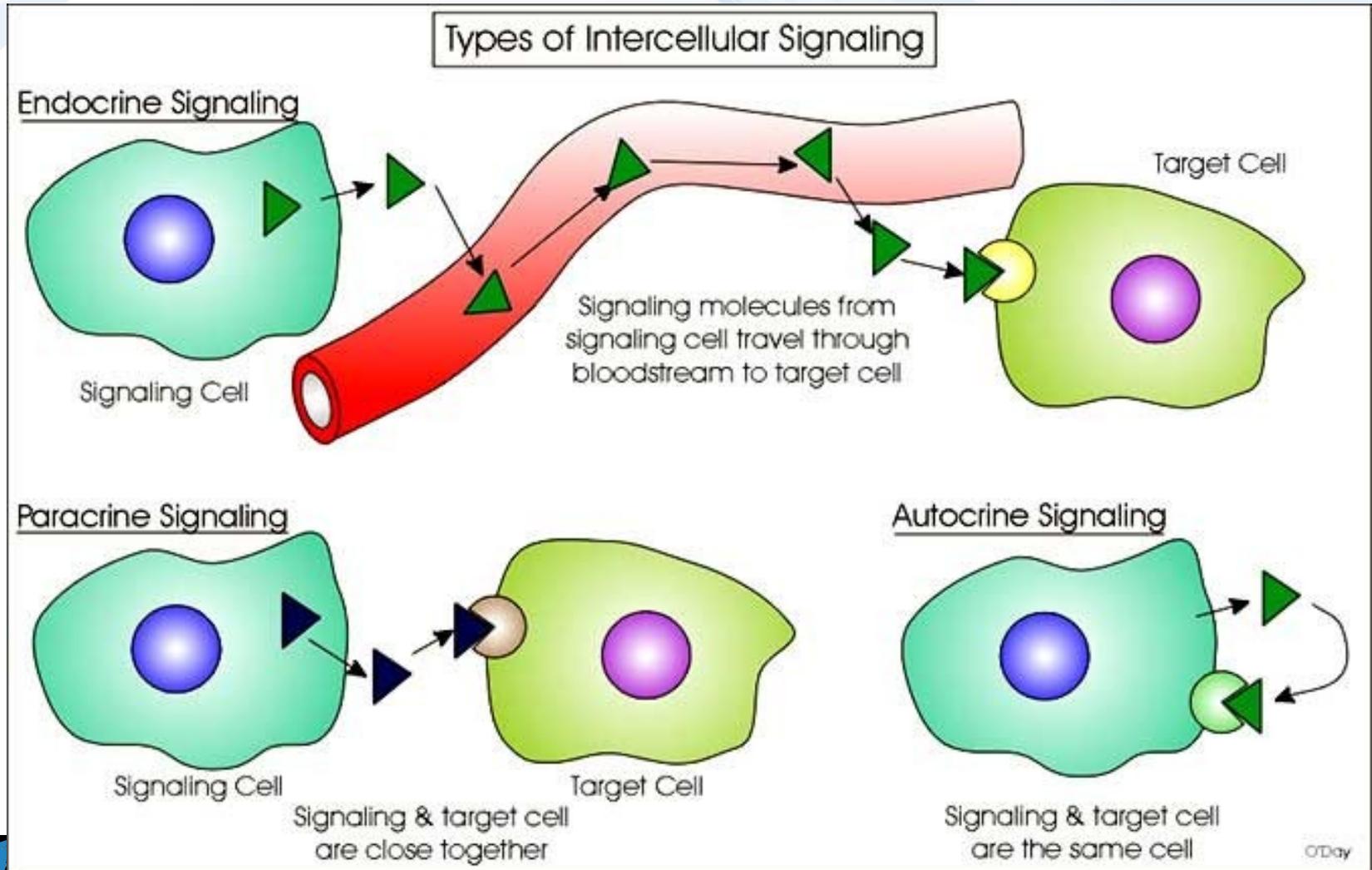


INTER-cellular signals

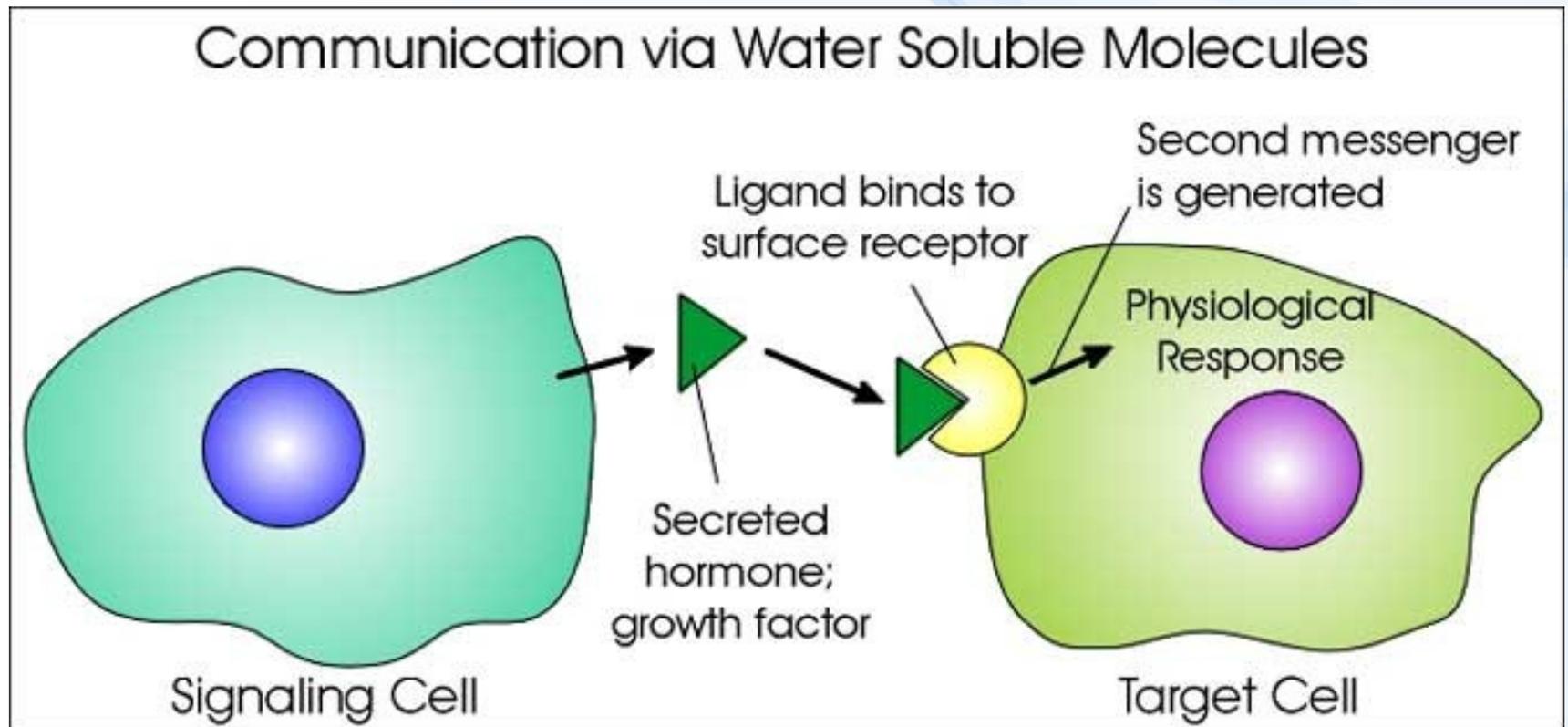
Overview



Cell to cell communication & regulation: a target for toxicants

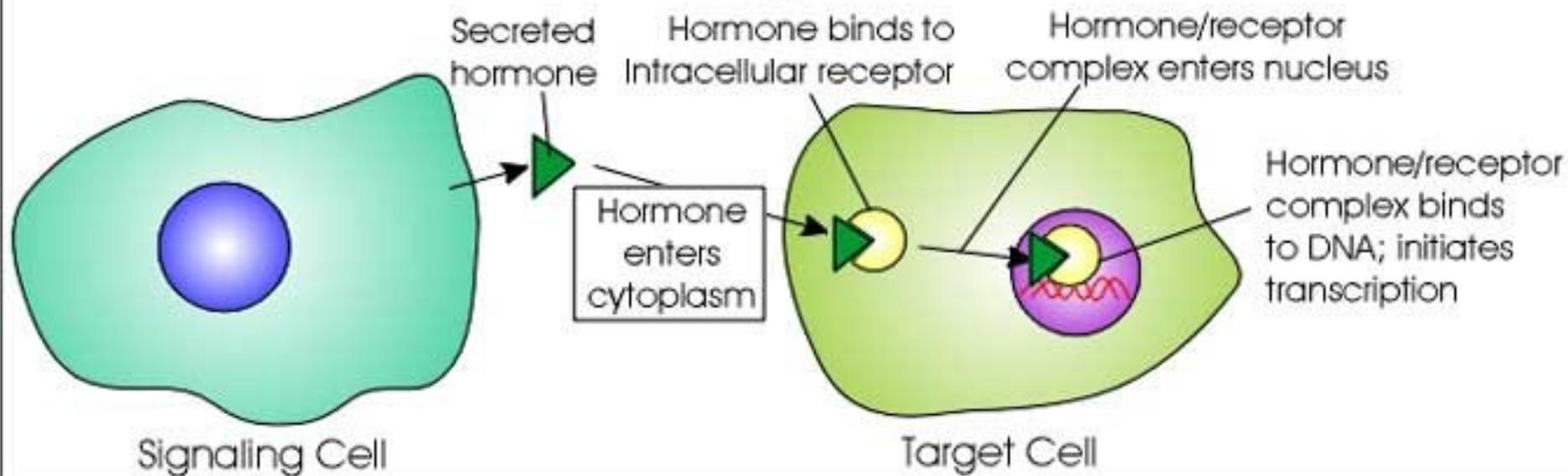


Cell to cell communication (1)



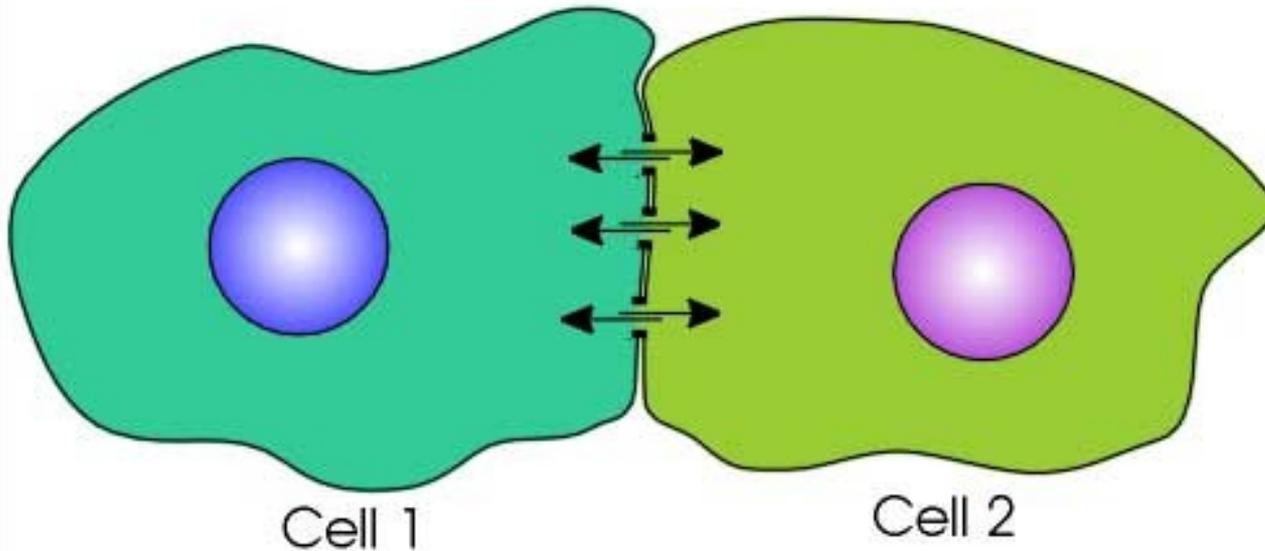
Cell to cell communication (2)

Communication via Lipid Soluble Molecules

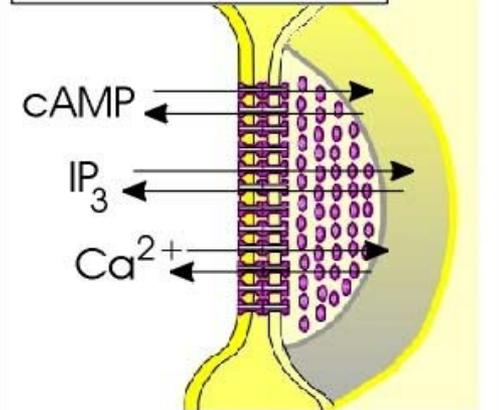


Cell to cell communication (3)

Communication via Cellular Continuities



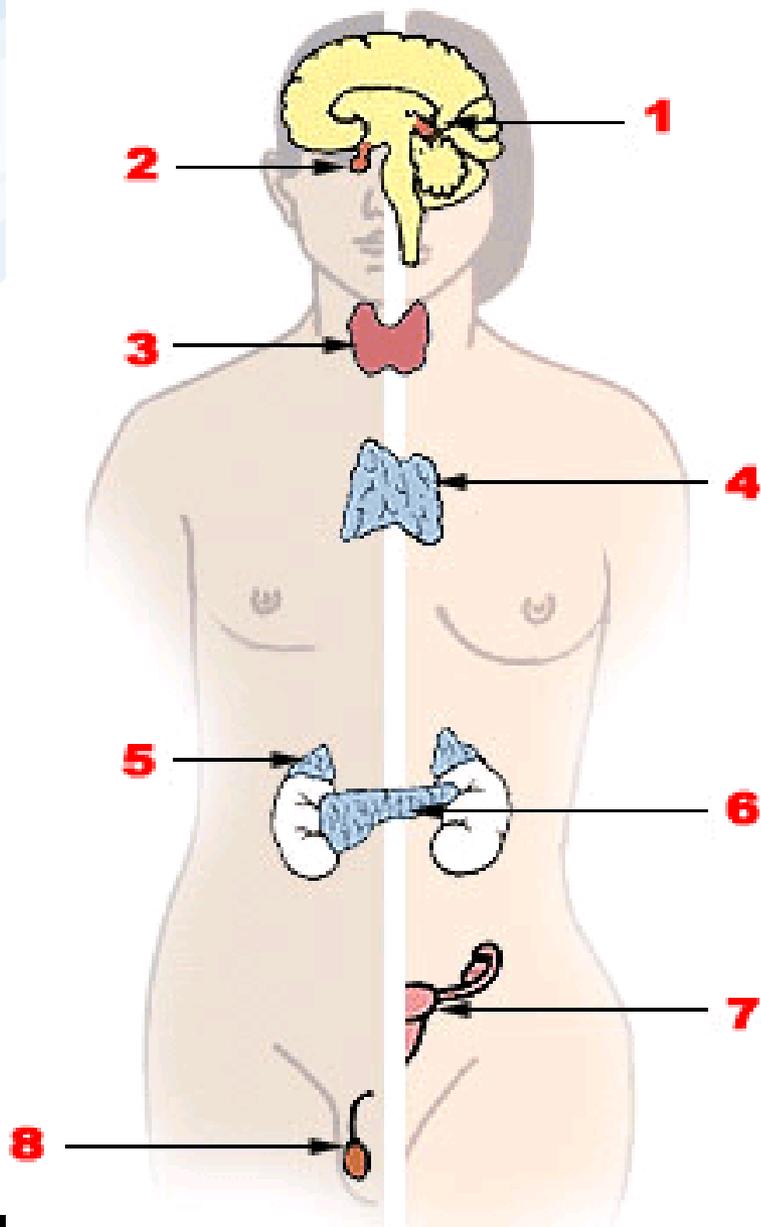
Gap Junction



INTER-cellular signals

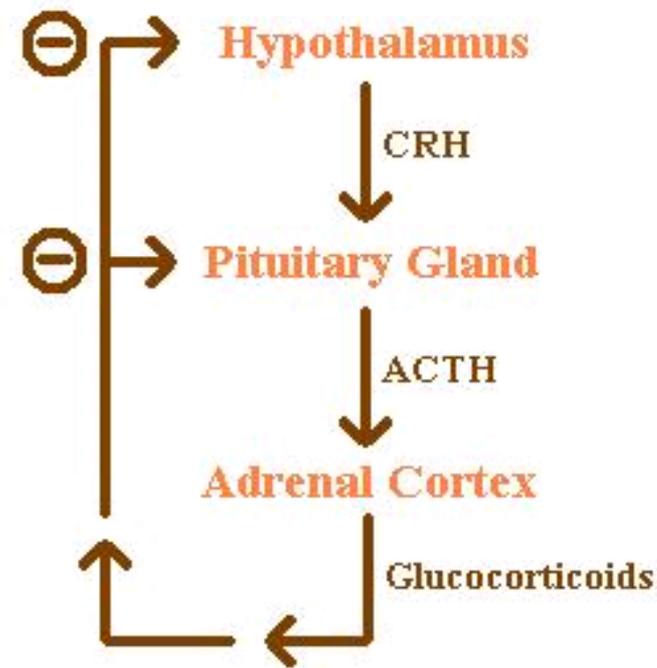
Hormones





Endocrine system:

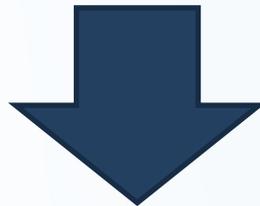
1. Pineal gland, 2. Pituitary gland, 3. Thyroid gland, 4. Thymus, 5. Adrenal gland, 6. Pancreas, 7. Ovary, 8. Testis



Example: feedback loop

FUNCTIONS OF HORMONES

- * stimulation or inhibition of growth
- * mood swings
- * induction or suppression of apoptosis
(programmed cell death)
- * activation or inhibition of the immune system
- * regulation of metabolism
- * preparation for fighting, fleeing, mating ...
- * preparation for a new phase of life
(puberty, caring for offspring, and menopause)
- * control of the reproductive cycle
.... etc.



Chemicals interfering with
various hormonal functions
→ **diverse impacts (effects)**

FATE OF HORMONES: target for toxicants

Toxic compounds can affect “hormone signalling” at various levels (highlighted):

1. Biosynthesis of a particular hormone in a particular tissue
2. Storage and secretion of the hormone
3. Transport of the hormone to the target cell(s)
4. Recognition of the hormone by an associated cell membrane or intracellular receptor protein.
5. Relay and amplification of the received hormonal signal via a signal transduction process -> cellular response.
6. The reaction of the target cells is recognized by the original hormone-producing cells (negative feedback loop)
7. Degradation and metabolism of the hormone

More details will be discussed
in the lectures dedicated to
nuclear receptors



Toxicity to hormone regulation = ENDOCRINE DISRUPTION

ED & EDCs (endocrine disrupting compounds)

= major problem in environmental toxicology

Effects at **all levels of hormonal action** have been demonstrated

→ *synthesis, transport, site of action*

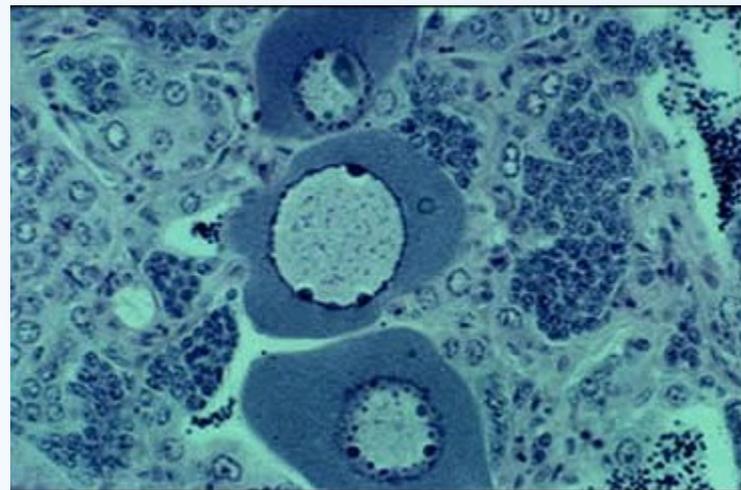
- **Multiple effects** due to ED (! Not only „xenoestrogenicity“ & feminization)

→ *immunotoxicity, developmental toxicity*

(ED - WILL ALSO BE DISCUSSED FURTHER)

Example of ED - Intersex roach testis

containing both oocytes and spermatozoa,
caused by exposure to environmental oestrogens



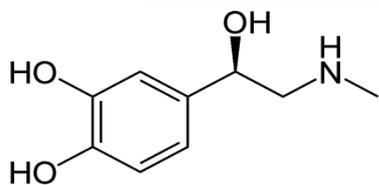
Types of hormones in vertebrates

Amine-derived hormones

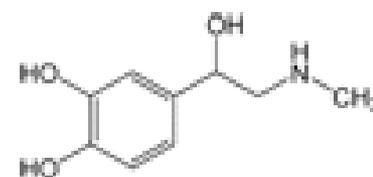
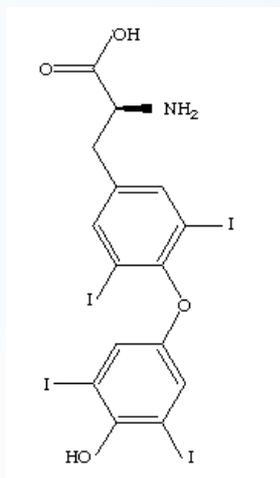
structure: derivatives of the amino acids tyrosine and tryptophan.
Examples - catecholamines and thyroxine.

(small molecules - **similar to organic toxicants** → **TOXIC EFFECTS**)

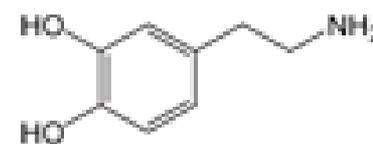
Adrenalin



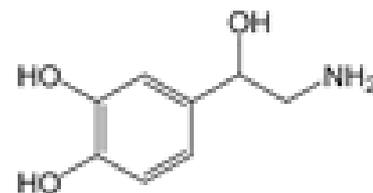
Thyroxin



Epinephrine



Dopamine



Norepinephrine



Types of hormones in vertebrates

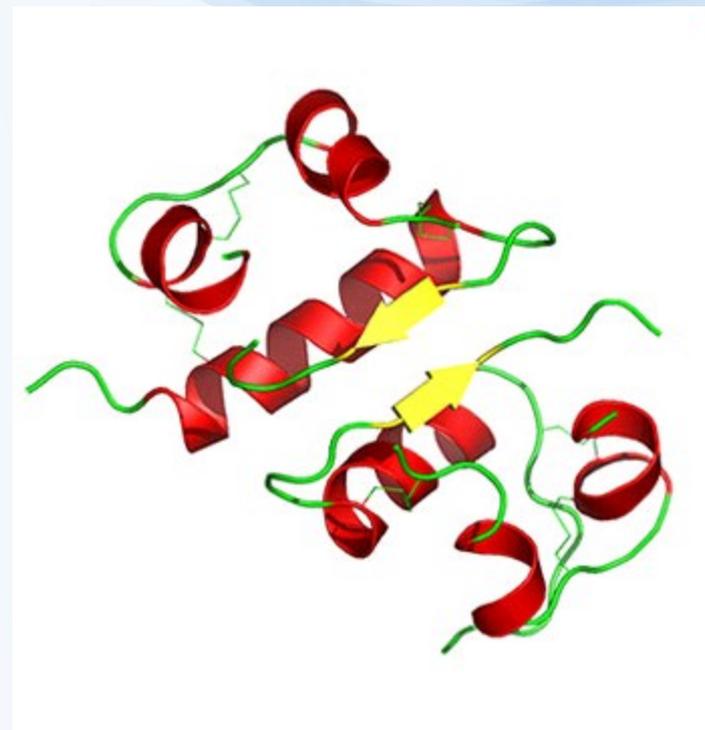
Peptide hormones

structure: chains of amino acids.

- small peptides: TRH and vasopressin;
- large proteins: insulin, growth hormone, luteinizing hormone, follicle-stimulating hormone and thyroid-stimulating hormone etc.

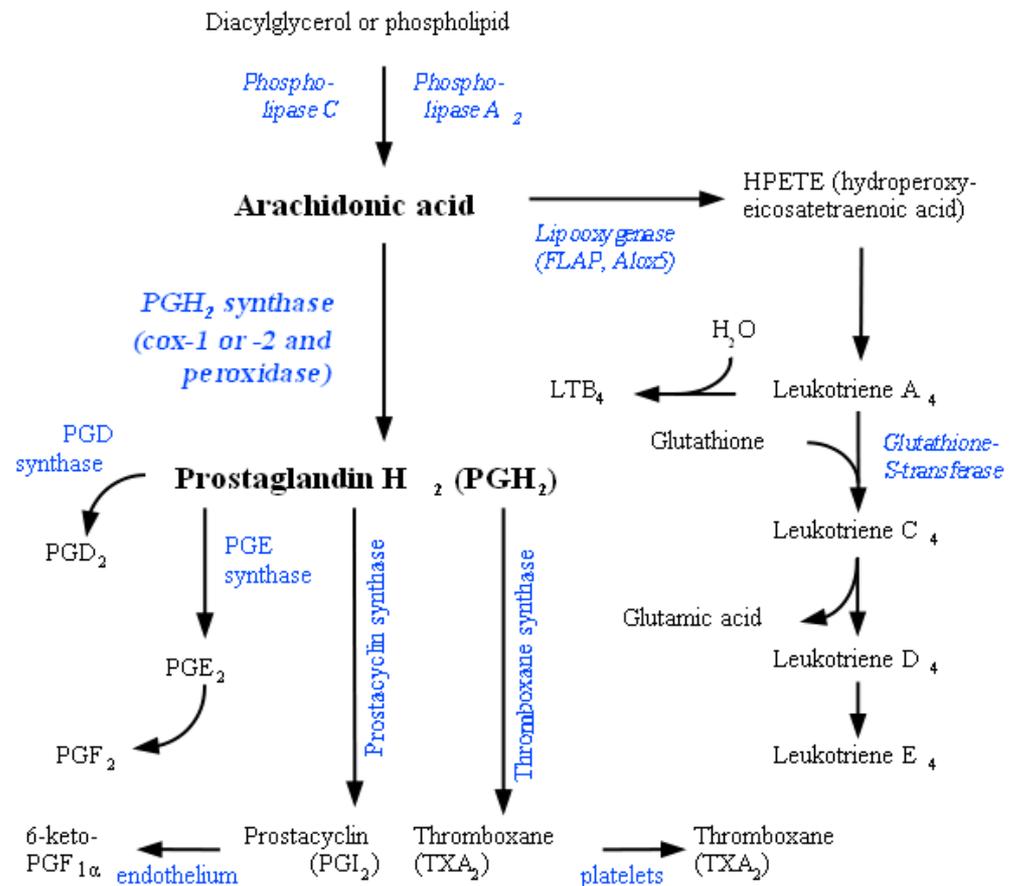
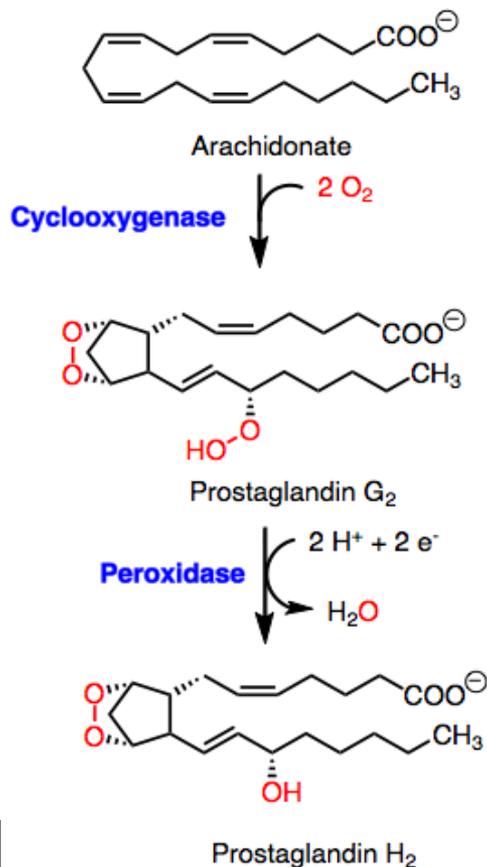
Large molecules;
receptors on surfaces of the cells
*(Interactions with toxic chemicals **less likely**)*

Example - insulin



Types of hormones (signal molecules) in vertebrates

Lipid derived “hormones” (1) - from linoleic acid, arachidonic acid - prostaglandins



Types of hormones in vertebrates

Lipid derived hormones 2 - steroid hormones

* Small molecules - similar to organic toxicants:

→ several compounds **interfere with steroid hormones** → **toxicity !!!**

Derived
from cholesterol

Examples:
testosterone,
cortisol,
estradiol ...

