Basic Endocrinology
Introduction

- System of ductless glands
- Produce chemical messengers called HORMONES
  - hormones help integrate body signals with neural and immune systems
- Hormones travel to target tissue/cell via
  - blood stream
  - intercellular space
Paracrine signaling

Secretory vesicle

Local regulator diffuses through extracellular fluid

Target cell

Secreting cell

Synaptic signaling

Nerve signals

Neurotransmitter diffuses across synapse

Nerve cell

(a) Local signaling

(b) Hormonal signaling

Endocrine cell

Blood vessel

Hormone travels in bloodstream

Target cell
Hormones

★ Come in two major forms
  ★ peptides / proteins
    ★ growth hormone, insulin, oxytocin
  ★ Lipid-based hormones
    ★ steroids and prostaglandins
Steroidogenesis

Cholesterol

P450ssc

P450c17

P450c17

17-OH Pregnenolone

P450c17

Dehydroepiandrosterone

3βHSD

Isomerases

Progesterone

P450c21

Deoxycorticosterone

P450c11

Corticoosterone

17-OH Progesterone

P450c17

17-OH Progesterone

P450c21

11 Deoxycortisol

P450c11

Cortisol

Androstenedione

17 Keto Reductase

Testosterone

P450 arom

17β Estradiol
Target Tissues

Endocrine gland
(source of hormone - H)

Cells of endocrine gland
Interstitial

Bloodstream

Blood
Receptors

- at the target cell, a hormone interacts with a RECEPTOR
- peptide hormones usually interact with membrane receptor
- steroid hormones interact with nuclear receptor
  - many steroid receptors are transcription factors
(a) Receptor in plasma membrane

SECRETORY CELL

Signal receptor

Hormone molecule

VIA BLOOD

TARGET CELL

Signal-transduction pathway

Response

(for example, an activated enzyme in the cytoplasm)

NUCLEUS

(b) Receptor in cell nucleus

SECRETORY CELL

VIA BLOOD

TARGET CELL

Signal receptor

Signal transduction and response

NUCLEUS

DNA

mRNA

Synthesis of specific proteins
1. Membrane receptor activates G protein
2. G protein + GTP activates adenylyl cyclase
3. ATP converted to cAMP (2° messenger)
4. Results = cellular response amplified @ each step
Amplification

Signal-transduction pathways allow for small amounts of a hormone to have a large effect.
1. Steroid binds to cytoplasmic or nuclear receptor (transcription factor)
2. Receptor hormone complex binds to DNA in nucleus
3. Stimulates transcription of mRNA
Nuclear Receptor Evolution

- Steroid receptors
  - Transcription factors
  - Large family of related molecules
    - Gene duplication
    - Ancestral form unknown
Evolution of Steroid Receptors

- Two serial duplications
- 1st = ER and 3-ketosteroid R
- 2nd = duplication of 3-KR
  - Corticoid receptor (CR)
  - 3-ketogonadal steroid R
    - Androgen
    - Progesterone
    - Or both
- These 3 duplicated again to form 6 common forms found today in vertebrates

Thornton (2001) PNAS 98:5671-5676
Hypothalamus - Pituitary

- Considered the master organs of the endocrine system
Hypothalamus

Saggital view

Frontal view
Hypothalamus

- Bottom of 3rd ventricle of brain
- Secretes
  - Neurohormones that influence synthesis and release of pituitary hormones
    - Examples:
      - Gonadotropin releasing hormone (GnRH)
      - Thyrotropin releasing hormone (TRH)
      - Dopamine - Prolactin releasing inhibiting factor
- Released into hypothalmo-hypophysial portal system
  - Blood vessel system between hypothalamus and pituitary
Hypothalamo-hypophysial Portal System

- A portal system
  - Vein - vein
  - Low pressure system
- Delivers hypothalamic factors to pituitary
Pituitary - Hypophysis

- center of the soul in classical times
- derived from two tissues embryologically
  - adenohypophysis (anterior pituitary) - derived from outpocketing of mouth - Rathke’s pouch
  - neurohypophysis (posterior pituitary) - derived from outpocketing of third ventricle and hypothalamus
- these two extensions meet, interact and form pituitary with two distinct regions as noted
Neurohypophysis

(a)

Hypothalamus

Neurosecretory cells of the hypothalamus

Posterior pituitary

Hormone

ADH

Oxytocin

Target

Kidney tubules

Mammary glands, uterine muscles

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