Endocrine Pharmacology

Growth Hormone (GH) – Molecular & Cellular Mechanism

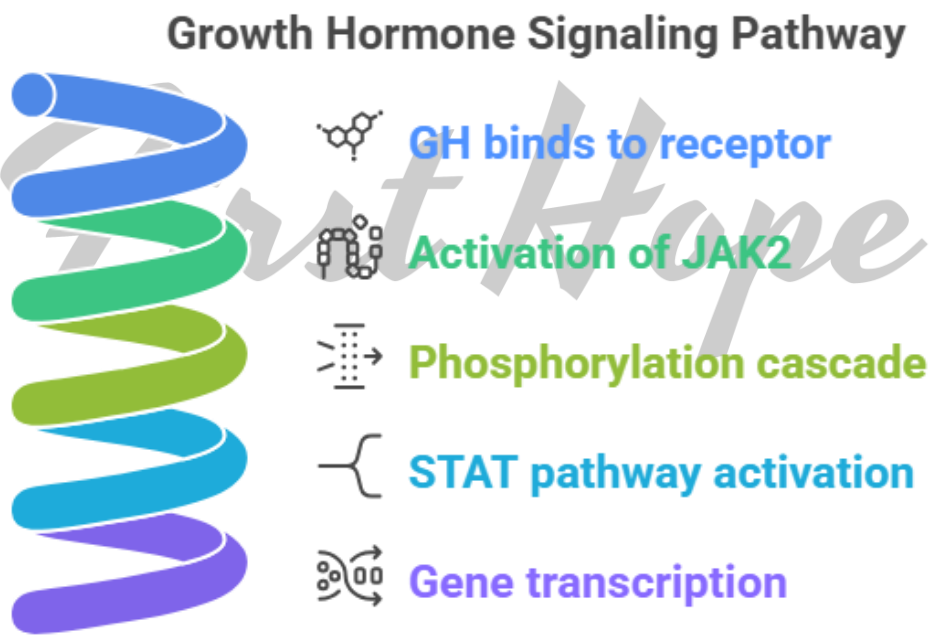
Basic Nature

- GH is a peptide hormone
- Synthesized and secreted by somatotroph cells of anterior pituitary
- Water-soluble → cannot enter cell, acts via cell surface receptors

Receptor Type

- GH receptor belongs to cytokine receptor superfamily
- It is intrinsic enzyme-linked receptor (no intrinsic kinase activity)
- Requires JAK (Janus kinase) for signaling

Step-by-step mechanism



1. **GH binds to receptor**
   - One GH molecule binds to two receptor molecules → causes dimerization.
2. **Activation of JAK2 (Janus Kinase 2)**
   - Receptor has no intrinsic enzyme activity.
   - It is associated with JAK2 (tyrosine kinase).
   - Binding → activates JAK2.
3. **Phosphorylation cascade**
   - JAK2 phosphorylates:
     - The receptor itself

Copyright by Engacy Learning Private Limited. All rights reserved. Reproduction or distribution without written consent is strictly prohibited.

- Intracellular proteins (STAT proteins)

4. STAT pathway activation

- **STAT (Signal Transducers and Activators of Transcription)** proteins:
  - Get phosphorylated
  - Form dimers
  - Move into nucleus

5. Gene transcription

- **STAT dimers activate genes → synthesis of:**
  - IGF-1
  - Proteins for growth and metabolism

IGF-1 Mediated Effects

- GH acts indirectly via IGF-1
- **IGF-1:**
  - Promotes bone growth (epiphyseal plate)
  - Increases cell division
  - Enhances protein synthesis

Metabolic Effects

- **Protein metabolism:** ↑ protein synthesis
- **Fat metabolism:** ↑ lipolysis
- **Carbohydrate metabolism**:
  - Anti-insulin effect
  - ↑ blood glucose

Prolactin – Molecular & Cellular Mechanism

Basic Nature

- Peptide hormone secreted by lactotroph cells
- Main role: milk production (lactation)

Receptor Type

- Prolactin receptor is also a cytokine receptor
- Uses JAK-STAT pathway (similar to GH)

First Hope

Copyright by Engacy Learning Private Limited. All rights reserved. Reproduction or distribution without written consent is strictly prohibited.

Mechanism

1. **Prolactin binds receptor**
   - Causes receptor dimerization
2. **JAK2 Activation**
   - Activates intracellular tyrosine kinase (JAK2)
3. **STAT activation**
   - STAT proteins are phosphorylated
   - Move into nucleus
4. **Gene transcription**
   - **Activates genes for:**
     - Milk protein synthesis (casein, lactalbumin)
     - Enzymes for lactose synthesis

Physiological Effects

- Development of mammary glands
- Initiation and maintenance of lactation

Regulation (Important for Pharmacology)

- **Dopamine inhibits prolactin**
  - Via D2 receptors
- **Drugs:**
  - Dopamine agonists (bromocriptine) → ↓ prolactin
  - Dopamine antagonists (antipsychotics) → ↑ prolactin

Thyroid Hormones (T3, T4) – Molecular & Cellular Mechanism

Basic Nature

- Derived from tyrosine + iodine
- Lipid-soluble → act like steroid hormones

Transport in Blood

- **Bound to proteins:**
  - Thyroxine-binding globulin (TBG)
- Only free hormone is active

Copyright by Engacy Learning Private Limited. All rights reserved. Reproduction or distribution without written consent is strictly prohibited.

Cell Entry

- T3/T4 enter cell via transporters
- T4 converted to T3 (active form) inside cell

Receptor Type

- Nuclear receptor (intracellular receptor)
- Located in Nucleus

Mechanism

1. **Conversion of T4 to T3**
   - Occurs inside cells by deiodinase enzymes
2. **T3 binds nuclear receptor**
   - TR is already bound to DNA at thyroid response elements (TRE)
3. **Receptor activation**
   - Without T3 → receptor suppresses gene expression
   - With T3 → receptor activates gene transcription
4. **Gene transcription changes**
   - **Increased synthesis of:**
     - Metabolic enzymes
     - Na^+/K^+-ATPase
     - β-adrenergic receptors

Cellular effects

- ↑ Basal metabolic rate (BMR)
- ↑ Oxygen consumption
- ↑ Heat production
- ↑ Sensitivity to catecholamines (via β-receptors)
- Essential for brain development and growth

Physiological Effects

- ↑ Basal metabolic rate (BMR)
- ↑ Oxygen consumption
- ↑ Heat production
- **Essential for:**
  - Brain development

First Hope

Copyright by Engacy Learning Private Limited. All rights reserved. Reproduction or distribution without written consent is strictly prohibited.

- Growth

Pharmacological Note

- Slow onset due to gene transcription mechanism
- Long duration due to protein binding

Insulin – Molecular & Cellular Mechanism

Basic Nature

- Peptide hormone from β-cells of pancreas
- **Main role:** decrease blood glucose

Receptor Type

- **Tyrosine kinase receptor**
- **Has:**
  - 2 α-subunits (outside)
  - 2 β-subunits (inside)

Mechanism

1. **Insulin binds receptor**
   - Binds to α-subunit
2. **Autophosphorylation**
   - β-subunits phosphorylate themselves (tyrosine residues)
3. **Activation of IRS (Insulin Receptor Substrates)**
   - IRS proteins get phosphorylated
4. **Two major pathways**
   a) **PI3K-AKT Pathway (Metabolic effects)**
      - IRS → activates PI3K
      - PI3K → activates AKT (Protein Kinase B)
      - **Effects:**
        - Translocation of **GLUT-4 to membrane** → ↑ glucose uptake (muscle, fat)
        - ↑ Glycogen synthesis
        - ↑ Lipid synthesis
        - ↓ Gluconeogenesis

First Hope

Copyright by Engacy Learning Private Limited. All rights reserved. Reproduction or distribution without written consent is strictly prohibited.

First Hope

FREE PREVIEW

Click here to visit our website

PHARMACY PREMIUM NOTES

Complete subject and semesters are available on FirstHope app only.

Scan or click here

Click here to get the app >

Available on Google Play

JOIN THE FIRSTHOPE COMMUNITY

Join our Telegram channel

Click here to join Telegram >

Scan or click here

@FirstHopeNotes

Instagram

@firsthope.official

Click here to follow >

YouTube channel

FirstHope-Pharmacy / Live streams

Click here to watch >

WhatsApp channel

Follow FirstHope on WhatsApp

Click here to join >

FirstHope website

firsthope.co.in

Click here to visit >

B.Pharm / D.Pharm / M.Pharm / Pharm.D

Preview notes. Complete subjects and semesters in the FirstHope app.