(a) Fed state: insulin dominates

Glucagon

Insulin

↑ Glucose oxidation
↑ Glycogen synthesis
↑ Fat synthesis
↑ Protein synthesis

(b) Fasted state: glucagon dominates

Glucagon

Insulin

↑ Glycogenolysis
↑ Gluconeogenesis
↑ Ketogenesis
(a) In the absence of insulin, glucose cannot enter the cell.

Glucose

Insulin receptor

ECF

Resting skeletal muscle or adipose cell

Secretory vesicle

GLUT-4 transport protein

(b) Insulin signals the cell to insert GLUT-4 transporters into the membrane, allowing glucose to enter the cell.

Insulin binds to receptor

Exocytosis

Signal transduction cascade

Glucose enters cell

GLUT-4
↓ Plasma glucose

α cells of pancreas

↑ Glucagon

Liver

Glycogenolysis

Gluconeogenesis

Ketones

↓ Insulin

Muscle and adipose tissue

Lactate, pyruvate, amino acids

Fatty acids

Prolonged hypoglycemia

For use by brain and peripheral tissues

Negative feedback

↑ Plasma glucose

KEY

Stimulus
Integrating center
Efferent path
Effector
Tissue response
Systemic response

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Stan Andrisse and Prof Fisher
Brain needs glucose
The large bottle (pile of cubes) per day
<table>
<thead>
<tr>
<th>Tissue location</th>
<th>$K_m$</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>All mammalian tissues</td>
<td>1 mM</td>
<td>Basal glucose uptake</td>
</tr>
<tr>
<td>Liver and pancreatic $\beta$ cells</td>
<td>15–20 mM</td>
<td>In the pancreas, plays a role in regulating insulin. In the liver, removes excess glucose from blood.</td>
</tr>
<tr>
<td>All mammalian tissues</td>
<td>1 mM</td>
<td>Basal glucose uptake</td>
</tr>
<tr>
<td>Muscle and fat cells</td>
<td>5 mM</td>
<td>Amount in muscle plasma membrane increases with endurance training.</td>
</tr>
<tr>
<td>Small intestine</td>
<td>—</td>
<td>Primarily a fructos transporter</td>
</tr>
</tbody>
</table>
Glucose

Insulin

IRα
IRβ

GLUT4

PI3-K

PIP3

PDK1

AKT

AS160

TBC1D1

Rab8A

Rab14

AMPK

ZMP

AICAR

Non-insulin dependent pathway

Contraction
Glucose Metabolism and Pharmacology Cory DeClue
When the system goes awry…

- **Type-1 diabetes (juvenile onset)**
  - Autoimmune reaction against the insulin-producing beta cells of the pancreas
  - No insulin can be produced

- **Type-2 diabetes (adult onset)**
  - Increased resistance to insulin in the muscles, liver, and adipose tissue in addition to decreased insulin production from pancreatic beta cells
**Hemoglobin A1C Test**

<table>
<thead>
<tr>
<th>A1C Now Value (%)</th>
<th>Average Blood Glucose (mg/dl)</th>
<th>Red blood cell</th>
</tr>
</thead>
<tbody>
<tr>
<td>10.5 and above</td>
<td>298</td>
<td>Glucose + Hemoglobin</td>
</tr>
<tr>
<td>8.5 – 10.4</td>
<td>269</td>
<td>Glycohemoglobin</td>
</tr>
</tbody>
</table>
| 7.1 – 8.4         | 240                           | |}
| 6.1 – 7.0         | 212                           | |}
| 4.0 – 6.0         | 185                           | |}

- **Non-Diabetic Levels**: 97 (68 – 126)
- **In Control**: 126 (127 – 155)
- **Monitor Closely**: 154 (156 – 195)
- **Elevated Levels**: 185 (196 – 252)
- **Seriously Elevated Levels**: 240 (253 and above)
The use of Manuka honey embedded dermal regeneration templates in normal and diabetic wound healing

Genevieve Hilliard
Laurie P Shornick, PhD
Department of Biology
Scott Sell, PhD
Department of Biomedical Engineering
Scaffold fabrication