Will The Real Glucose Transporter Please Stand Up!

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Why Study Glucose Transporters?

This is Your Brain On Glucose.  This is Your Brain Off Glucose.
Why Study Glucose Transporters?

**Type II Diabetes Mellitus**
- Insulin Resistance
- Glucose Metabolism Deficiency

**Obesity**
- Glucose Metabolism Deficiency
- Insulin Resistance

**Antioxidant Defense**
- GLUT1 transports oxidized vitamin C (DHA)
- Vitamin C = most efficient antioxidant
Glucose Transporters

• Facilitated Diffusion

• Structure
  – 12TM
  – Intracellular N- & C- term
  – ~500aa

• SGLT-1 & 2
  – Na⁺/Glc Co-Transporter

• SLC2 Family
  – 13 GLUTs

• Differences
  – Tissue Expression
  – Substrate Specificity
  – Kinetics
  – Physiological Regulation
Most Studied Glucose Transporters

<table>
<thead>
<tr>
<th>Name</th>
<th>Tissue location</th>
<th>$K_m$</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>GLUT1</td>
<td>All mammalian tissues</td>
<td>1 mM</td>
<td>Basal glucose uptake</td>
</tr>
<tr>
<td>GLUT2</td>
<td>Liver and pancreatic $\beta$ cells</td>
<td>15–20 mM</td>
<td>In the pancreas, plays a role in regulation of insulin</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>In the liver, removes excess glucose from the blood</td>
</tr>
<tr>
<td>GLUT3</td>
<td>All mammalian tissues</td>
<td>1 mM</td>
<td>Basal glucose uptake</td>
</tr>
<tr>
<td>GLUT4</td>
<td>Muscle and fat cells</td>
<td>5 mM</td>
<td>Amount in muscle plasma membrane increases with endurance training</td>
</tr>
<tr>
<td>GLUT5</td>
<td>Small intestine</td>
<td>—</td>
<td>Primarily a fructose transporter</td>
</tr>
</tbody>
</table>

- Pancreas (GLUT2)
  - High $K_m$ relative to concentration of blood glucose (4-5mM)
- Glucose transport into cell will rise linearly with [glucose] in the blood
GLUT1

• Refer to Poster
GLUT4

• Discovered in 1980s

• Most Studied GLUT

• Still Unknown
  – Trafficking???

• Whole Body Glc Homeostasis

• Regulation of Insulin
  – Insulin-dependent

• Insulin Resistance Diseases
  – Type II Diabetes
  – Obesity
GLUT4 Signaling

(Youngren 2010)
GLUT4 Trafficking

(Brogan 2010)
Glucose Sensing: Glucose-Stimulated Insulin Release

(Schuitt 2001)
Blood Glucose

**Hyperglycemia**
- >180 mg/dl (>10 mM)
  - Noticeable 270-360 mg/dl (15-20 mM)
- Symptoms
  - Organ damage
  - Blood vessel damage
- Causes
  - Diabetes (>126 mg/dl or >7 mM)
  - Drugs
    - Beta Blockers, anti-psychotics, meth, many others
  - Illness - Stroke, heart attack, etc

**Hypoglycemia**
- 40-50 mg/dl (2-2.5 mM)
  - Normal = 70-110 mg (4-5 mM)
- Brief Duration = brain damage/fatal
  - GLUT3 Km = 1.6 mM (neural)
- Symptoms
  - Sweating, hunger, fatigue
  - Palpitations, tremors
  - Coma, convulsions
  - Death
Literature Cited