Will The Real Glucose Transporter Please Stand Up!

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Glucose Transport: Exercise vs. Insulin effects (How Sweet are you?)

https://www.facebook.com/AmericanDiabetesAssociation

https://www.facebook.com/Diabetes.n.Diabetics

https://www.facebook.com/Diabetes.n.Diabetics
Exercise Increases Life Expectancy And Decreases Disease

(Mora 2006)

**HOW??**

(Mora 2007)
Why Study Glucose Transporters?

This is Your Brain On Glucose.  
This is Your Brain Off Glucose.
The amount of sugar your brain needs (per day).

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**Nutrition Facts**

**Serving Size 1 Banana (124g)**

<table>
<thead>
<tr>
<th>Amount Per Serving</th>
<th>% Daily Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calories 270</td>
<td></td>
</tr>
<tr>
<td>Calories from Fat 130</td>
<td></td>
</tr>
<tr>
<td>Total Fat 15g</td>
<td>23%</td>
</tr>
<tr>
<td>Saturated Fat 10g</td>
<td>49%</td>
</tr>
<tr>
<td>Trans Fat 0g</td>
<td></td>
</tr>
<tr>
<td>Cholesterol 0g</td>
<td>0%</td>
</tr>
<tr>
<td>Sodium 25mg</td>
<td>1%</td>
</tr>
<tr>
<td>Potassium 320mg</td>
<td>9%</td>
</tr>
<tr>
<td>Total Carbohydrate 38g</td>
<td>13%</td>
</tr>
<tr>
<td>Dietary Fiber 5g</td>
<td>18%</td>
</tr>
<tr>
<td>Sugars 25g</td>
<td></td>
</tr>
<tr>
<td>Protein 3g</td>
<td></td>
</tr>
</tbody>
</table>

Vitamin A 2%
Vitamin C 15%
Calcium 2%
Iron 6%
Riboflavin (Vitamin B2) 4%
Niacin 4%
Vitamin B6 15%
Folate 4%
Magnesium 6%
Copper 4%
Manganese 10%

* Percent Daily Values are based on a 2000 calorie diet. Your daily values may be higher or lower, depending on your calorie needs:

<table>
<thead>
<tr>
<th>Calories</th>
<th>Total Fat</th>
<th>Sat Fat</th>
<th>Cholesterol</th>
<th>Sodium</th>
<th>Total Carbohydrate</th>
<th>Dietary Fiber</th>
</tr>
</thead>
<tbody>
<tr>
<td>2,000</td>
<td>Less than 65g</td>
<td>Less than 20g</td>
<td>Less than 300mg</td>
<td>Less than 2,400mg</td>
<td>300g</td>
<td>25g</td>
</tr>
<tr>
<td>2,500</td>
<td>80g</td>
<td>25g</td>
<td>300mg</td>
<td>2,400mg</td>
<td>375g</td>
<td>30g</td>
</tr>
</tbody>
</table>

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SugarsStacks.com
Why Study Glucose Transporters?

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

**Obesity**
- Glucose Metabolism Deficiency
- Insulin Resistance
- 1960 = 13%  2012 = ~40% (CDC)
  - Children = 17%

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

• Facilitated Diffusion

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

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

• SLC2 Family
  – 13 GLUTs
  – GLUT1 & GLUT4 (today’s focus)

• 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; 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 (4-5 mM)
- Glucose transport into cell will rise linearly with [glucose] in the blood
GLUT4

• Discovered in 1980s
• Most Studied GLUT
• Still Unknown
  – Trafficking???

• Whole Body Glc Homeostasis

• Regulation
  – Insulin-dependent
  – Non-insulin dependent

• Insulin Resistance
  – Inability to activate glucose uptake
  – Conditions (metabolic disease)
    • Type II Diabetes
    • Obesity

• Conditions (metabolic disease)
Dysfunctional in Type 2 diabetics

GLUT4 translocation Signaling

Ho K CJASN 2011;6:1513-1516
GLUT4 Trafficking

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

Dysfunctional in Type 1 diabetics

(Schuitt 2001)
Blood Glucose

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

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

Phun Week 2012

Other Contributing members:
Benjamin Booker, Vivek Vallurapalli, Emma Dwyer, Chuwuemeka Obi.

Jonathan Fisher, Ph.D.

Stan and Gaytri

Joseph Chen

Rikki Koehler

Gaytri Patel

Allyson Renth

Andrea Webber
GLUT1

- Refer to Posters

Proposed Model

\[\text{ROS} = \text{metabolic disease}\]

\[\text{ATM activity} \quad \uparrow \quad \text{GLUT}1 \quad \rightarrow \quad \downarrow \quad \text{ROS} = \text{disease}\]
Literature Cited

• Younggren JF. 2010. Exercise and Regulation of Blood Glucose. Diabetes Manager.