Will The Real Glucose Transporter Please Stand Up!

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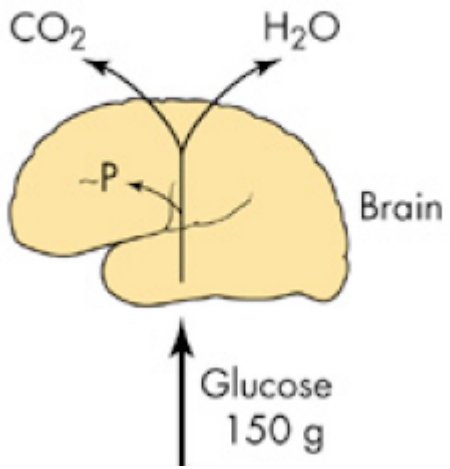
Physiology Lab Spring 2011

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

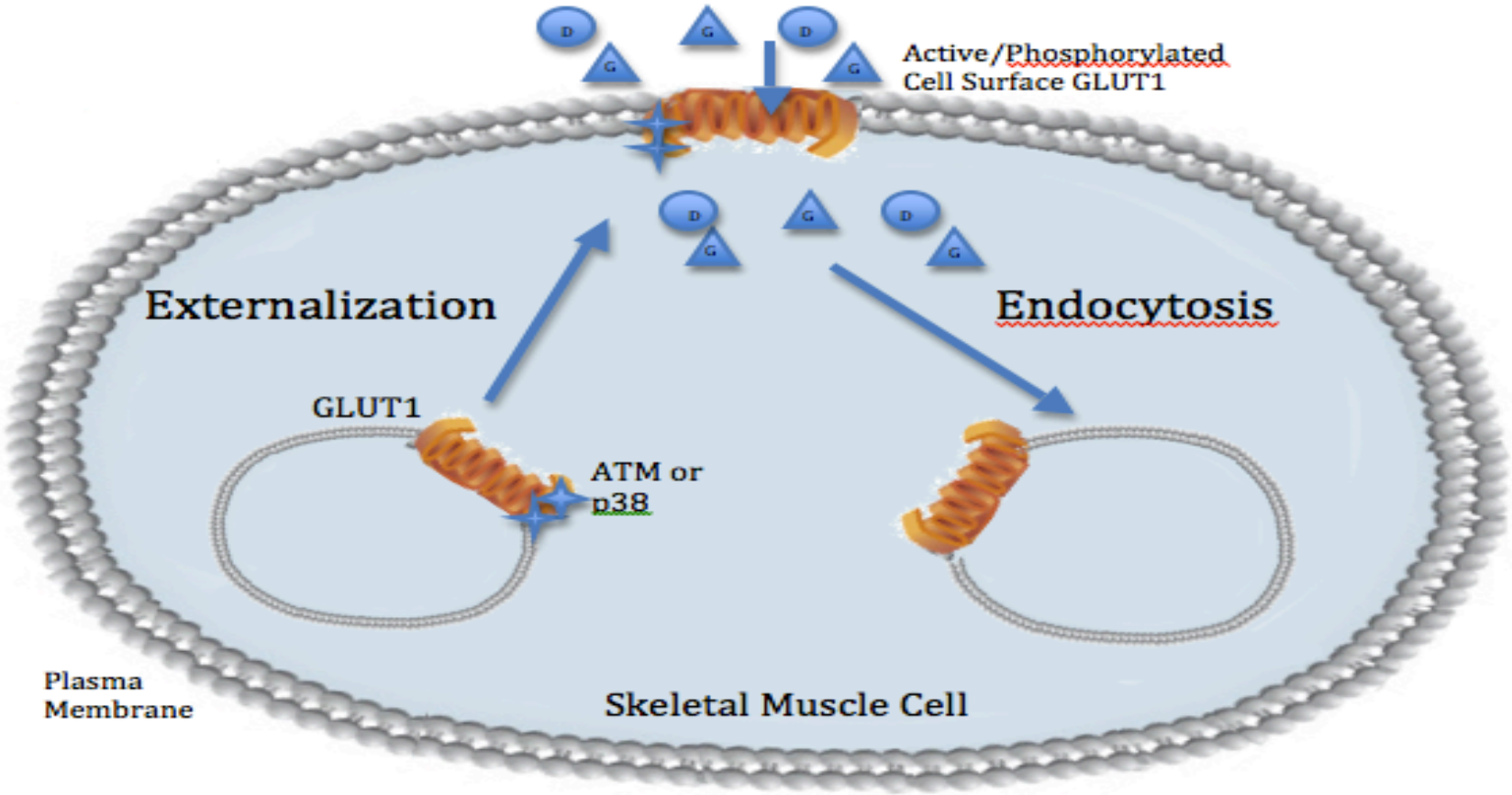
Most Studied Glucose Transporters

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

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

GLUT1

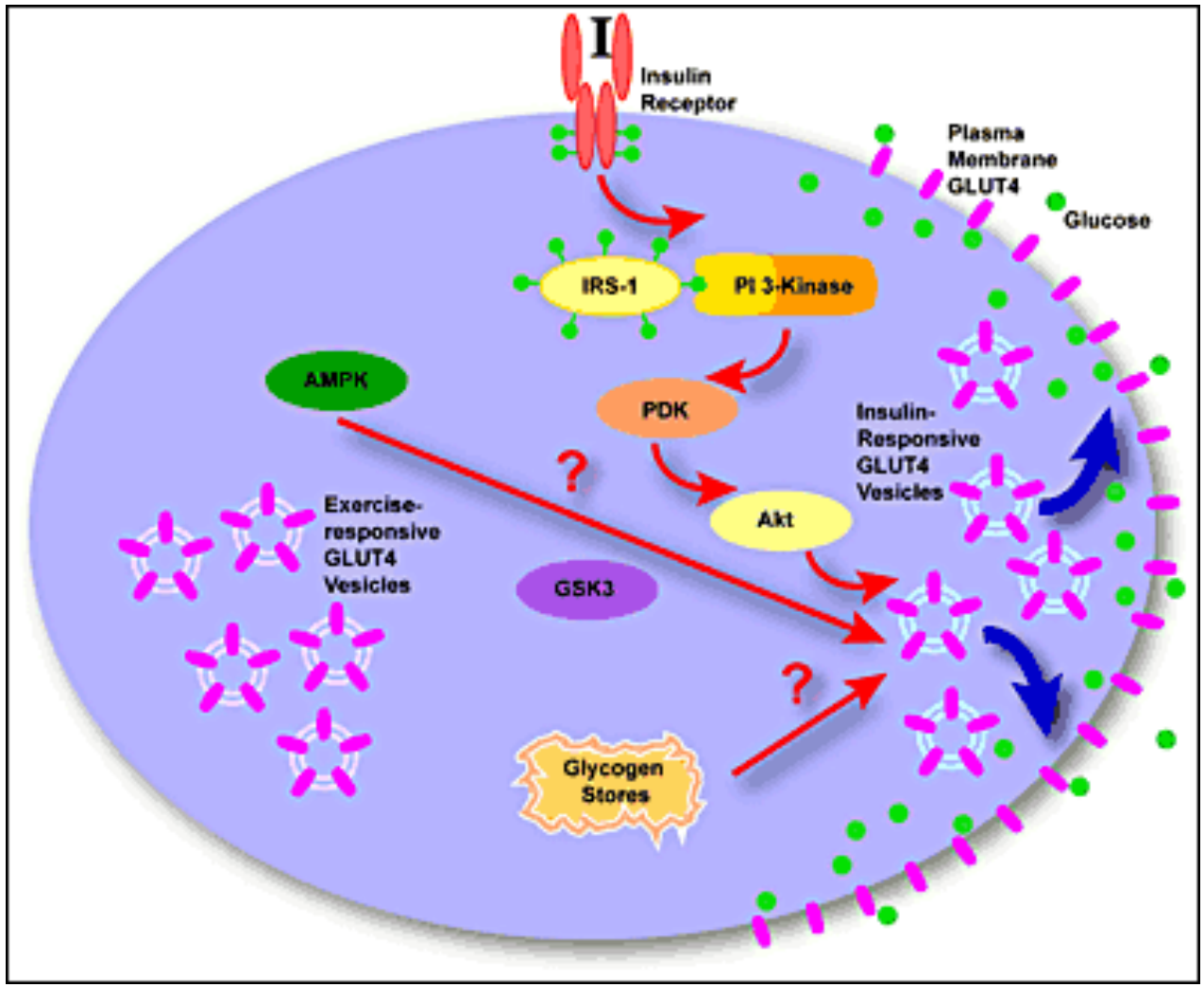
- Refer to Poster



GLUT4

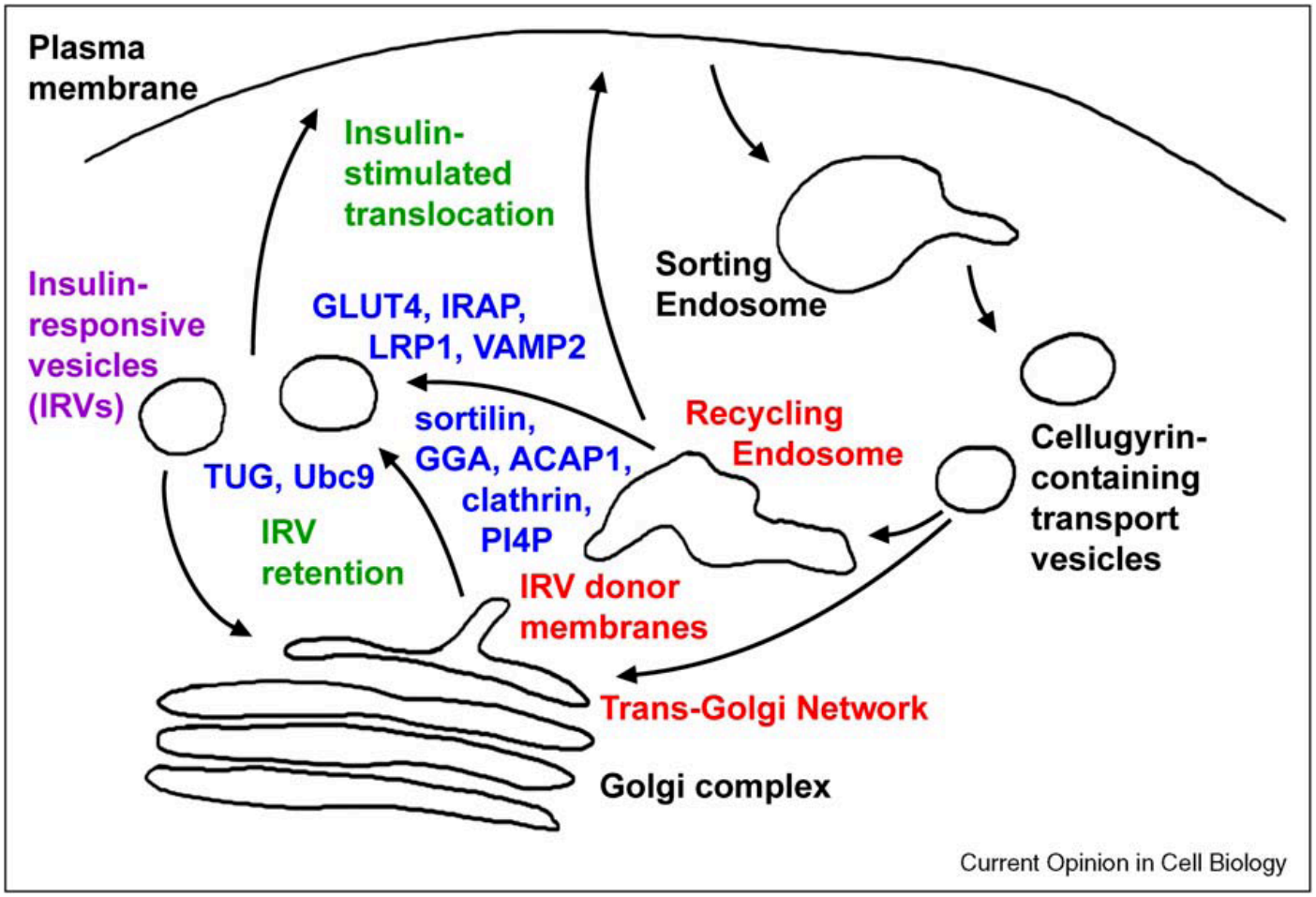
- Discovered in 1980s
- Most Studied GLUT
- Still Unknown
  - Trafficking???
- Whole Body Glc Homeostasis
- Regulation of Insulin
  - Insulin-dependent
- Insulin Resistance Diseases
  - Type II Diabetes
  - Obesity

GLUT4 Signaling



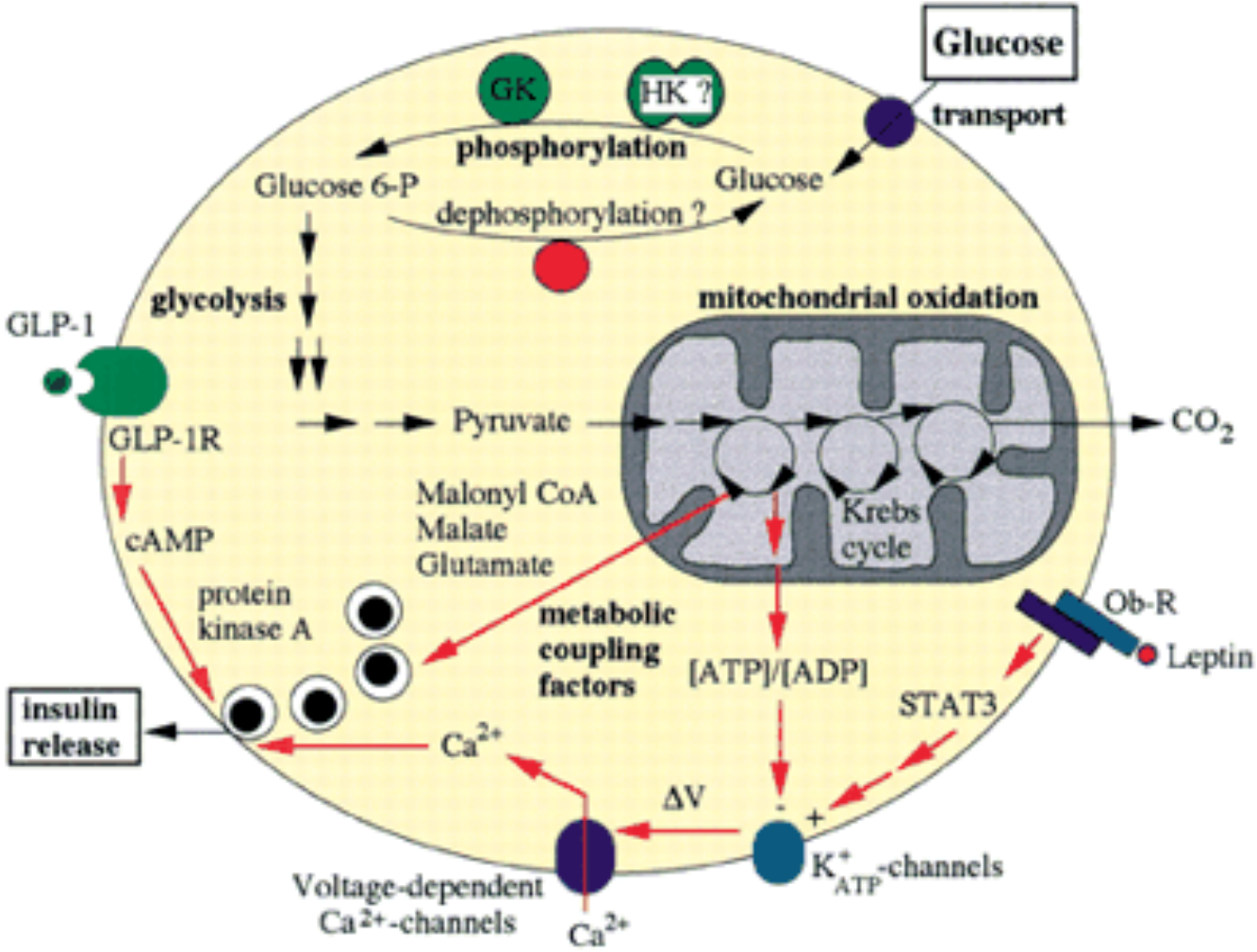
(Youngren 2010)

GLUT4 Trafficking



(Brogan 2010)

Glucose Sensing: Glucose-Stimulated Insulin Release



(Schuitt 2001)

Blood Glucose

Hyperglycemia

- >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

Literature Cited

- Brogan JS, Kandror KV. 2010. *Biogenesis and regulation of insulin-responsive vesicles conataining GLUT4.* Cur Op in Cell Bio 22: 506-512.
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