**Review Sessions for MT 1**

- **FRI (4/17):** Kleiber Hall, 5 - 7 p.m.
- **Mon (4/20):** Kleiber Hall, 5 - 7 p.m.

- See *ESSENTIALS for MIDTERM 1*
- Problem sets and Midterms of 2008 and 2007

posted on the “real” 103 website (My UCDavis)
http://www.plantsciences.ucdavis.edu/bis103
**MIDTERM 1**

Next Tuesday (4/21 from 1:40 – 3:00 p.m.)

*Seating Assignments (last name initial)*


(I-Z) ➔ 198 Young Hall

Bring a calculator supporting log functions!
Lecture 6

- Degradation of other carbohydrates
- Pyruvate Dehydrogenase Complex (PDH)

Co-Factors, Reactions, Enzymes
The “Powertrain” of Human Metabolism (Overview)

CARBOHYDRATES
- Glucose
- Glucose-6-P
- Oxaloacetate
- Ribose-5-P
- NADPH
- NADH

GLYCOLYSIS

PROTEINS
- Amino acids

LIPIDS
- Fatty acids
- Ketone bodies
- Cholesterol

ATP

NADH

O2

CO2

H2O

aerobic

anaerobic

Lactate
The "Powertrain" of Human Metabolism (Overview)

**CARBOHYDRATES**
- Sucrose
- Lactose
- Fructose
- Mannose
- Glycerol
- Galactose
- Starch

**PROTEINS**
- Amino acids
- Oxaloacetate

**LIPIDS**
- Fatty acids
- Acetyl-CoA
- NADH

**GLYCOLYSIS**
- Glycogen → Glucose-6-P → Pyruvate
- Lactate
- Ribose-5-P
- NADPH → NADH

**Anaerobic**
- Lactate

**Aerobic**
- Acetyl-CoA → CO₂ → H₂O → ATP

**Additional Metabolites**
- Ketone bodies
- Cholesterol
Hydrolysis of Sucrose and Lactose

\[
\text{Sucrose } + \text{ H}_2\text{O} \rightarrow \text{ Glu } + \text{ Fru}
\]

Enzyme (Hydrolase): Invertase (saliva, small intestines)
Lactose

\[ \text{Lactose} + \text{H}_2\text{O} \rightarrow \text{Gal} + \text{Glu} \]

Enzyme (Hydrolase): Lactase (babies, weaning animals)

Lactose Intolerance

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Metabolism of Fructose, Mannose, and Glycerol

A. Fructose

\[
\text{Fructose} \xrightarrow{1} \text{F-6-P} \xrightarrow{14} \text{F-1-P} \xrightarrow{15} \text{Dihydroxyacetone-P (DHAP)} \xrightarrow{16} \text{GA-3-P}
\]

\[
\begin{align*}
\text{Fructose} & \quad \xrightarrow{1} \quad \text{ATP} \quad \text{ADP} \\
\text{F-6-P} & \quad \xrightarrow{14} \quad \text{ATP} \quad \text{ADP} \\
\text{F-1-P} & \quad \xrightarrow{15} \\
\text{Dihydroxyacetone-P (DHAP)} & \quad + \\
\text{GA-3-P} & \quad \xrightarrow{16} \quad \text{ATP} \quad \text{ADP}
\end{align*}
\]
B. Mannose

\[
\begin{align*}
\text{CHO} & \quad \text{HO} \\
\text{HO} & \quad \text{H} \\
\text{H} & \quad \text{OH} \\
\text{H} & \quad \text{OH} \\
\text{CH}_2\text{OH} & \quad \text{ATP} \quad \text{ADP}
\end{align*}
\]

Mannose

\[
\begin{align*}
\text{CHO} & \quad \text{HO} \\
\text{HO} & \quad \text{H} \\
\text{H} & \quad \text{OH} \\
\text{H} & \quad \text{OH} \\
\text{CH}_2\text{OPO}_3^{2-} & \quad 1
\end{align*}
\]

Mannose-6-P (M-6-P)

\[
\begin{align*}
\text{CHO} & \quad \text{HO} \\
\text{HO} & \quad \text{H} \\
\text{H} & \quad \text{OH} \\
\text{H} & \quad \text{OH} \\
\text{CH}_2\text{OPO}_3^{2-} & \quad 20
\end{align*}
\]

F-6-P
C. Glycerol

Glycerol

\[
\begin{align*}
\text{CH}_2\text{OH} & \quad \text{OH} \\
\text{CH}_2\text{OH} & \quad \text{ADP} \\
\text{ATP} & \quad \text{17}
\end{align*}
\]

Glycerol-3-P

\[
\begin{align*}
\text{CH}_2\text{OH} & \quad \text{OH} \\
\text{CH}_2\text{OPO}_3^{2-} & \quad \text{ADP} \\
\text{NAD}^+ & \quad \text{18}
\end{align*}
\]

DHAP

\[
\begin{align*}
\text{CH}_2\text{OH} & \quad \text{OH} \\
\text{CH}_2\text{OPO}_3^{2-} & \quad \text{NADH} + \text{H}^+
\end{align*}
\]
Enzymes for Converting Other Carbohydrates into Intermediates of Glycolysis

• **Hydrolases** (di-, oligo-, and polysaccharides)

• **Kinases** (phosphotransferases; “phosphorylation”)

• **Isomerase**s (ketol isomerase, epimerase, mutase)

• **Dehydrogenases** (NADH-dependent)
Metabolism of Galactose

Galactose (Gal) $\rightarrow$ Gal-1-P $\rightarrow$ Glc-1-P

$\text{UMP}^\sim\text{P}$-Glc $\rightarrow$ $\text{UMP}^\sim\text{P}$-Gal

$\text{UMP}^\sim\text{P} = \text{UDP}$

Reactions:
1. Galactose $\rightarrow$ Gal-1-P
2. Gal-1-P $\rightarrow$ Glc-1-P
3. $\text{UMP}^\sim\text{P}$-Glc $\rightarrow$ $\text{UMP}^\sim\text{P}$-Gal
4. $\text{UMP}^\sim\text{P}$-Gal $\rightarrow$ $\text{UMP}^\sim\text{P}$-Glc
Metabolism of Galactose

\[
\begin{align*}
\alpha-D-Gal\text{-}1-P & \quad \text{ATP} \quad \text{ADP} \\
\alpha-D-Gal\text{-}1-P & \quad \text{UDP-Gal} \\
\alpha-D-Gal\text{-}1-P & \quad \text{UDP-Glc}
\end{align*}
\]
Metabolism of Galactose

\[ \alpha-D-Glc-1-P \rightarrow 24 \text{ Phosphoglucomutase} \rightarrow \alpha-D-Glc-6-P \]
Source of UDP-Glucose

\[ \text{UDPGlc} = \alpha\text{-D-Glc-1-P} + \text{UTP} \]

\[ \text{Pyrophosphate (PPi)} + \text{UDP-Glc} \rightarrow 2 \times \text{Phosphate (Pi)} \]

\[ \text{H}_2\text{O} \]

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Degradation of Polysaccharides
(Starch, Glycogen)
Intracellular Polysaccharides (Glycogen Reserve)

Blood

Digestive Tract

“Dietary” Polysaccharides (Starch, Glycogen)

“Hydrolysis” (unregulated)

Glucose

Liver, Skeletal Muscles

Intracellular Polysaccharides (Glycogen Reserve)

Synthesis (ATP-dep.)

“Phosphorolysis” (highly regulated)

Glucose

Glc-1-P (Glycolysis)

Blood

Glucose
Structure of Glycogen and Starch

![Diagram of glycogen and starch structures with annotations for (α1 → 4) linkages and (α1 → 6) branch points.](image-url)
Structure of Glycogen and Starch
Starch Grains in Sweet Potato Tuber Cells

mse.iastate.edu/images/microscopy/
Hydrolysis of Dietary Starch and Glycogen

- Beta-Amylase
- Beta-Amylase
- Beta-Amylase (exoglucosidase, plants)
- Alpha(1→6) Glucosidase (debranching enzyme)
- Alpha-Amylase (endoglucosidase)
- Maltase

Water (all glucosidases)

H2O

Glc

2 Glc

Maltose
Glc (α1→4) Glc

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Intracellular Polysaccharides (Glycogen Reserve)

Blood

Digestive Tract

“Dietary” Polysaccharides (Starch, Glycogen)

“Hydrolysis” (unregulated)

Glucose

Liver, Skeletal Muscles

Intracellular Polysaccharides (Glycogen Reserve)

Synthesis (ATP-dep.)

Glucose

“Phosphorolysis” (highly regulated)

Glc-1-P (Glycolysis)

Blood

Glucose

Synthesis (ATP-dep.)

Glucose

“Phosphorolysis” (highly regulated)

Glc-1-P (Glycolysis)

Blood

Glucose
Glycogen Granules in Muscle Fibers (white)

www.neuro.wustl.edu/neuromuscular/pathol/acdmchi.htm
**Phosphorolysis of Intracellular Glycogen**

Glycogen phosphorylase (or Starch phosphorylase) catalyzes the conversion of glycogen to Glc-1-P, which is then converted to limit dextrin. The key steps are:

- **Non-reducing ends**
- **α1,4 linkages**
- **Branch point** one α1,6 linkage
- **Reducing end**

The reaction proceeds as follows:

1. Glycogen phosphorylase (or Starch phosphorylase) removes 11 HPO$_4^{3-}$ (Pi) from the glycogen, forming 11 Glc-1-P.

2. The Glc-1-P is then converted to limit dextrin.

3. Limit dextrin is a linear polysaccharide with α-(1,6) linkages.

Limit dextrin is linked to protein.
Debranching enzyme
(the glucanotransferase activity)

Limit dextrin

\( \alpha-(1,6) \) linkage

Debranching enzyme
(the \( \alpha 1,6 \) glucosidase activity)

\( \text{H}_2\text{O} \)

Glucose

Glycogen phosphorylase

\( 15 \text{ HPO}_4^{3-} \)

\( 15 \text{ Glc-1-P} \)

..........linked to protein

..........linked to protein

..........linked to protein

..........linked to protein

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The “Powertrain” of Human Metabolism (Overview)

CARBOHYDRATES

PROTEINS

LIPIDS

Glucose → Glucose-6-P → Pyruvate → Acetyl-CoA → NADH → ATP

Glycogen → Glucose-6-P

Oxaloacetate → Lactate

Glycolysis

Other Carbohydrates

Amino acids

Fatty acids

Ketone bodies

Cholesterol

O2

CO2

H2O

NADPH → NADH
Overall Goal: $\text{C}_6\text{H}_{12}\text{O}_6 + 6\text{O}_2 \rightarrow 6\text{CO}_2 + 6\text{H}_2\text{O}$

CARBOHYDRATES

Glycolysis

Glucose

Other Carbohydrates

Glycogen → Glucose-6-P → Pyruvate → Acetyl-CoA → PDH → CO$_2$ → ATP

Lactate

O$_2$ → CO$_2$ → H$_2$O
Inner-Membrane Transporters Are Powered by the Proton-Gradient
A. Additional Coenzymes

- Flavin Adenine Dinucleotide (FAD)
- Lipoic Acid (Lipoamide)
- Coenzyme A (CoA-SH)
Riboflavin (Vitamin B₂)

FAD, FADH₂, FMN, FMNH₂

FADH₂ or FMNH₂
Lipoic Acid (Lipoamide)

Lysine residue of enzyme (isopeptide bond)
Coenzyme A (CoA-SH)
B. Reactions of the Pyruvate Dehydrogenase Complex

Overall Reaction

\[
\text{Pyruvate} + \text{NAD}^+ + \text{CoA-SH} \rightarrow \text{Acetyl-CoA} + \text{CO}_2 + \text{NADH} + \text{H}^+
\]

\[\Delta G^o' = -33.5 \text{ kJ mol}^{-1}\]

Five Co-factors:
- NAD\(^+\)
- Coenzyme A
- TPP
- Lipoic Acid
- FAD
C. Mechanism of Pyruvate Dehydrogenase (E1)

"Business end" of TPP is thioazolium ring

Carbanion

Intermediates common to both PDC and PDH enzymes

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Intermediates common to both PDC and PDH enzymes.

- **Acetyl-CoA**
  - **H₃C-C-ScoA**
  - **SH HS**
  - **(CH₂)₄-C O-N-E₂**
  - **FADH₂**
  - **NAD⁺**
  - **NADH + H⁺**

- **Coenzyme A** (CoA or CoASH)
  - **(CH₂)₄-C-N-Enzyme (E₂)**

- **Lipoamide**
  - **(CH₂)₄-C-O-N-Enzyme (E₂)**

- **Enzyme (E₂)**
Glucose $\rightarrow$ 2 Pyruvate

Glycolysis

Cytosol

2H$_2$O $\rightarrow$ 2ATP $\rightarrow$ 2Pyruvate $\rightarrow$ 2NAD$^+$ $\rightarrow$ 2NADH + H$^+$

Mitochondria

2 Pyruvate $\rightarrow$ 2Pyruvate $\rightarrow$ 2NAD$^+$ $\rightarrow$ 2CoA-SH $\rightarrow$ 2CO$_2$ $\rightarrow$ 2 Acetyl~CoA $\rightarrow$ 2NADH + H$^+$

PDH Complex