複製動物

阮雪芬
Jun 11
@NTU
【由體細胞複製羊桃莉過程】

1. 取出雌羊體細胞（乳腺細胞）
2. 血清（營養）依平常稀釋二十分之一倍，保持營養飢餓狀態培養體細胞，由於此操作體細胞永久關閉基因又打開。
3. 取出另一雌羊之未受精卵
4. 以吸將未受精卵之去核
5. 已除核之未受精卵移植到飢餓培養之體細胞中。
6. 將卵胞以電壓瞬間讓細胞融合為一
7. 細胞融合活化的受精卵
8. 細胞融合活化的受精卵
9. 複製羊桃莉誕生（雌性）
受精卵

體細胞複製（核移植複製）

乳腺的上皮細胞

將分割細胞的核植入核處理之未受精卵中

出生的複製小羊具有兩親代各一半特性，如同雙胞胎，並非真正來自親代體細胞的複製生物

與提供乳腺細胞完全相同遺傳特性的複製羊誕生。沒有父親，與代理孕母遺傳上完全無關

受精卵複製與體細胞複製
Ch14 Basic Concepts of Cellular Metabolism and Bioenergetics

阮雪芬
Jun 11
@NTU
Outline

• Introduction
• Intermediary metabolism
• The chemistry of metabolism
• Concepts of Bioenergetics
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• Introduction
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• Concepts of Bioenergetics
Introduction

• Metabolism
  – Sum total of all chemical reactions in an organism

• Energy input
  – Fats and carbohydrates
Introduction

• Specific questions to answer:
  – How do organism transform the potential energy
  – How much energy
  – How do cells regulate the metabolic processes
  – How do photosynthetic organisms harness energy from the sun to make carbohydrates

• Most organism use the same general pathways for extraction and utilization of energy.
Autotrophs and Heterotrophs

- **Autotrophs**
  - Self-feeding organisms
- **Heterotrophs**
  - Feeding on others
  - Aerobes and anaerobes
Metabolic Processes in Heterotrophic Cells

Route A
Organic compounds from environment are absorbed into organism, e.g., fats, carbohydrates, amino acids

Route B
Special organic compounds that cannot be biosynthesized, e.g., vitamins, essential amino acids, and fatty acids

Nucleus

Range of organic compounds taken into cell

Intermediary metabolites

Organic compounds of the cell + complex biomolecules

Mitochondrion

Water

Oxygen

Mineral ions

CO₂ + H₂O + waste nitrogen-containing compounds

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Outline

• Introduction
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Intermediary Metabolism

• The process of metabolism in all organisms takes place via sequences of consecutive enzyme-catalyzed reactions.

• Each step is usually a single, highly specific, chemical change leading to a product that becomes the reactant for the next step.
Metabolic Pathways

- A sequence of reactions that has a specific purpose
Two paths of Metabolism

• Catabolism
  – The degradative path
  – Characterized by oxidation reactions and by release of free energy

• Anabolism
  – Characterized by the construction of large, complex biomolecules from smaller precursor molecules.
  – Characterized by reduction reaction and energy input
<table>
<thead>
<tr>
<th>Catabolism</th>
<th>Anabolism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leads to degradation of biomolecules</td>
<td>Synthesis of biomolecules</td>
</tr>
<tr>
<td>Overall process of chemical oxidation and formation of reduced cofactors of NADH, NADPH, FADH₂</td>
<td>Overall process of chemical reduction and formation of oxidized cofactors NAD⁺, NADP⁺, FAD</td>
</tr>
<tr>
<td>Release of chemical energy (exothermic) and production of ATP from ADP</td>
<td>Requirement for energy input (endothermic) and use of ATP</td>
</tr>
<tr>
<td>Convergence of pathways</td>
<td>Divergence of pathways</td>
</tr>
</tbody>
</table>
The ATP Energy Cycle (I)
Anaerobic Metabolism

Lactate
or
Ethanol + CO₂

Oxidizable substrate

ADP + Pᵢ

ATP

Synthetic work (anabolism)
Concentration work (transport)
Electrical work
Mechanical work

(a) Anaerobic metabolism

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The ATP Energy Cycle (II)
Aerobic Metabolism

(b) Aerobic metabolism

CO₂ + H₂O
O₂
Oxidizable substrate

ADP + Pᵢ

ATP

Synthetic work (anabolism)
Concentration work (transport)
Electrical work
Mechanical work
The Structure of Adenosine Triphosphate (ATP)
The Stages of Catabolism and Anabolism

- **Stage I**: No energy release
- **Stage II**: Some energy is released and captured in the form of NADH and ATP
- **Stage III**: Citric acid cycle

Citric acid cycle:
- Fatty acids, glycerol
- Hexoses, pentoses
- Amino acids

Some energy is released and captured in the form of NADH and ATP.
Catabolism and Anabolism

• **Different in types of cells**

  – **Catabolism**
    • Glucose degradation predominates in active muscle cells
    • Fatty acids synthesis in the cytoplasm of adipose cells

  – **Anabolism**
    • Glucose synthesis takes place primarily in liver cells
    • Fatty acids degradation in mitochondria or resting muscle cells
Outline

• Introduction
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• Concepts of Bioenergetics
### Six Categories of Biochemical Reactions

**Table 14.2**

Types of chemical reactions in metabolism correlated to enzyme classes

<table>
<thead>
<tr>
<th>Type of Reaction</th>
<th>Enzyme Class</th>
<th>Description of Reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Oxidation–reduction</td>
<td>Oxidoreductases (dehydrogenases)</td>
<td>Transfer of electrons</td>
</tr>
<tr>
<td>2. Group transfer</td>
<td>Transf erase s</td>
<td>Transfer of a functional group from one molecule to another or within a single molecule</td>
</tr>
<tr>
<td>3. Hydrolytic cleavage (hydrolysis)</td>
<td>Hydrolases</td>
<td>Cleavage of bonds by water (transfer of functional groups to water)</td>
</tr>
<tr>
<td>4. Nonhydrolytic cleavage</td>
<td>Lyases</td>
<td>Splitting a molecule by nonhydrolytic processes</td>
</tr>
<tr>
<td>5. Isomerization and rearrangement</td>
<td>Isom erases</td>
<td>Rearrangement of functional groups to form isomers</td>
</tr>
<tr>
<td>6. Bond formation using energy from ATP</td>
<td>Ligases</td>
<td>Formation of carbon–carbon and other bond with energy from ATP</td>
</tr>
</tbody>
</table>
Oxidation-Reduction Reactions

• $\text{AH}_2 + B \rightleftharpoons A + \text{BH}_2$

• Enzymes: oxidoreductases or dehydrogenases
<table>
<thead>
<tr>
<th>Functional Group</th>
<th>Name</th>
<th>Geometry of Carbon Center</th>
<th>Relative Oxidation Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH₄</td>
<td>Methane</td>
<td>Tetrahedral</td>
<td>Lowest</td>
</tr>
<tr>
<td>CH₃</td>
<td>Methyl</td>
<td>Tetrahedral</td>
<td></td>
</tr>
<tr>
<td>CH₂</td>
<td>Methylene</td>
<td>Tetrahedral</td>
<td></td>
</tr>
<tr>
<td>RHC=CHR'</td>
<td>Methene</td>
<td>Planar</td>
<td></td>
</tr>
<tr>
<td>RCHR' OH</td>
<td>Alcohol</td>
<td>Tetrahedral</td>
<td></td>
</tr>
<tr>
<td>RCH</td>
<td>Aldehyde</td>
<td>Planar</td>
<td></td>
</tr>
<tr>
<td>RCR'</td>
<td>Ketone</td>
<td>Planar</td>
<td></td>
</tr>
<tr>
<td>RCX</td>
<td>Carboxylic acid or derivative</td>
<td>Planar</td>
<td></td>
</tr>
<tr>
<td>O=O</td>
<td>Carbon dioxide</td>
<td>Planar</td>
<td>Highest</td>
</tr>
</tbody>
</table>

*The carbon center undergoing oxidation is in red.

ⁿ, ᵅ — alkyl or aryl group; X = —OH (acid), —OR (ester), —NH₂ (amide).
Many Oxidation-reduction Reactions are Coupled to the Coenzyme Redox Pairs

- $\text{CH}_3\text{CH}_2\text{CH}_3\text{C}$ $\rightarrow$ $\text{CH}_3\text{C}$ $\rightarrow$ $\text{CH}_3\text{COOH}$

  - Ethanol $\rightarrow$ Acetaldehyde $\rightarrow$ Acetic acid
  - Alcohol dehydrogenase
  - Acetaldehyde dehydrogenase

  - NAD$^+$ $\rightarrow$ NADH + H$^+$ $\rightarrow$ NAD$^+$

Electron donors
<table>
<thead>
<tr>
<th>Name</th>
<th>Structure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phosphoryl</td>
<td><img src="image" alt="Phosphoryl Structure" /></td>
</tr>
<tr>
<td>Acyl</td>
<td><img src="image" alt="Acyl Structure" /></td>
</tr>
<tr>
<td>Glycosyl</td>
<td><img src="image" alt="Glycosyl Structure" /></td>
</tr>
</tbody>
</table>
Example of a Group-transfer Reaction

\[
\text{α-D-Glucose} + \text{ATP} \rightleftharpoons \text{α-D-Glucose 6-phosphate} + \text{ADP}
\]
Acyl Group

\[ \text{RC-}X + \text{CoASH} \rightleftharpoons \text{CoAS-C-R} + \text{XH} \]

Coenzyme A  Thioester
Thioesters-Ancient, But Still lots of Energy

\[
R-SH + R'-COOH \rightleftharpoons R-S-C-R' + H_2O
\]

Thioesters
Coenzyme A

- The most common reactive thioesters in the cell are produced from the thiol coenzyme A.
- Acetyl CoA is an important metabolite formed in the stages II catabolism of carbohydrates, fats, and amino acids.

\[
\text{CoA} - \text{SH} + \text{C} - \text{CH}_3 \rightleftharpoons \text{CoA} - \text{S} - \text{C} - \text{CH}_3
\]

Coenzyme A    Acetyl    Acetyl CoA
CoASH Structure

β-Mercaptoethylamine  
Pantothenic acid  
CoASH structure  
Adenosine 3′-phosphate 5′-diphosphate
Acetyl CoA and Other Thioesters

- Are participants in many reactions where ATP is used and recycled.

\[
\text{CoA-S-C-CH}_3 + \text{H}_2\text{O} \rightleftharpoons \text{CoA-SH} + \text{CH}_3\text{COOH} \quad \Delta G^\circ' = -31.4 \text{ kJ/mol}
\]

ATP: \( \Delta G^\circ' = -30.5 \text{ kJ/mol} \)
Hydrolysis Reactions (I)
Ester Hydrolysis

\[
\text{CH}_2\text{OCR} + \text{H}_2\text{O} \xrightleftharpoons{\text{lipase}} \text{CH}_2\text{OH} + \text{CH}_2\text{OCR}' + \text{RCOOH}
\]

Triacylglycerol  \rightarrow  2,3-Diacylglycerol  \rightarrow  Fatty acid

(a) Ester hydrolysis
Hydrolysis Reactions (II)
Amide Hydrolysis

(b) Amide hydrolysis
Hydrolysis Reactions (III)
Glycoside Hydrolysis

Lactose $\xrightarrow{\text{lactase}}$ Galactose + Glucose

(c) Glycosidic bond hydrolysis
Nonhydrolytic Cleavage Reactions

• Molecular are split without the use of water.
• Include the addition of functional groups to double bonds or the removal of functional groups to form double bonds.
Nonhydrolytic Cleavage Reactions - Carbohydrate Metabolism by Glycolysis

Fructose 1,6-bisphosphate $\rightarrow$ Dihydroxyacetone phosphate + Glyceraldehyde 3-phosphate

(a) aldolase reaction
Nonhydrolytic Cleavage Reactions - Carbohydrate Metabolism by Glycolysis

\[ \text{2-Phosphoglycerate} \xleftrightarrow{\text{enolase}} \text{Phosphoenolpyruvate} \]
The Reaction of Glycrosis

- Fig 15.2
The Reaction of Glycosis - Continued

- Fig 15.2

Each of these reactions occurs twice because two glyceraldehyde 3-phosphates are produced from one glucose.
The Citric Acid Cycle

- Fig 16.1
Important Bioprocess and Their Location in the Mitochondrion

- **Fig 16.2**

  **Inner membrane**
  - Impermeable to most small molecules and ions, including $H^+$
  - Contains:
    - Respiratory electron carriers (Complexes I–IV)
    - ATP synthase
    - Other membrane transporters

  **Outer membrane**
  - Freely permeable to small molecules and ions

  **Matrix**
  - Contains:
    - Pyruvate dehydrogenase complex
    - Citric acid cycle enzymes
    - Fatty acid $\beta$-oxidation enzymes
    - Amino acid oxidation enzymes
    - DNA, ribosomes
    - Many other enzymes
    - ATP, ADP, $P_i$, $Mg^{2+}$, $Ca^{2+}$, $K^+$
    - Many soluble metabolic intermediates

  **Cristae**
  - ATP synthase
  - Ribosomes
How the Mitochondrion is Involved in Energy Metabolism

- Fig 16.2
Isomerization and Rearrangement Reactions

- Fig 14.10 isomerase
  
  Glyceraldehyde $\rightarrow$ Dihydroxyacetone

   
   Phosphoglucomutase

   $\beta$-D-Glucose 6-phosphate $\rightarrow$ $\beta$-D-Glucose 1-phosphate

- Two kinds of chemical transformations:
  - Intramolecular hydrogen atom shifts changing the location of a double bond.
  - Intramolecular rearrangements of functional groups.
Bond Formation Reactions Using Energy from ATP (I)

- In glucose synthesis

\[
\begin{align*}
\text{CH}_3\text{CCOO}^- + \text{CO}_2 + \text{ATP} \rightleftharpoons \text{CH}_2\text{CCOO}^- + \text{ADP} + \text{P}_i
\end{align*}
\]

Pyruvate \quad \text{pyruvate carboxylase} \quad \text{Oxaloacetate}

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Bond Formation Reactions Using Energy from ATP (II)

- In the citric acid cycle

\[
\text{Acetyl CoA} + \text{Oxaloacetate} \xrightleftharpoons{\text{citrate synthase}} \text{Citroyl CoA}
\]
Bond Formation Reactions Using Energy from ATP (III)

\[ \text{CH}_3\text{C} \leftrightarrow \text{CH}_2\text{C} + \text{H}^+ \]

\[ \text{H}_2\text{C}\equiv\text{C} \]
Metabolism
How Do We Know the Pathways

• Biochemical characteristics
• Control of the pathway
• The physiological function of the pathway and how it coordinates with the overall metabolism of the organism.
NMR
Outline

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Standard Free Energy Change

• ATP: the universal carrier of energy
• A fundamental concept of metabolism:
  – The overall process of catabolism releases energy; the overall process of anabolism requires energy input.
\( \Delta G^\circ \) The Standard Free Energy Change

- \( A + B \rightleftharpoons C + D \)
- \( K'_{eq} = \frac{[C][D]}{[A][B]} \)
- \( \Delta G^\circ = -2.303RT \log K'_{eq} \)
Experimental Measurement of $\Delta G^\circ$’

- Glucose 6-phosphate $\rightleftharpoons$ fructose 6-phosphate
  
  $[\text{Glucose 6-phosphate}] = 1.33 \text{M}$
  $[\text{fructose 6-phosphate}] = 0.67 \text{M}$

Keq’ = $0.67/1.33 = 0.5$

$\Delta G^\circ = (-2.303)(8.315 \text{ J/mol})(298 \text{ K}) \log 0.5$

$= +1.718 \text{ kJ/mol}$
Table 14.5
Significance of $\Delta G^{\circ'}$ values

<table>
<thead>
<tr>
<th>Value and Sign of $\Delta G^{\circ'}$</th>
<th>Thermodynamic Consequences</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\Delta G^{\circ'} = 0$</td>
<td>The reactants and the products are at the same energy level. The reaction under standard conditions is at equilibrium. No release of or requirement for energy.</td>
</tr>
<tr>
<td>$\Delta G^{\circ'} &lt; 0$ (negative values)</td>
<td>The reaction releases energy as it approaches equilibrium. The reactants are at a higher energy level than products. Useful energy is released and available to do work.</td>
</tr>
<tr>
<td>$\Delta G^{\circ'} &gt; 0$ (positive values)</td>
<td>The reactants are at a lower energy than products. The reaction requires an input of energy to proceed as written.</td>
</tr>
</tbody>
</table>
\[ \Delta G^\circ' \]
kJ/mol

Glucose + ATP $\rightleftharpoons$ glucose 6-phosphate + ADP $\Delta G^\circ' = -16.7$

Glucose 6-phosphate + H\textsubscript{2}O $\rightleftharpoons$ glucose + Pi $\Delta G^\circ' = -13.8$

**Sum:** ATP + H\textsubscript{2}O $\rightleftharpoons$ ADP + Pi $\Delta G^\circ' = -30.5$

Spontaneous reaction
Energy Diagram for the Reaction

\[ \text{ATP} + \text{H}_2\text{O} \rightarrow \text{ADP} + \text{Pi} \]

- Resonance stabilization
Resonance Stabilization of ADP and Pi

Three resonance forms of Pi

\[
\text{HO-PO}_3^- \quad \leftrightarrow \quad \text{HO-P=O} \quad \leftrightarrow \quad \text{HO-PO}_3^- \quad \leftrightarrow \quad \text{etcetera}
\]

Two resonance forms of ADP

\[
\text{Adenosine-O-P-O-P-O}^- \quad \leftrightarrow \quad \text{Adenosine-O-P-O-P}=O \quad \leftrightarrow \quad \text{etcetera}
\]
The more negative the $\Delta G^\circ$, the greater the tendency to transfer the phosphoryl group

Table 14.6
$\Delta G^\circ$ values and relative ranking for phosphoryl group transfer potential of important phosphorylated biochemicals

<table>
<thead>
<tr>
<th>Phosphorylated Compounds</th>
<th>$\Delta G^\circ$ (kJ/mol)$^a$</th>
<th>Phosphoryl Group Transfer Potential</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phosphoenolpyruvate</td>
<td>$-61.9$</td>
<td>Highest</td>
</tr>
<tr>
<td>1,3-Biphosphoglycerate</td>
<td>$-49.3$</td>
<td></td>
</tr>
<tr>
<td>Phosphocreatine</td>
<td>$-43.0$</td>
<td></td>
</tr>
<tr>
<td>ATP</td>
<td>$-30.5$</td>
<td></td>
</tr>
<tr>
<td>ADP</td>
<td>$-30.5$</td>
<td></td>
</tr>
<tr>
<td>Glucose 1-phosphate</td>
<td>$-20.9$</td>
<td></td>
</tr>
<tr>
<td>Glucose 6-phosphate</td>
<td>$-13.8$</td>
<td></td>
</tr>
<tr>
<td>Glycerol 1-phosphate</td>
<td>$-9.2$</td>
<td>Lowest</td>
</tr>
</tbody>
</table>

$^a$These values are for hydrolysis reactions (the transfer potential of the phosphoryl group to $H_2O$).
Transfer of Phosphoryl Groups
Exercises

• 14.1
• 14.2
• 14.4
• 14.5
• 14.8
• 14.14
• 14.16