第四單元 蛋白質功能 - 與氧結合的蛋白質
Protein functions: Oxygen binding proteins

學習目標：

1. 熟悉肌紅素與血紅素之組成與結構特徵 (含血基質)
2. 熟悉蛋白質與受質之結合曲線圖 (結合率, 親和力與 K_d)
   (a) 肌紅素與氧氣之結合曲線圖 – 雙曲線 Hyperbola
   (b) 血紅素與氧氣之結合曲線圖 – S 型曲線 Sigmoid
3. 熟悉異位調控 Allosterism
   (a) 協同作用– Cooperativity, Hill plot
   (b) 調控血紅素與氧氣結合之因子: O_2, H^+, CO_2, CO, BPG
4. 血紅素突變引起的疾病: 例如: 鐮刀型貧血(sickle-cell anemia)

天堂筆記：

1. Globin family (球蛋白家族): Myoglobin (Mb，肌紅素) and hemoglobin (Hb，血紅素)
   - Heme (血基質) = Fe^{2+} + porphyrin (紫質或卟啉)
     - Heme containing protein:
       - Mb, Hb (血基質含 Fe)
       - Cytochrome (細胞色素，血基質含 Fe and Cu)
       - Chlorophyll (葉綠素，血基質含 Mg)
   - Protein-ligand (受質) binding curve (O_2 binding curve, Figure 1)
     - θ (or Y): 蛋白質與受質的結合率或結合百分比
     - K_d:
       - Dissociation constant (解離常數);
       - Binding affinity (親和力);
       - [L] at half-saturation
         (蛋白質結合達一半飽和時之受質濃度)

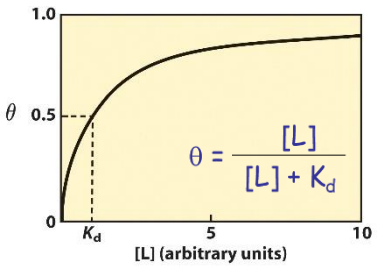

Figure 1. Binding curve of Protein (P) and ligand (L).

2. Myoglobin: Hyperbolic (hyperbola,雙曲線) binding curve,
   - Small K_d, high affinity (Figure 1)
   - Sequence homology vs Structural homology

3. Hb: Sigmoid (S-shape) binding curve, Figure 2a
   - Hb is an allosteric (異位調控) protein (2 conformations)
     - T (taut) state: low O_2 affinity
       - Stable at low pO_2, unstable at high pO_2
     - R (relaxed) state: high O_2 affinity
       - Unstable at low pO_2, stable at high pO_2
     - T-R transition – dependent pO_2

- Cooperativity (協同作用): Cooperative O_2 binding (subunit interactions)
  - Hill plot; Hill coefficient; Figure 2b

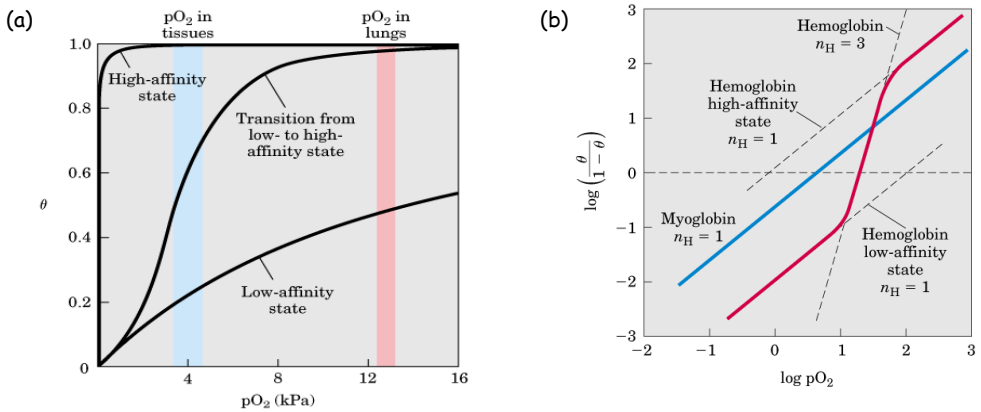

Figure 2. (a) O_2 binding curve of Hb; (b) Hill plot of Mb and Hb.

- Allosteric interaction (異構作用): change activity by changing conformation
  - Sigmoid binding curve; Multimer; Conformational change;
  - Models:
    - Symmetry (MWC, or Concerted) model
    - Sequential model
  - Allosteric modulators (effector) for Hb-O_2 binding
    - Homotropic (同質的): modulator (O_2)= ligand (O_2)
    - Hetertropic (異質的): modulator (O_2) ≠ ligand (CO, H^+, CO_2, BPG)
  - Bohr effect: Figure 3a
    - CO_2, H^+ bind Hb and affect (reduce) O_2 affinity
  - BPG (2,3-bisphosphoglycerate) or DPG bind Hb: Figure 3b
    - Stabilized the T state, reduce O_2 affinity
    - Adaptation to high altitude.

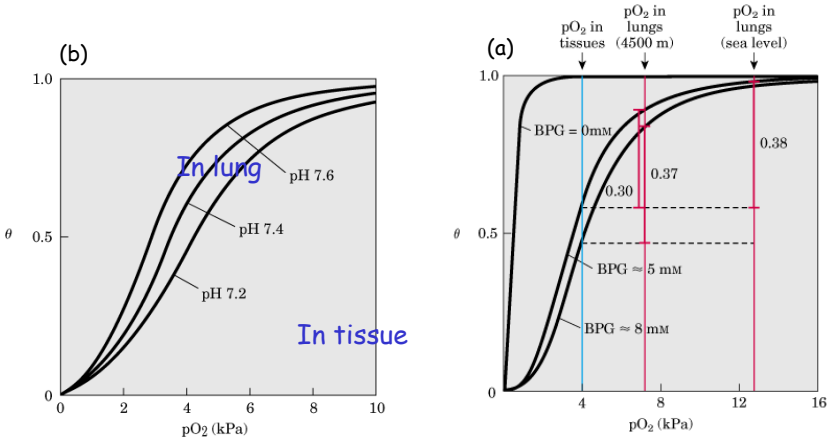

Figure 3. O_2 binding curve of Hb showing (a) Bohr effect, and (b) BPG effect.

- Hb isoforms:
  - The primary structures of the β, γ, and δ chains of human Hb are highly conserved.
  - HBA ($\alpha_2\beta_2$, normal adult Hb)
  - HbF ($\alpha_2\gamma_2$, fetal Hb)
  - HbS (α_2S_2, sickle cell Hb) → sickle cell anemia, sticky patch on HbS.

單位換算:

1 atmosphere (atm) = 101.325 kPa (760 Torr ≈ 760 mmHg, or 14.696 psi)

魔咒關鍵詞：

Globin: myoglobin (Mb) and hemoglobin (Hb)
    Heme, Porphyrin
Protein-ligand binding curve (O_2 binding curve): θ (or Y), K_d, Affinity
    Mb: Hyperbolic (hyperbola) binding curve,
    Hb: Sigmoid (S-shape) binding curve
Allosteric protein (allosterism)
    Cooperativity: Hill plot; Hill coefficient
    Bohr effect
    Homotropic vs Hetertropic modulator (effector)

魔法參考書目:

1. 台大莊榮輝教授教學網頁: http://juang.bst.ntu.edu.tw/BCbasics/index.htm
2. Lehninger Principles of Biochemistry (2013), 6th ed, David L. Nelson, and Michael M. Cox, Freeman and Company, New York.
3. Principles of Biochemistry (2013) 4th ed. Voet, Voet, and Pratt. Wiley.
4. Biochemistry, a short course. (2015) John L. Tymoczko, Jeremy M. Berg, Lubert Stryer (3rd ed) W.H. Freeman & Company.

魔法練習題:

1. 請將肌紅素與血紅素與氧氣的結合曲線畫在同一個圖上；比較兩個蛋白質的特徵並以此說明為什麼肌紅素適合儲存氧氣，而血紅素適合運送氧氣。
2. O_2, H^+, CO_2, CO, BPG等分子都能與血紅素結合，請分別說明結合後對血紅素與氧氣的結合有何影響? 例如: 使親和力增加或降低? 使結合曲線向左移或右移?
3. 25歲病患因頭痛、昏眩、噁心來到急診，經檢查後懷疑可能是一氧化碳中毒。下列有關一氧化碳對血紅素（hemoglobin）的影響，何者敘述正確？_____(101-1-2101)
   (a) 它會增加血液酸度，導致氧合血紅蛋白（oxyhemoglobin）沈澱
   (b) 它會改變血紅蛋白結合的鐵離子的氧化態
   (c) 它會將肌球蛋白（myoglobin）直接轉變成碳氧血紅蛋白（carboxyhemoglobin）
   (d) 它會與氧分子競爭，導致氧合血紅蛋白（oxyhemoglobin）減少