

• 計畫中文名稱	營養素對粒線體生合成及功能調控對能量利用之控制		
• 計畫英文名稱	Various Nutrients Modulate Mitochondrial Biogenesis and Function to Regulate Energy Utilization		
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• 英文關鍵字	mitochondrial biogenesis, glycolysis, fatty acid β oxidation, animal model		
• 中文摘要	<p>不同細胞型態對於能量來源有不同的選擇，可能偏賴糖解作用或依賴脂肪酸 β-氧化作用，而飲食中營養素種類及含量改變，也會影響細胞代謝的路徑，當細胞對能量代謝路徑的選擇改變時，通常也意謂此細胞的行為與功能也有所變化。粒線體是真核生物細胞專司能量代謝的胞器，藉由電子傳遞及氧化磷酸化的反應製造 ATP。雖然已知粒線體在生理上的重要性，但已見的報告關於營養物質對於粒線體生合成的調控及對於能量利用的影響並不如預期中的詳盡，需要有更多 的研究來瞭解其對於粒線體生合成的調控機制。在本實驗室的先前實驗已證實利用營養素包括 9-cis retinoic acid, 1,25-dihydroxyvitamin D3 及脂肪酸對粒線體生合成的調控，同時也建立粒線體功能缺陷之細胞模式以評估粒線體之生合成。為進一步瞭解營養物質的供給對細胞選擇其能量代謝路徑及粒線體生合成的影響，因此進行本計劃。葡萄糖與脂肪酸雖都是細胞能量的主要來源，兼以目前已初步瞭解其亦扮有調控基因表現的角色，對粒線體生合成及相關代謝基因調控具有顯著的不同，以其為代表探討不同能量代謝狀況下，代謝酵素的表現狀況及其相關調控機轉。本計劃主要有三個目標，分別為：一、糖類及脂肪酸對細胞粒線體生合成、功能及能量利用的影響；二、高糖及高脂飲食對粒線體生合成、功能及能量利用之老鼠離體細胞(ex vivo)研究；三、營養素對粒線體生合成及功能評估之老鼠體內(in vivo)即時偵測模式建立。本計畫涵蓋細胞株及離體細胞(ex vivo)的細胞模式及小鼠體內(in vivo)即時(real-time)的動物評估模式來驗證上述之假設，尤其動物體內即時偵測的模式，可提供營養素介入後即時及長時間的觀察。本研究預期可幫助瞭解不同營養物質對粒線體生合成的控制及對於能量代謝途徑的調節，也建立一個研究營養物質及荷爾蒙對粒線體生合成的模式，對於粒線體生合成控制路徑的瞭解也將有助於提供因粒線體</p>		

功能缺陷或代謝途徑改變 所造成的各式疾病(如心臟衰竭、代謝症候群)可能的預防及治療方法。

Choices of energy sources of different cell types are dependent on preferred metabolic pathways including glycolysis and fatty acid beta-oxidation. Changes in contents of nutrients in diets can also contribute alternative cellular metabolic pathway. Changed requirement for metabolic pathway to provide energy occurs during changed in cellular behavior and function. Mitochondria are the organelle major in energy metabolism in eukaryotic cells. ATP production by mitochondria is through electron transfer and oxidative phosphorylation. Given this physiological importance of the mitochondria, the observation that nutrients regulate mitochondrial biogenesis was not unexpected, but requires new studies in order to characterize the pathways involved in this regulation. The preliminary data of our studies presented that nutrients including 9-cis retinoic acid, 1,25-dihydroxyvitamin D3, and fatty acids could modulate mitochondrial biogenesis. We also established cell model system with defected mitochondria for evaluation mitochondrial biogenesis. In order to further understand the effects of nutrients supplement on cellular requirement for metabolic pathways and mitochondrial biogenesis, this study will be processed. Three specific aims of this plan are listed: 1. Estimation of regulations of glucose and fatty acid on cellular mitochondrial biogenesis, function and energy utilization. 2. Determination of high glucose and fatty acids diets how to modulate mitochondrial biogenesis, function and energy utilization through ex vivo animal model. 3. Create a real-time bioluminescence tracking animal model to examine the effects of various nutrients on mitochondrial biogenesis and function. This plan include two cell models, cell lines and cells from ex vivo study, and one real-time bioluminescence tracking in vivo animal model to evaluate the proposals. Importantly, this animal model will provide real-time tracking concept and long-term monitoring to follow the fates of nutrients intervention. In this study, we plan to characterize regulation of nutrients on mitochondrial biogenesis, modulation effect on energy metabolic pathway and establish a model to study how nutrients or hormones to regulate mitochondrial biogenesis, this knowledge could bring new ways to better understand mitochondrial defect related diseases and possible preventive and therapeutic treatment.

• 英文摘要