在膀胱癌中脂質代謝對於巨噬細胞分化之影響

學生: 顏岑璇
指導教授: 陳永恩教授
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根據世界衛生組織統計資料顯示，癌症是全球第二大死因，而膀胱癌發生率在所有癌症中佔據第十名。膀胱癌的成因有抽菸、含砷飲用水使用等等。目前膀胱癌的治療方式包含手術切除、化療、放射線治療與免疫療法等，然而其易復發性與抗藥性導致患者五年存活率較低，因此找到新型的治療方式為目前迫切所需要的。

腫瘤微環境 (Tumor microenvironment, TME) 其中的免疫細胞的種類在對抗癌症的免疫反應裡扮演重要的角色。癌細胞為了逃避免疫攻擊，會釋放多種因子來誘導抑制發炎的免疫細胞分化。近年研究指出，Myc 在癌症中所調控的脂質代謝可能會透過脂質的受體 CD36 使抗癌的 M1 巨噬細胞轉換成促癌的 M2 巨噬細胞。從這個觀點來看，以癌症中的脂質代謝作為目標可能可以作為一個重新活化抗腫瘤的免疫反應的策略。我們先前的研究發現，脂蛋白酶抑制劑的基因 ANGPTL4 表現量在膀胱癌中透過表觀遺傳的調控給靜默。過度表達 ANGPTL4 基因後，可以抑制腫瘤生長，因此可以推測其為一種腫瘤抑制基因。在本篇研究中，我們要探討表觀基因是否可以回復癌症中 ANGPTL4 的表現量並抑制脂質代謝，也會透過使用不同的表觀基因調控藥物後的膀胱癌細胞，來探討 THP-1 往巨噬細胞的分化。

The role of lipid metabolism on the differentiation of macrophages in urothelial carcinoma

Student: Tsen Hsuan Yen

Advisor: Dr. Michael Chan

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According to the statistical data from World Health Organization, urothelial carcinoma (UC) ranks the tenth most common cancer in the world. The risk factors of urothelial carcinoma include smoking and arsenic-contain drinking water. The standard treatments of urothelial carcinoma include surgery, chemotherapy, radiation therapy and immunotherapy. Nevertheless, because of the chemoresistance accompanied with high recurrence rate, the 5-year survival rate is still low. Therefore, a novel therapeutics for UC is urgently needed.

Tumor microenvironment (TME), including various subtypes of immune cells, plays an important role in the immune response against cancer. To escape immune attack, cancer cells may secrete various factors to induce the differentiation of immune cells immuno-suppressive subtypes. Recent studies suggested that Myc-mediated lipid metabolism of the cancer cells may turn the M1 anti-tumor macrophage into M2 pro-tumor subtype, via CD36 lipid receptor. In this regard, targeting the lipid metabolism in cancer may be a strategy to “reactivate” the anti-tumor immunity. Our previous study showed that ANGPTL4, a lipoprotein lipase inhibitor, was silenced by epigenetic regulation in urothelial carcinoma. Overexpression of ANGPTL4 gene can inhibit tumor growth, suggesting that it is a tumor suppressor. In this study, we aim to examine if epigenetic treatment can restore the expression of ANGPTL4 and inhibit the lipid metabolism in cancer. The differentiation of THP-1 induced macrophage will also be examined in UC cells treated with various epigenetic modifiers.