褐藻黃素經由粒線體依賴性細胞凋亡途徑抑制口腔鱗狀細胞癌

演講者:黃國瑋　　指導教授:陳浩仁　　日期: 2023/09/15

口腔癌是頭頸癌的一種，是全球十大癌症之一。根據世界衛生組織的估計，每年約新增657,000口腔癌病例，死亡人數超過330,000人。台灣衛生福利部的一份報告顯示，男性口腔癌的發病率明顯高於女性。而在所有口腔癌病例中，90%以上是屬於口腔鱗狀細胞癌（oral squamous cell carcinoma, OSCC）。儘管目前口腔癌的治療策略有很多，但術後復發率仍屬偏高，並且對目前的第一線化療藥物如順鉑和5-FU逐漸產生了抗藥性。因此，新藥的開發就顯得尤為重要。許多研究顯示藻類中的化合物具有抗腫瘤效果，可以抑制細胞增殖並誘導細胞凋亡等，使得藻類成為新藥開發的潛在目標。在本論文中，我使用了從食用褐藻中分離出來的褐藻黃素(fucoxanthin, Fx)為目標，因為褐藻黃素是一種類胡蘿蔔素，已被認為具有多種功能，包括抗發炎、抗氧化、神經保護和保肝活性，許多研究論文皆證明褐藻黃素對不同類型的癌症具有抗癌活性。然而，其對口腔癌的影響尚未被發表。所以我試著探討褐藻黃素對口腔癌細胞株的影響和可能機轉。

通過 MTT 測定和集落形成實驗證實本土口腔癌細胞株 OC2 和 OCSL 的存活率會隨著褐藻黃素濃度的增加而逐漸下降。當與 Z-VAD-FMK（一種廣泛型凋亡抑製劑）聯合處理時可使細胞存活率回升，顯示細胞死亡的機制可能是經由細胞凋亡。為了進一步證實這是否與線粒體依賴性細胞凋亡有關，進行了 JC-1 測定實驗，結果顯示褐藻黃素確實會引起線粒體內膜的通透化，阻止 JC-1 染料的附著並導致綠色螢光的產生。

未來，將使用流式細胞儀、Tunnel assay 和西方墨點等技術，去更加確定是否經由粒線體依賴性的細胞凋亡造成的死亡。此外，相關文獻中也提到褐藻黃素也可造成細胞週期停滯，因此也將以流式細胞儀檢測細胞週期的停滯狀況。

Fucoxanthin suppresses oral squamous cell carcinoma via mitochondrion-dependent apoptotic signaling pathway

Speaker：Guo-Wei Huang　Advisor: Hau-Ren Chen　Date: 2023/09/15

Oral cancer, a subtype of head and neck cancer, is among the top ten cancers worldwide. According to statistical research by the World Health Organization, an estimated 657,000 new cases of oral cancer are diagnosed, resulting in over 330,000 deaths each year. Another report from Taiwan's Ministry of Health and Welfare indicates that the incidence of oral cancer is significantly higher in males than in females. Furthermore, more than 90% of all oral cancer cases are belonged to oral squamous cell carcinoma (OSCC). Despite the availability of numerous treatment strategies for oral cancer, the recurrence rate remains high. Besides, the resistance to current first-line chemotherapy drugs such as cisplatin and 5-FU has been observed. Therefore, the development of new drugs becomes critically important. Many studies have suggested that compounds derived from algae possess anti-tumor properties by inhibiting cell proliferation and inducing apoptosis. This makes algae to be the potential targets for new medications. In this study, fucoxanthin extracted from edible brown algae was use for test. Fucoxanthin is a type of carotenoid with multiple functions, including anti-inflammatory, antioxidant, neuroprotective, and hepatoprotective activities. Several researches have suggested that fucoxanthin exhibits anti-cancer activity against various types of cancer. However, its impact on oral cancer has not been investigated. Therefore, in this research, I tried to investigate the effect and the mechanisms of fucoxanthin in oral cancers.

Firstly, the effects of fucoxanthin on two domestic cell lines OC2 and OCSL were evaluated through MTT assays and colony formation assays. It was observed that the cell survival rates decreased as the concentration of fucoxanthin increased. When treated with fucoxanthin in combination with Z-VAD-FMK (an apoptosis inhibitor), the cell survival rates rebounded by roughly, suggesting that the mechanism of cell death may be through apoptosis pathway. From JC-1 assays, it was speculated to be related to mitochondrion-dependent apoptosis since fucoxanthin induced permeabilization of the mitochondrial inner membrane, preventing the attachment of JC-1 dye and resulting in the production of green fluorescence significantly.

In the future, flow cytometry and Tunnel assay for apoptosis and Western blot for apoptosis marker proteins will be evaluated to further confirm whether the death is caused by mitochondrion-dependent apoptosis. It has also been seen observed that fucoxanthin can arrest the cell cycle in many literatures. I will investigate the effect of fucoxanthin on cell cycle arrest by flow cytometry.