褐藻黃素透過粒線體依賴型凋亡訊號途徑抑制口腔鱗狀細胞癌的細胞活力並誘導凋亡

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口腔癌，是頭頸部癌症的亞型之一，被列為全球十大癌症之一。根據世界衛生組織的統計數據，每年約有657,000例新發口腔癌病例，造成超過330000人死亡。儘管口腔癌有多種治療策略，但復發率仍然很高。尤其是對目前第一線化療藥物如順鉑和5-氟尿嘧啶的抗藥性已經被觀察到，這意味著開發新藥物的重要性。許多研究表明，從海藻中提取的化合物具有抗腫瘤特性，可以抑制細胞增殖並誘導細胞凋亡。在海藻萃取物中豐富的褐藻黃素對各種癌症表現出抗癌活性。然而，其對口腔癌的影響尚未被研究。因此，本研究旨在評估褐藻黃素對口腔癌的影響，並探討其對口腔癌細胞的分子機制。

隨著褐藻黃素濃度的增加，口腔癌細胞的存活率呈現劑量依賴性下降。 透過傷口癒合實驗觀察到口腔癌細胞遷移能力的顯著抑制。使用褐藻黃素與各種抑制劑合併處理細胞。褐藻黃素加Z-VAD-FMK（一種凋亡抑制劑）幾乎完全恢復了存活率，顯示主要凋亡途徑的參與。流式細胞儀與Annexin V和PI染色證實了褐藻黃素誘導的細胞凋亡。此外，JC-1染色顯示褐藻黃素誘導的粒線體膜通透性增加和凋亡因子釋放。最後，Western blot顯示褐藻黃素可以增加促凋亡蛋白Bax和剪切的caspase 3的表達，同時降低抗凋亡蛋白Bcl-2的表達。總之，褐藻黃素有效抑制了口腔鱗狀細胞癌的存活和遷移，可能透過粒線體依賴的凋亡途徑。

未來將進行深入研究，以確認線粒體依賴的凋亡途徑和其他潛在相關途徑。例如，外源性凋亡和內質網壓力誘導的凋亡途徑將是研究的首要任務。 此外，值得探索褐藻黃素是否可能誘導其他獨立於凋亡的死亡途徑。 通過深入研究這些不同的死亡途徑，將有助於更深入了解褐藻黃素功能的分子機制。

Fucoxanthin suppresses cell viability and induces apoptosis in oral squamous cell carcinoma via mitochondrion-dependent apoptotic signaling pathway

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Oral cancer, a subtype of head and neck cancer, is listed as one of the top ten cancers worldwide. According to statistics from the World Health Organization, approximate 657,000 new cases of oral cancer are diagnosed each year, resulting in over 330,000 deaths. Despite various treatment strategies available for oral cancer, recurrence rates remain high. Especially, resistance to current frontline chemotherapy drugs such as cisplatin and 5-fluorouracil has been observed, implying the importance of developing new drugs. Many studies indicated that compounds extracted from seaweed possessed anti-tumor properties by inhibiting cell proliferation and inducing apoptosis. Fucoxanthin, which is abundant in seaweed extracts, exhibits the anticancer activity against various cancers. However, the effect on oral cancer was not investigated. Therefore, the aims of this study focused on evaluating the effects of fucoxanthin and investigating the molecular mechanisms of such effects on oral cancer on oral cancer cells.

As the concentration of fucoxanthin increases, the survival rate of oral cancer cells decreases in a dose-dependent. Significant inhibition of the migration ability of oral cancer cells was observed from wound healing experiments. Various inhibitors in combination with fucoxanthin were used to treat cells. Fucoxanthin plus Z-VAD-FMK (an apoptosis inhibitor) almost fully restored the survival rates, indicating involvement of major apoptosis pathway. Fucoxanthin-induced apoptosis was confirmed by flowcytometry with Annexin V and PI staining. Furthermore, JC-1 staining revealed increased mitochondrial membrane permeability induced by fucoxanthin and the release of apoptotic factors. Finally, Western blot showed that fucoxanthin could increase the expression of pro-apoptotic proteins Bax and cleaved-caspase 3, while decrease the expression of anti-apoptotic protein Bcl-2. In conclusion, fucoxanthin effectively inhibits the survival and migration of oral squamous cell carcinoma might be through the mitochondrion-dependent apoptosis pathway.

In the future, intensive studies to confirm the mitochondrion-dependent apoptosis pathway and potential other related pathways will be performed. For example, extrinsic apoptosis and endoplasmic reticulum stress-induced apoptosis pathways will be the first priority for study. Additionally, it will be worth exploring whether fucoxanthin may also induce other apoptosis-independent death pathways. By delving into these different death pathways, it will be helpful for a more intensive understanding about the molecular mechanisms of fucoxanthin functions.