探討Omega-3脂肪酸對NME1調節之人類頭頸部鱗狀上皮細胞癌SAS細胞之影響

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一. 前言

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摘要

腫瘤發展過程中，癌細胞具持續增生、無限複製、轉移入侵、代謝重整等特徵。頭頸癌因容易早期轉移、對化學放射治療具抗性，使患者五年存活率低於 50%，其中患者癌組織中 NME1 (NME/NM23 nucleoside diphosphate kinase 1; Nm23-H1) 表現量與預後呈正相關性；以口腔鱗狀上皮癌 SAS 細胞建立 NME1 低表現量之穩定轉殖株 ($SAS_{shRNAnm23}$) 與其正控制組 (SAS_{shRNA})，證實 NME1 可抑制癌細胞遷徙及提升化療敏感性，並降低對糖解作用之依賴性。本研究目的為評估水產活性成分抑制頭頸癌惡化之潛力並探討可能的作用機制。本研究先將臺灣蜆 (*Corbicula fluminea*) 以乙醇萃取脂溶性成分，利用氣相層析儀 (gas chromatography, GC) 分析其脂肪酸組成發現含有 EPA (1.86%) 及 DHA (1.42%)。將細胞以 trypan blue exclusion assay 觀察細胞存活率與輔助化療敏感性之結果，並以流式細胞儀 (cell cytometry) 分析細胞週期變化與西方墨點法 (Western blotting) 分析細胞週期調節蛋白之表現量。癌幹細胞 (cancer stem cells) 特徵則以球體生成能力 (sphere formation) 及 Aldehyde dehydrogenase (ALDH) 活性為指標。脂質代謝重整現象則以細胞中性脂質含量及細胞內外脂肪酸組成變化為指標。研究發現 $SAS_{shRNAnm23}$ 及 SAS_{shRNA} 經 EPA 及 DHA 作用 24、48 與 72 小時後，可抑制細胞存活率，並呈現濃度效應，$SAS_{shRNAnm23}$ 及 SAS_{shRNA} 經 6 μM EPA 及 DHA 作用後，存活率分別為 68.8%、78.8%與 72.0%、77.7%。此外，兩株細胞存活率於 6 μM EPA 及 DHA 作用後與僅處理 cisplatin 組相比，已無顯差，說明 6 μM EPA 及 DHA 可提升化療藥物 cisplatin 對 $SAS_{shRNAnm23}$ 細胞之治療效果，並增加細胞週期 S 期 (33.7±0.9 增至 35.0±1.5) 及 G2M 期 (58.4±2.3 增至 61.1±1.6)、促進細胞週期蛋白 cyclin A 與 cyclin B 之表現量 (分別為 SAS_{shRNA} 組之 1.4 倍及 2.1 倍)，因此 EPA 及 DHA 可能經由阻滯細胞週期而提升 $SAS_{shRNAnm23}$ 細胞化療敏感性。處理 EPA 及 DHA 也抑制癌幹細胞球狀生成，且 6 μM 及 12 μM EPA 及 DHA 皆抑制 ALDH 之活性。$SAS_{shRNAnm23}$ 中性脂質之含量顯著高於 SAS_{shRNA}，以 GC 分析發現 $SAS_{shRNAnm23}$ 內 C18:0 及 C16:0 高於 SAS_{shRNA}。總結上述，EPA 及 DHA 抑制頭頸癌 SAS 細胞增生、提升 NME1 低表現細胞之化療敏感性，為具有輔助治療頭頸癌之潛力活性成分。

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