Development of self-assembled fucoidan nanoparticle to perform photodynamic therapy on triple-negative breast cancer in a hypoxic environment

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中文摘要:

癌症，近年在全球十大死因一直居高不下，在台灣更為十大死因之首，而乳癌是女性最常見的惡性腫瘤之一，在女性惡性腫瘤中發病率最高。而治療乳癌目前都以手術切除為主要的治療方式，雖在治療過後患者大多都能回復健康，但因要切除整個乳房，所以大多數的女性患者對此治療方式的意願也較低，而在治療癌症的療法中，光動力療法（photodynamic therapy）治療相較於其他治療方式表現出較多的優點，如較低入侵性、較輕微的副作用、較少的傷口，其利用特定波長的光來激發光敏劑，產生對細胞具有毒性的活性氧及 ROS，使細胞走向死亡，而光動力療法在臨床上還有一些需要克服的課題，如光敏劑的水溶性不佳、無法專一性的靶向腫瘤細胞、腫瘤微環境（tumor microenvironment, TME）的缺氧環境造成的藥物效果失效，為了克服上述缺點，我們使用離子交聯的方式將帶負電的褐藻醣膠（Fucoidan）與帶正電的樹枝狀高分子聚合物 polyamidoamine dendrimers(PAMAM)結合形成自組裝奈米載體，並封裝光敏劑二氫卟吩(Chlorin e6)，及過氧化氫酶（Catalase），最後形成具有多功效的奈米載體 FP@CA。此奈米載體可以使其他藥物得以發揮作用，也可以阻止腫瘤細胞放出 HIF-1 的訊息傳遞，防止腫瘤的轉移發生，最後再利用 660 nm 的紅光來激發二氫卟吩（Chlorin e6）產生 ROS 及活性氧，使三陰性乳癌細胞走向死亡。此研究可提供更具安全性及生物相容性的奈米載體，並結合標靶治療及光動力療法，改善腫瘤缺氧環境並增加光動力療法的效果以達到抑制三陰性乳癌生長的治療方式。

英文摘要:

Cancer has been one of the top ten causes of death in the world in recent years. Breast cancer is one of the most common malignant tumors in women, with the highest incidence among female malignant tumors. At present, the main treatment for breast cancer is surgical resection. Although most patients can recover after treatment, most female patients are less willing to take this treatment because of the need to remove the entire breast. Among the treatments for cancer, photodynamic therapy (PDT) shows many advantages over other treatment modalities, such as less invasiveness, less side effects, less wounds. In PDT, light at a specific wavelength is used to excite a photosensitizer producing reactive oxygen species and ROS that are toxic to cells, causing cells to die. causing the cells to die. However, there are still some clinical issues to be overcome in PDT, such as the poor water solubility of photosensitizers and non-specific targeting to tumor cells. Furthermore, the effect of PDT is weakened due to the hypoxic environment of the tumor microenvironment. In order to overcome the above shortcomings, based on the ionic cross-linking, we plan to use negatively charged fucoidan and positively charged dendritic polymer polyamidoamine dendrimers (PAMAM) to form self-assembled nanocarriers for encapsulation of the photosensitizer (chlorin e6) and catalase (Catalase). As the result, a multifunctional nanocarrier FP@CA is formed. This nanocarrier can be a payload for other drugs, and can also prevent tumor cells from releasing HIF-1 signaling, preventing tumor metastasis. Finally, PDT is performed using 660 nm red light to stimulate chlorin e6 to generate ROS resulting apoptosis of triple-negative breast cancer cells. Overall, this research can provide a biocompatible nanocarrier, and combine with targeting therapy for photodynamic therapy to function in a hypoxic environment and increase the effect of photodynamic therapy to inhibit the growth of triple negative breast cancer.