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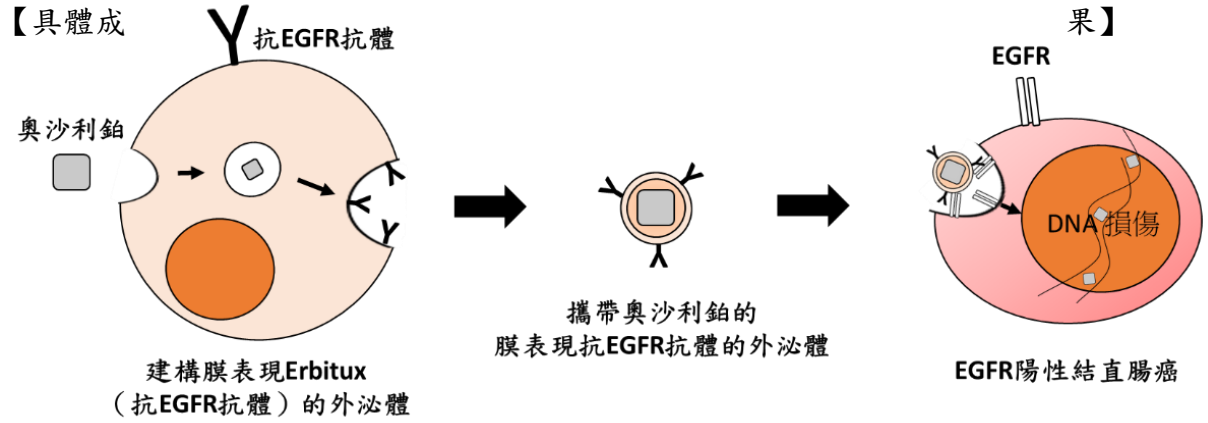
本研究主題為，透過標靶外泌體技術，最大化奧沙利鉑在 EGFR 陽性結直腸癌中的療效。主要是為了克服癌症治療面臨幾個主要挑戰，例如化療藥物奧沙利鉑（Oxaliplatin, OXA）缺乏針對性，容易傷害正常細胞，引發嚴重副作用。此外，藥效不足或患者產生耐藥性，也常影響治療效果。為了解決這些問題，我們研究了一種創新的藥物遞送方式，利用「外泌體」作為載體，提高藥物治療效率。外泌體是細胞分泌的小型囊泡，具有天然的生物相容性與低免疫反應，非常適合用來運送藥物。我們利用人類胚胎腎細胞（HEK293 細胞）生產外泌體，並透過基因改造，在其表面修飾針對「表皮生長因子受體」（EGFR）的抗體，使外泌體能精準累積於 EGFR 陽性的癌細胞中，同時載送奧沙利鉑進入目標細胞。實驗結果顯示，這些改良型外泌體顯著提升了奧沙利鉑對癌細胞的毒性，同時降低對正常細胞的影響。在動物實驗中，我們觀察到這些外泌體能特異性累積於 EGFR 陽性腫瘤，並有效抑制腫瘤生長，其效果優於單純使用奧沙利鉑。這項研究展示了外泌體在癌症治療中的潛力，不僅能解決現有治療的針對性不足和副作用問題，還有助於提升治療效果。我們相信這種技術未來能廣泛應用於其他癌症類型，但目前仍需進一步提升藥物包覆效率。我們將持續努力，期望這項成果能早日造福更多患者。

建構膜表現Erbitux（抗EGFR抗體）的外泌體來提升奧沙利鉑在EGFR陽性結直腸癌中的治療效能

【具體成果】



【具體成果】

曾帶領學生開發標靶外泌體技術，並指導學生參加第 11 屆高醫校園創業競賽，榮獲第二名的佳績；此外，成功帶領學生參與第 17 屆戰國策競賽並順利入圍決賽。這項技術的研究成果已發表於 Chien et al., Cancer Nanotechnology (2024) 15:45，展現其在癌症治療領域的創新價值與潛力。

【研究團隊】

團隊成員：莊智弘

https://sites.google.com/gap.kmu.edu.tw/cchkmulab/%E8%8E%8A%E6%99%BA%E5%BC%98%E8%80%81%E5%B8%AB%E7%B0%A1%E4%BB%8B?pli=1

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Purpose: To investigate the ability of extracellular vesicles (EVs) to deliver oxaliplatin to epidermal growth factor receptor ($EGFR^+$) colorectal cancer cells and increase oxaliplatin's cytotoxicity.

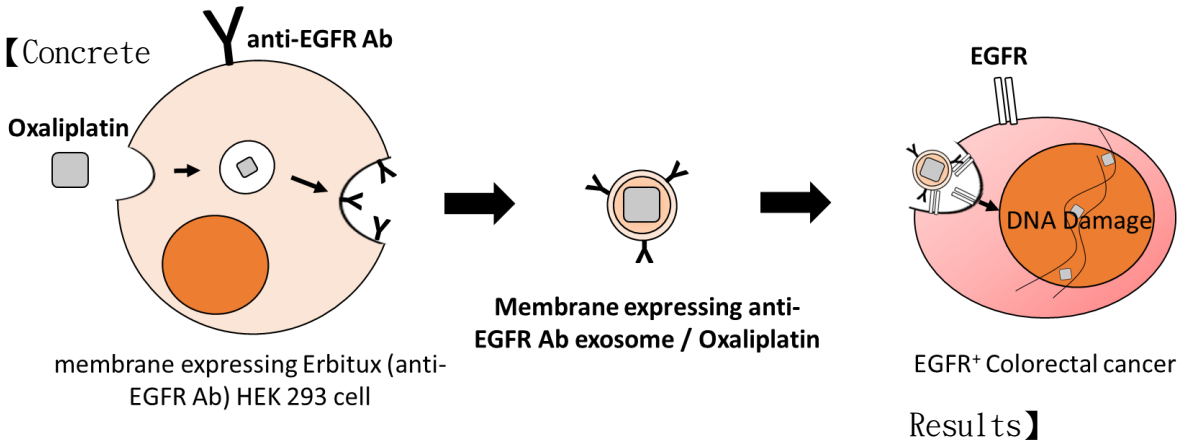
Method: Oxaliplatin was passively loaded into a stable cell line expressing cetuximab in membranes. EVs were collected and characterized for size, and their ability to target $EGFR^+$ cells was tested. Cytotoxicity experiments were performed, and a

xenograft cancer animal model was used to confirm the specific accumulation of oxaliplatin-loaded EVs with cetuximab-expressing membranes in EGFR$^+$ cells.

Results: EVs with cetuximab-expressing membranes were successfully produced and used to encapsulate oxaliplatin, resulting in consistently sized oxaliplatin-loaded EVs with cetuximab-expressing membranes. The oxaliplatin-loaded EVs with cetuximab-expressing membranes were specifically internalized by EGFR$^+$ cells, leading to significant cytotoxic effects on these cells. In the animal model, the oxaliplatin-loaded EVs with cetuximab-expressing membranes accumulated specifically in EGFR$^+$ cells and significantly enhanced oxaliplatin's therapeutic efficacy against EGFR$^+$ cancer cells.

Conclusion: EVs with membrane-expressed bioactive molecules are a promising strategy for delivering therapeutic agents to EGFR$^+$ colorectal cancer cells.

The membrane expressing Erbitux (anti-EGFR Ab) exosome enhances the therapeutic efficacy of oxaliplatin in EGFR$^+$ colorectal cancer



Concrete Results:

Guided students in developing targeted extracellular vesicle technology, leading to a remarkable second-place achievement in the 11th KMU Campus

Entrepreneurship Competition. Additionally, mentored students to successfully advance to the finals of the 17th Warring States Policy Competition. The outcomes of this groundbreaking technology were published in Chien et al., Cancer Nanotechnology (2024) 15:45, highlighting its innovative contributions and potential in advancing cancer treatment.

【Research Team】

Team Members: Chih-Hung Chuang

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