



**HKU
Med**

School of Clinical Medicine
Department of Paediatrics
& Adolescent Medicine
香港大學兒童及青少年科學系

港大醫學院發現 $\gamma\delta$ -T細胞外泌體聯合放療可作為治療鼻咽癌的新方法

HKUMed develops a novel therapeutic approach against nasopharyngeal carcinoma by using exosomes derived from $\gamma\delta$ -T cells synergised with radiotherapy

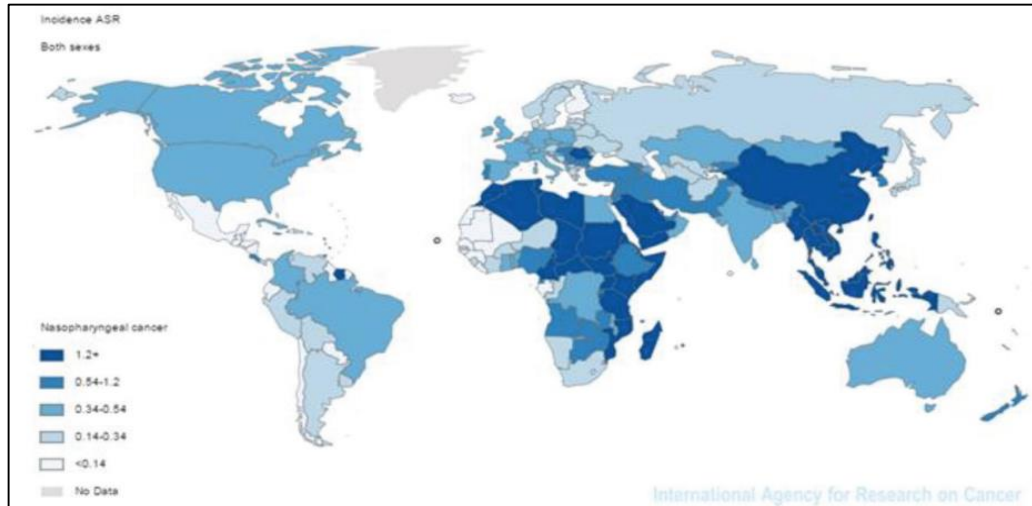
涂文偉教授 & 王系偉博士、張延梅女士
香港大學李嘉誠醫學院臨床醫學學院兒童及青少年科學系

Prof Tu Wenwei & Dr Wang Xiwei, Ms Zhang Yanmei

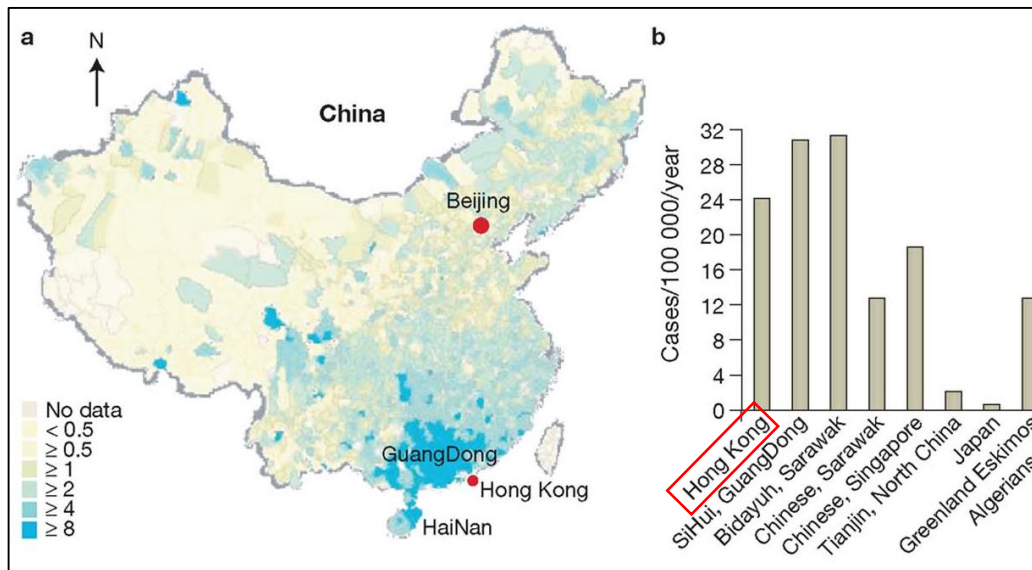
Department of Paediatrics & Adolescent Medicine, School of Clinical Medicine,
LKS Faculty of Medicine, The University of Hong Kong (HKUMed)

鼻咽癌於香港十分常見

Nasopharyngeal carcinoma (NPC) is highly prevalent in Hongkong



1. **鼻咽癌**每年約130,000多新病例，而高於70%的病例發生在中國東南部和東南亞，包括**香港**。
2. 與愛潑斯坦-巴爾病毒（Epstein-Barr virus, EBV）感染高度相關
3. 在**香港**，鼻咽癌發病率約13~24/100,000。



1. **Nasopharyngeal carcinoma (NPC)** causes around 130,000 cases of cancer each year, with more than 70% reported in South China and Southeast Asia, including **Hong Kong**.
2. Highly associated with EBV infection
3. **NPC incidence in Hong Kong** is 13~24 per 100,000 male.

放射治療是鼻咽癌的首選治療方法

Radiotherapy is the primary treatment for NPC

Treatment recommendations for NPC

Early stage	Stage I	Radiation alone
Intermediate stage	Stage II	Concurrent chemoradiotherapy (I, B)
Advanced stage	Stage III, IVA, IVB	Concurrent chemoradiotherapy +/- adjuvant chemotherapy (I, A)
Problematic radiation therapy (RT) planning (e.g. tumor abutting chiasm)	Stage IVA, IVB	Induction chemotherapy followed by concurrent chemoradiotherapy (II, B)

Nasopharyngeal cancer: EHNS-ESMO-ESTRO Clinical Practice Guidelines

優勢:

1. 安全性高, 避免手術損傷神經血管
2. 精確度高, 對神經及面部結構影響較小
3. 殺傷力強, 早期鼻咽癌可達到80%的5年治癒率

局限:

1. 腫瘤幹細胞**對放療抵抗力強, 造成療效下降、復發**
2. 易出現副作用

Advantages:

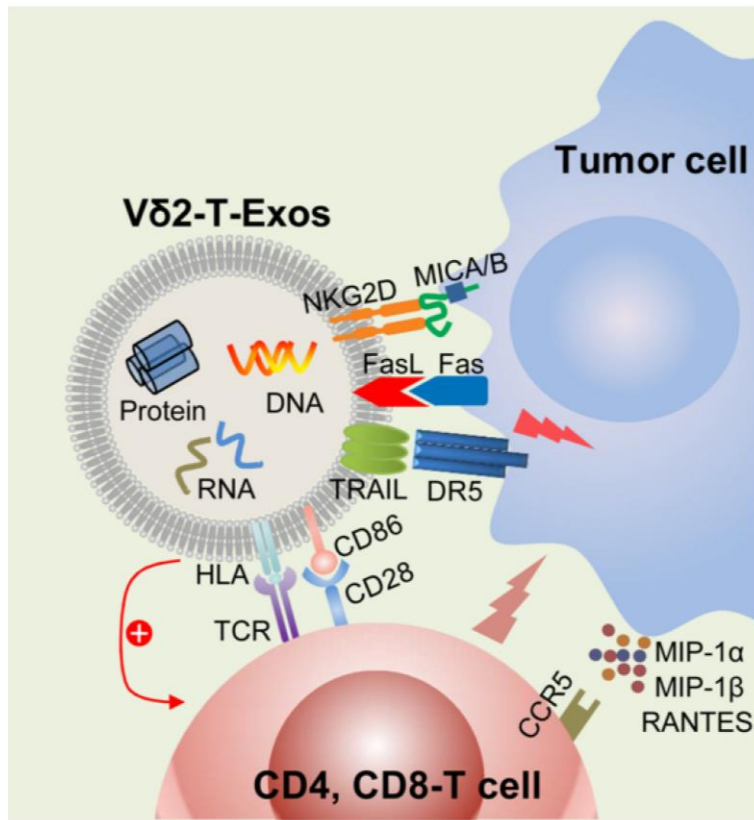
1. Higher safety and avoid surgical injury of nerve vessels
2. Higher accuracy and less impact on nerve and facial structure
3. Stronger killing ability and the 5-year cure rate of early nasopharyngeal cancer can reach to 80%

Limitations:

1. Cancer stem cells cause **radioresistance, leading to decreased efficacy and reoccurrence**
2. Easy to produce side-effects

$\gamma\delta$ -T細胞來源的外泌體具有抗EBV-相關腫瘤的活性

$\gamma\delta$ -T cells-derived exosomes display potent anti-tumour activities



SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE

CANCER

Exosomes derived from Vδ2-T cells control Epstein-Barr virus-associated tumors and induce T cell antitumor immunity

Xiwei Wang¹, Zheng Xiang¹, Yinping Liu¹, Chunyu Huang¹, Yujun Pei¹, Xia Wang², Hui Zhi³, Wilfred Hing-Sang Wong¹, Haiming Wei⁴, Irene Oi-Lin Ng², Pamela Pui-Wah Lee¹, Godfrey Chi-Fung Chan¹, Yu-Lung Lau¹, **Wenwei Tu^{1*}**

(*Science Translational Medicine*: the world's leading journal of translational medicine research)

$\gamma\delta$ -T 細胞外泌體的優點：雙重抗腫瘤活性，易於生產，同種異體外泌體仍有效。

Advantages of $\gamma\delta$ T-Exos: dual antitumor activities, easiness in production, allogeneic counterpart also works

$\gamma\delta$ -T 細胞外泌體於體外實驗可誘導鼻咽癌細胞凋亡

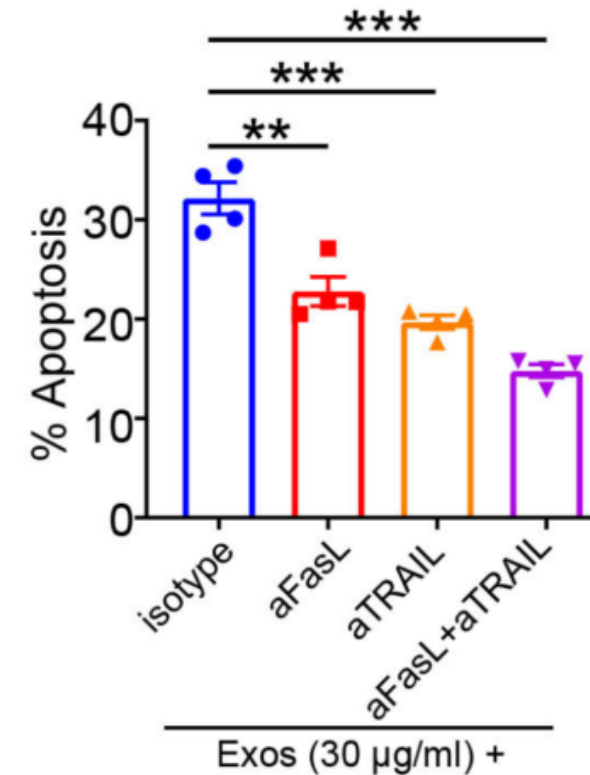
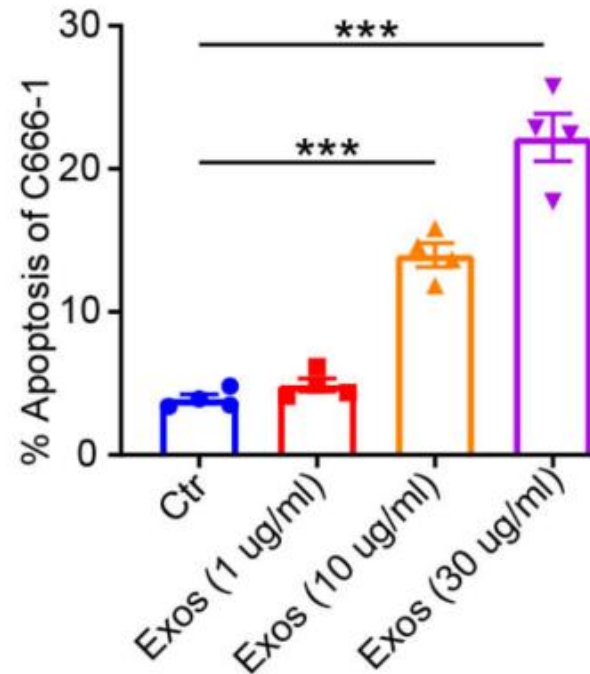
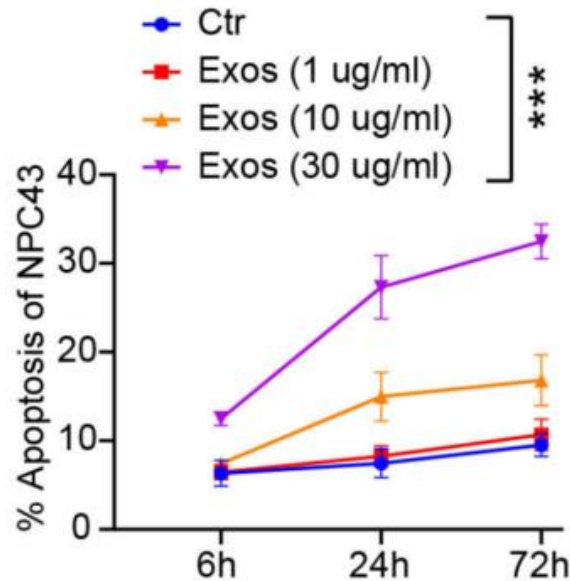
$\gamma\delta$ -T-Exos induce apoptosis of nasopharyngeal carcinoma cells

誘導鼻咽癌細胞凋亡

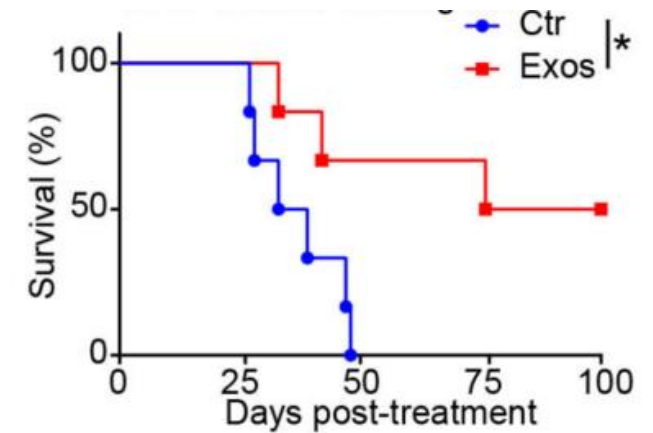
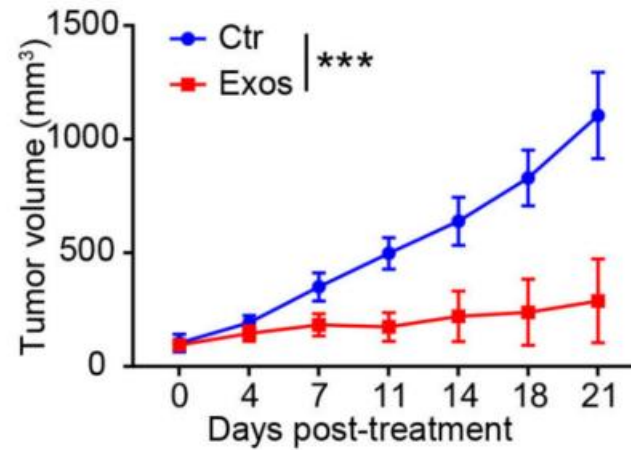
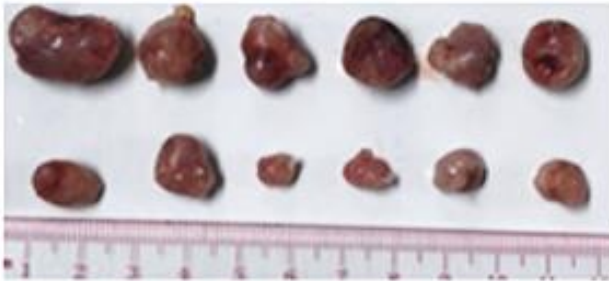
induced nasopharyngeal carcinoma cells
apoptosis

通過激活腫瘤細胞表面的死亡受體介導凋亡

induced apoptosis by ligating death receptors on tumour cells

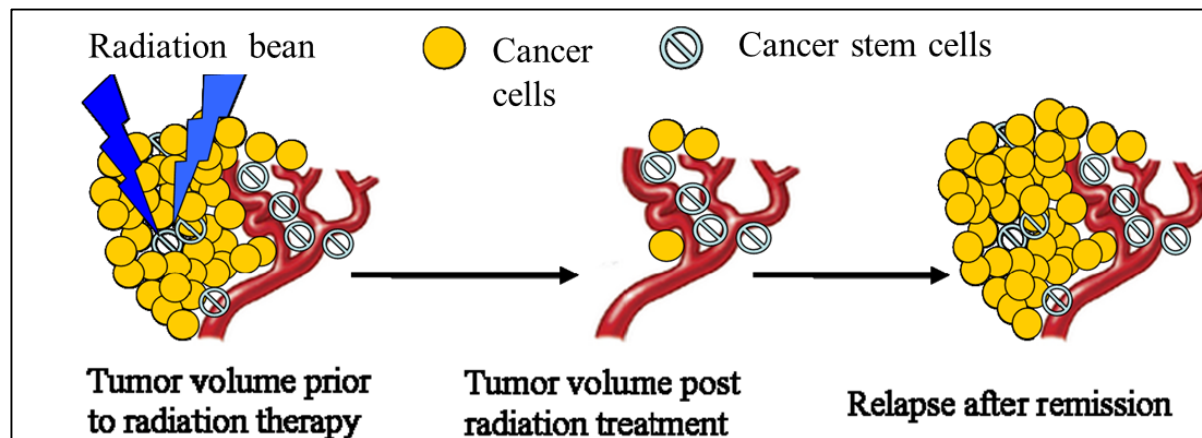


$\gamma\delta$ -T 細胞外泌體在體內模型中可控制NPC腫瘤的進展 $\gamma\delta$ -T-Exos inhibit the progression of NPC tumours in vivo



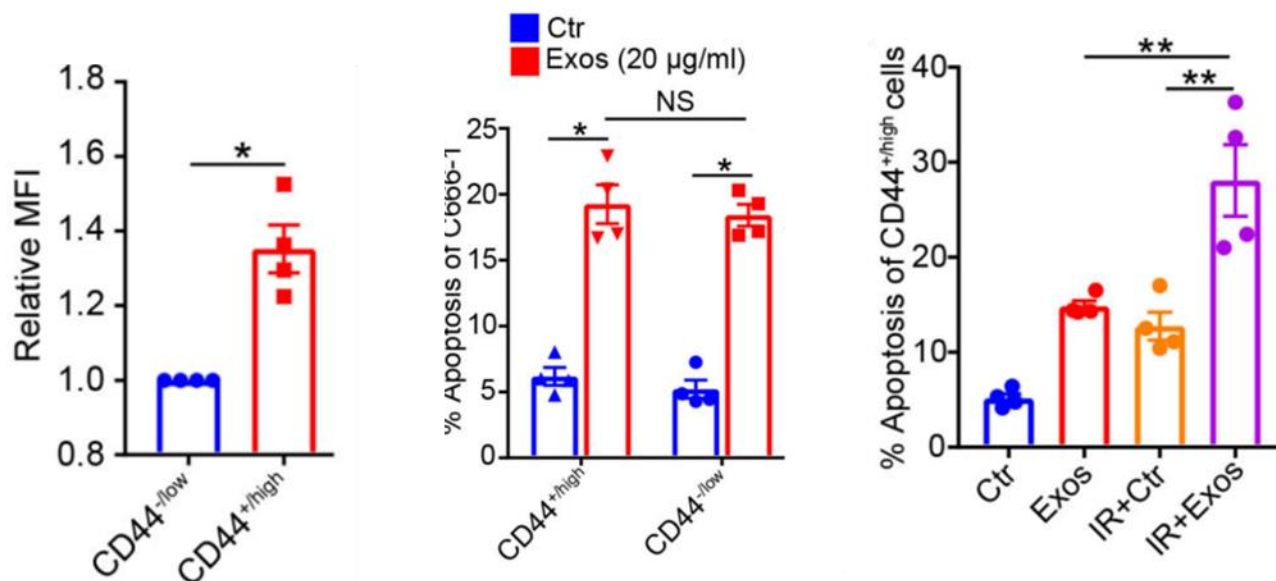
$\gamma\delta$ -T細胞外泌體可與放療協同治療鼻咽癌

$\gamma\delta$ -T-Exos synergise with radiotherapy to eradicate NPC tumour cells



腫瘤幹細胞 (CD44陽性) 具有放射抵抗特性，與腫瘤復發和轉移相關

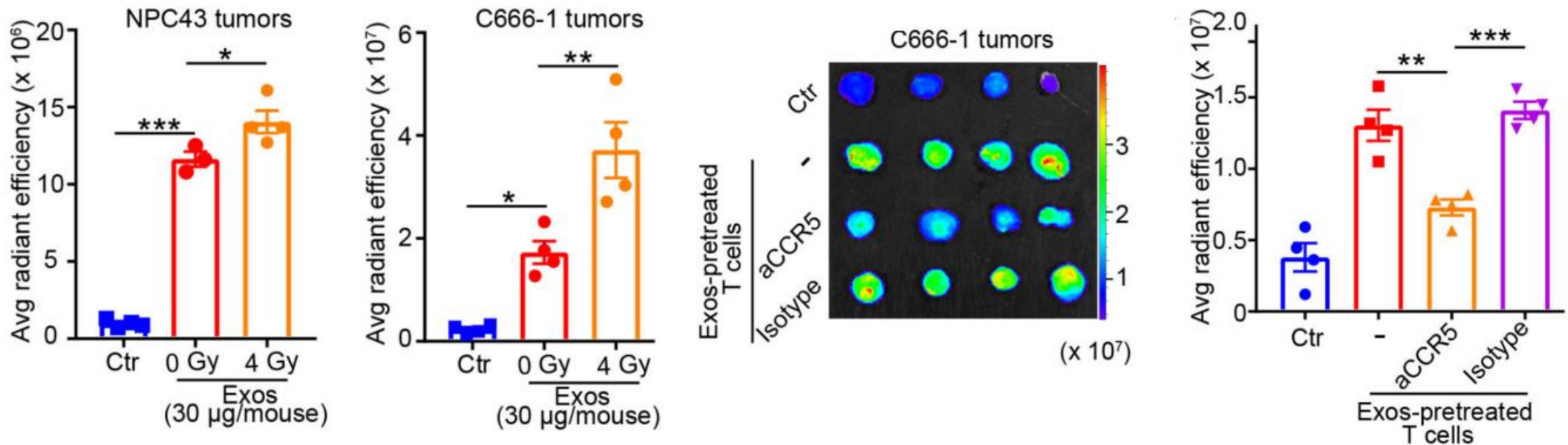
CSCs (CD44⁺) are radioresistant and associated with tumour recurrence and metastasis



$\gamma\delta$ -T細胞外泌體有效殺傷鼻咽癌的腫瘤幹細胞

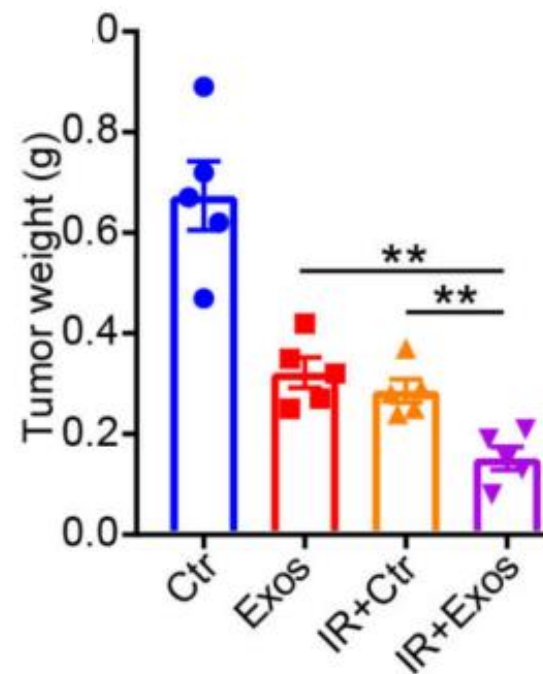
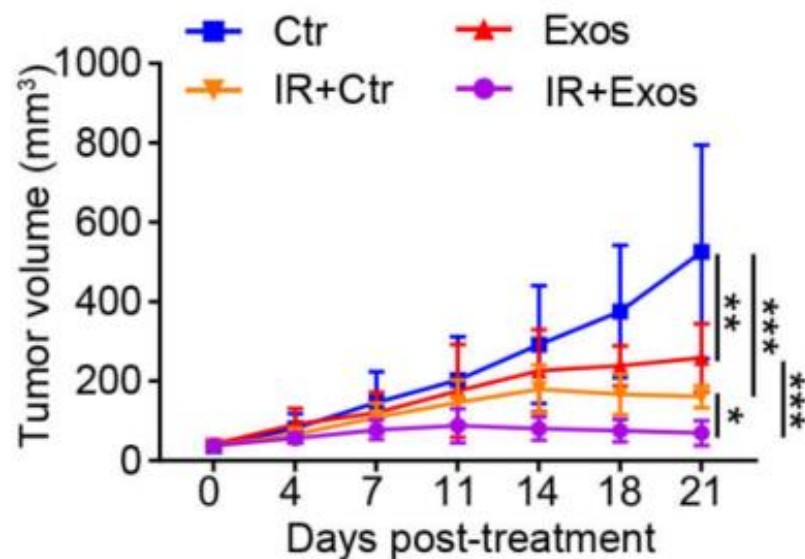
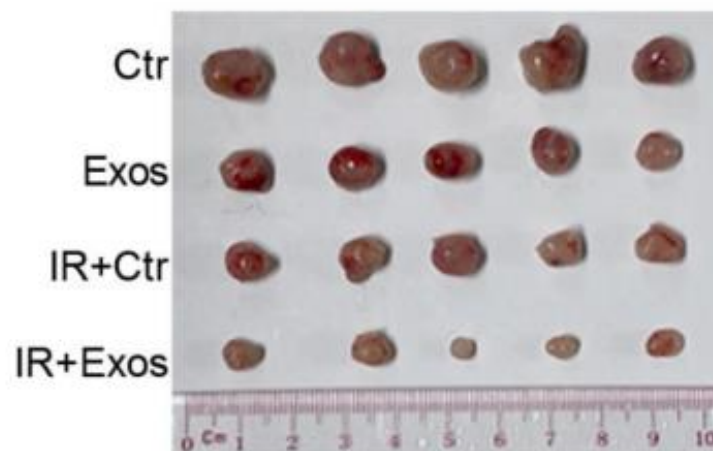
$\gamma\delta$ -T-Exos efficiently killed NPC CSCs

放療促進鼻咽癌組織吸收 $\gamma\delta$ -T細胞外泌體，進而促進T細胞進入腫瘤微環境 Radiotherapy enhances NPC tumours to uptake $\gamma\delta$ -T-Exos that promote T-cell migration into tumour microenvironment



$\gamma\delta$ -T細胞外泌體在體內模型中與放療協同治療鼻咽癌

$\gamma\delta$ -T-Exos synergise with radiotherapy to control NPC tumour growth in vivo

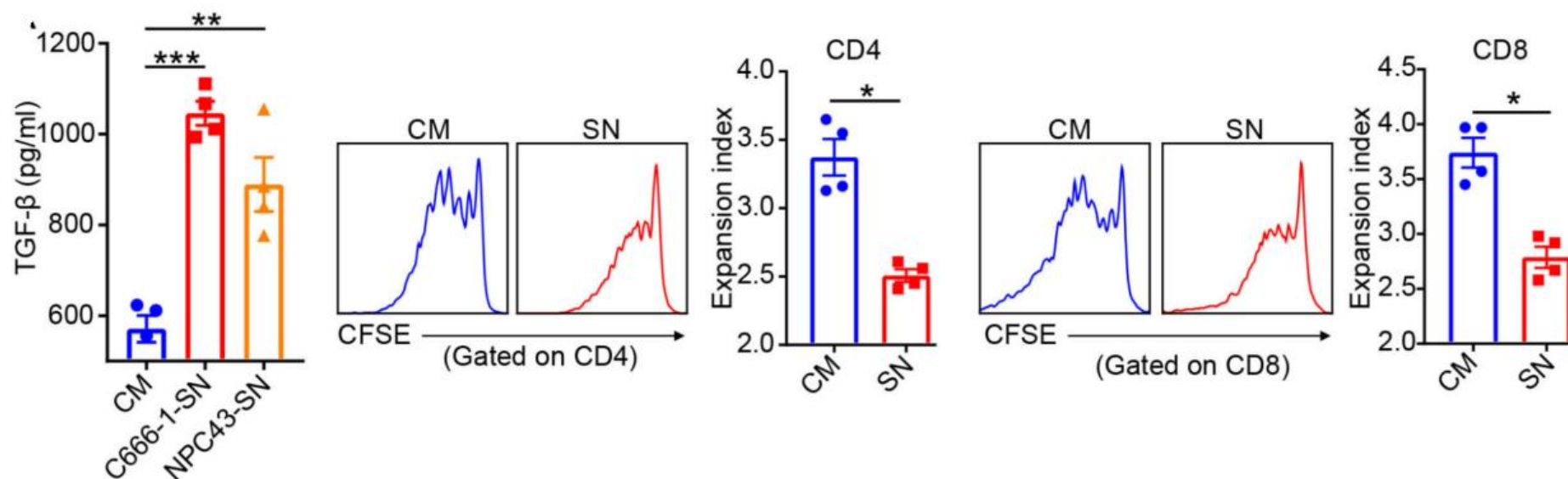


$\gamma\delta$ -T細胞外泌體在免疫抑制性的腫瘤微環境中仍保留抗腫瘤活性

$\gamma\delta$ -T-Exos preserve anti-tumour activities in immunosuppressive NPC tumour microenvironment

腫瘤微環境中T細胞功能減弱

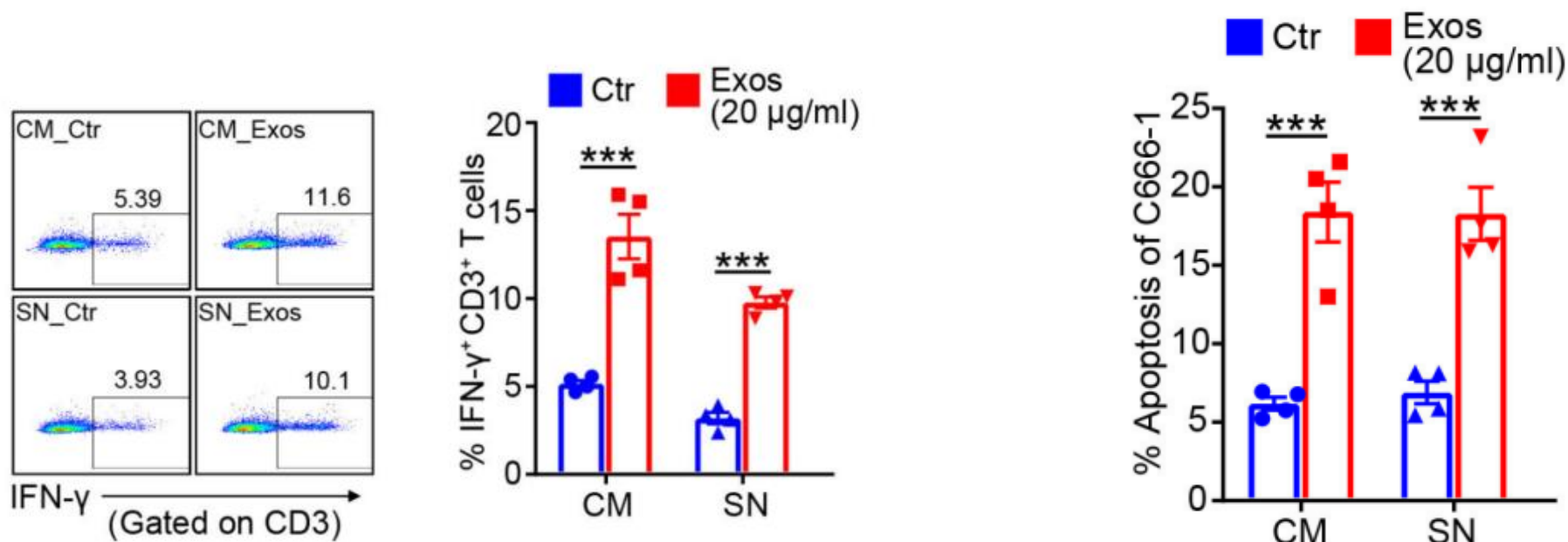
T cells are significantly suppressed in tumour microenvironment



$\gamma\delta$ -T細胞外泌體在免疫抑制性的腫瘤微環境中仍保留抗腫瘤活性

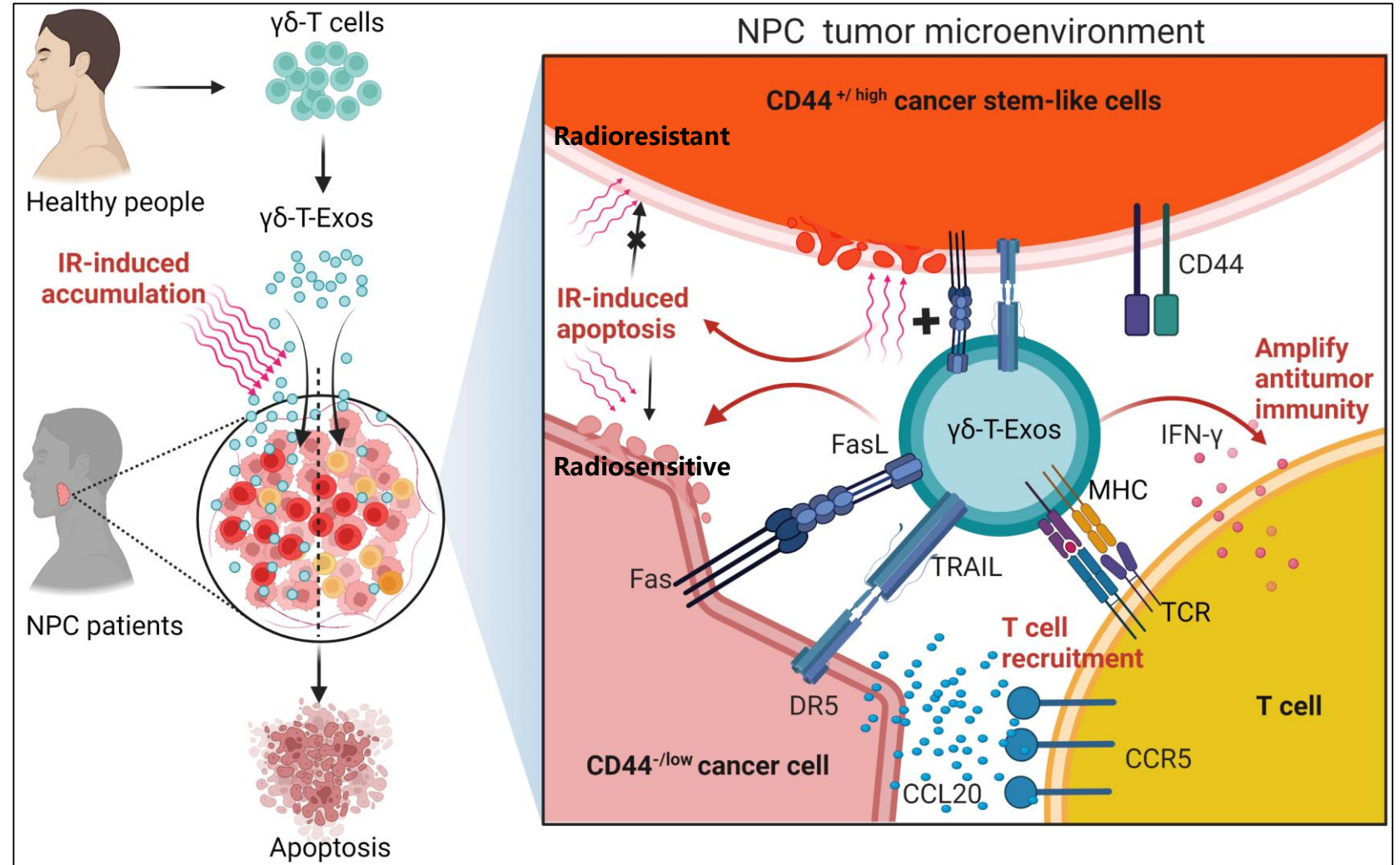
$\gamma\delta$ -T-Exos preserve anti-tumour activities in immunosuppressive NPC tumour microenvironment

細胞外泌體於腫瘤微環境仍保持雙重抗瘤活性
 $\gamma\delta$ -T-Exos induce T-cell anti-tumour immunity



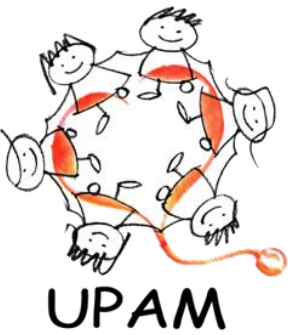
總結 Summary

1. 放療促進腫瘤微環境中外泌體的累積
IR induces the accumulation of Exos into TME
2. 外泌體增強腫瘤幹細胞的放療敏感性
Exos increase the sensitivity of CSCs to IR
3. 腫瘤微環境中外泌體維持雙重抗癌功能
Exos preserve dual anti-tumour activities in TME
4. 外泌體和放療具有協同效應, 增強治療鼻咽癌的療效
Exos synergise with IR to improve NPC therapy



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