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研究興趣

本實驗室研究重點以臨床生醫技轉為重心所開發的創新生物科技：

• 開發抗聚乙二醇雙功能抗體專一性遞送奈米醫藥以治療抗原消失型復發性淋巴癌

B淋巴癌標靶療法，例如CD19抗體-藥物和CD19-雙功能T細胞抗體銜接器療法，在臨床試驗中皆展現卓越的成果。然而單一抗原標靶策略，往往產生復發風險。CD19-雙功能T細胞抗體銜接器療程後，約有30%復發的淋巴癌為CD19陰性。主因可能是CD19抗原突變和腫瘤異質性。本實驗室將開發一種可切換的雙功能抗體平台，能將聚乙二醇奈米藥物標靶至B淋巴癌，以克服抗原突變的復發。

• 開發雙功能抗體以通過血腦屏障遞送奈米藥物

大約10-20%的非小細胞肺癌（NSCLC）患者發生腦轉移。腦癌的治療通常需要有效地將藥物突破穿越血腦屏障（BBB），而這是將藥物遞送到大腦中的主要瓶頸。轉鐵蛋白受體（TfR）介導的轉胞吞作用對於穿越BBB運輸藥物具有高度的潛在用途，但是由於轉胞吞作用運輸過程中無法有效地釋放藥物，因此藥物穿透BBB效果不佳。我們提出了一種新穎方法，可以有效促進聚奈米藥物在腦部血管內皮細胞中釋放，進而增加奈米藥物的腦中攝取。

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Research Interests

My research focus is to develop biotechnology with an emphasis toward clinical translation, including methods:

• Development of switchable bispecific antibodies for cancer-specific delivery of PEGylated nanomedicine to treat antigen-loss relapse in B cell malignancies

Targeted therapies for B malignancies such as CD19 targeted antibody-drug conjugates and CD19-targeted bi-specific T-cell engagers (BiTEs) therapy showed impressive results in clinical trials. However, single-antigen targeting is associated with the risk of relapse, with up to 30% of relapses after CD19-mediated BiTE therapy found to be CD19-negative population. This might be due to antigen-loss mutations and tumor heterogeneity. We hypothesize that subsequently targeting multiple antigens (e.g. CD19, CD22, and CD52) will improve therapy outcomes of B malignancies and control disease progression during CD19-negative relapse. In this study, we propose to develop a switchable bispecific antibody platform for redirecting PEGylated nanomedicines to B malignancies to overcome antigen-loss relapse.

• Development of bispecific antibodies for delivery of nanomedicines across the Blood-Brain Barrier

Approximately 10-20% of patients with non-small cell lung cancers (NSCLC) developed brain metastasis. Treatments of brain cancers typically require efficient drug delivery across the blood-brain-barrier (BBB) which is the main bottleneck for the delivery of therapeutics into the brain. Transferrin receptor (TfR) mediated transcytosis has potential use for transportation of therapeutics across the BBB, however it usually showed poor BBB penetration due to the inefficient release of the payload during transcytosis. We propose a novel approach to boost the brain uptake of nanoparticles by facilitating efficient nanoparticles release in brain endothelial cells.