附件四、技術說明表

利用脂質奈米顆粒遞送抑制 RAS 之 mRNA 以治療神經纖維瘤第一型之相關腫瘤

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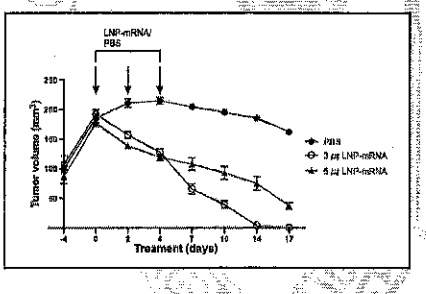
簡　歷：請參閱
https://www.ntuh.gov.tw/neur/Vcard.action?q_type=-1&q_itemCode=270

市場及需求: 神經纖維瘤第一型(NF1)相關腫瘤缺乏有效治療方式，為高度未滿足之醫療需求。NF1 盛行率為 1/3000- 1/4000，推估台灣約有 7,000 到 8,000 名 NF1 病人，其中 900 - 2,300 人為適用本技術族群，美國約有 100,000 名患者，可接受治療族群約 1.5 - 2.5 萬人。

技術摘要(含成果):
本技術是以脂質奈米顆粒(LNP)為載體遞送可表達抑制 RAS 活性蛋白的 mRNA，此 LNP-mRNA 複合體經由腫瘤內注射途徑送入腫瘤內，當 LNP-mRNA 進入細胞後表達蛋白，抑制腫瘤生長。在以 NF1 惡性神經鞘腫瘤細胞株為目標的體外細胞實驗中，LNP-mRNA 複合體顯著抑制細胞生長；在 NF1 惡性神經鞘腫瘤細胞異種移殖(xenograft)的小鼠實驗，LNP-mRNA 複合體注射腫瘤，一週後腫瘤明顯縮小。我們的結果顯示此 LNP-mRNA 具有治療 NF1 相關腫瘤的潛力。



優勢:
最近，使用脂質奈米顆粒包覆訊息 RNA 的治療方式，在蛋白缺陷治療、疫苗免疫及 RNAi 治療上，有長足進步，且個別技術上已證實可行。本技術創新之處在於應用脂質奈米顆粒，包覆大量合成的標的訊息 RNA，再以腫瘤內注射遞送。脂質奈米顆粒並無嚴重的生物毒性，而訊息 RNA 在體內也容易被降解，NF1 相關的腫瘤尤其叢狀神經纖維瘤通常長於體表，腫瘤內注射容易成功。因此使用本技術來治療 NF1 相關的腫瘤不但效果好，其全身性不良反應機率很低。

競爭產品:
目前唯一核准用於治療 NF1 相關腫瘤的藥物只有 MEK 抑制劑 Koselugo。但是服用此藥物能達到腫瘤體積減少 20% (partial response)的比率約 68%，再加上藥物使用後常有副作用，因此目前這藥物的藥效並不理想。

專利現況:

本技術目前沒有任何相關專利。

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Utilizing lipid nanoparticles to deliver RAS-inhibiting mRNA to treat NF1-related tumors

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Experience: Please refer to

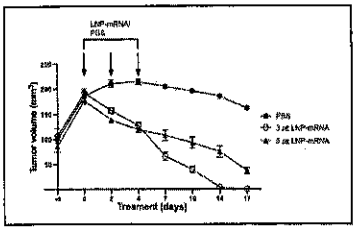
https://www.ntuh.gov.tw/neur/Vcard.action?q_type=-1&q_itemCode=270

Market Needs:

Neurofibromatosis type 1 (NF1)-related tumors currently lack effective treatment options, highlighting a critical unmet medical need. With a global prevalence of 1 in 3,000-4,000, NF1 affects approximately 100,000 individuals in the United States and roughly 7,000 to 8,000 in Taiwan. Within these populations, the estimated eligible patient groups for this technology are 15,000 to 25,000 in the U.S. and 900 to 2,300 in Taiwan.

Our Technology:

This technology leverages lipid nanoparticles (LNPs) to deliver mRNA encoding a RAS-suppressing protein. Administered via intratumoral injection, the LNP–mRNA complex facilitates localized protein expression, effectively inhibiting tumor progression. In *in vitro* studies using NF1-associated malignant peripheral nerve sheath tumor (MPNST) cell lines, the complex demonstrated significant growth inhibition. These results were further validated in mouse xenograft models, where intratumoral administration led to a marked reduction in tumor volume within one week. Collectively, these findings highlight the therapeutic potential of this LNP–mRNA platform for treating NF1-related malignancies.



Strength:

Recent breakthroughs in lipid nanoparticle (LNP)-mediated RNA delivery have demonstrated significant efficacy across the fields of protein replacement therapies, vaccinations, and RNA interference (RNAi). This technology innovates by utilizing LNPs to encapsulate high concentrations of synthetic target mRNA for direct intratumoral delivery. A key advantage of this platform is its favorable safety profile; LNPs exhibit minimal biotoxicity, and the encapsulated RNA is readily degraded *in vivo*, mitigating long-term risks. Furthermore, the superficial location of many NF1-related tumors, particularly neurofibromas, facilitates accessible and precise intratumoral injection. Consequently, this localized approach maximizes therapeutic impact while significantly reducing the likelihood of systemic adverse effects.

Competing Products:

At present, the MEK inhibitor Koselugo (selumetinib) is the only FDA-approved pharmacological treatment for NF1-related tumors. However, its clinical efficacy remains limited; the partial response rate—defined as a ≥20% reduction in tumor volume—is approximately 68%. When weighed against its systemic side-effect profile, there remains a significant need for more effective and better-tolerated therapeutic alternatives.

Intellectual Properties:

There are currently no patents related to this technology.

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