

## 致 謝

想當年，從一個懵懂無知的私立大學的畢業生，經過了交大的兩年的洗禮之後，如今已成為了一個能夠對自己所作所為負責的研究生。這重大的自我革新，就在於當初的那一剎那間的決定，進入了黃國華老師實驗室，在老師的細心的教導與學長們的熱心幫忙解惑下，我才能夠有今日的成就。畢竟，成功不是一朝一夕之間造成的，唯有不斷的犯錯與改過之下，才能到達光輝燦爛的一天。因此必須感謝這兩年所有陪伴我，幫助我和甚至喚醒我的人。首先當然是老師的不厭其煩的對我們進行傳道，授業與解惑，才能讓我快速的從材料領域方面，快速地跨越到生物相關領域，成為專業的跨領域人才。再者，當然是師母，總是熱心的在咪挺前，準備許多豐盛的佳餚，填飽我們的肚子，溫暖我們的心。第三則是洪醫師，每個禮拜五特地從台中趕上來參加我們的咪挺，並且散播歡樂，散播愛給大家。實驗室兩大支柱，昱勳學長與敘安學長，在專業知識方面的傳授與實驗經驗的分享方面，更是讓人精益求精。新堯學長與高超學長，在電腦軟體與開車技術上的教導，甚至帶我上去台北拿老鼠，真是讓我感激萬分。與我一同奮鬥的世明，煌孟和宏書，除了常一同研究如何改進實驗方法外，還常一起分享許多內心的喜悅，寫到這，真讓我不禁感動流淚。再來則是一年級的生力軍，佳慧、玉蘋、洪寧、家偉、忠瀚和順華，這幾位新生命的灌注，我相信你們在不久的將來，一定可以為實驗室灌注更多的歡樂與能量，還有感謝婷婷，在颱風天陪我瘋狂飆高音，希望改天能在多尬幾首。其他實驗室的同學，青翔，感謝你在半導體技術的分享與開車帶我們去內灣兜風。嘉琦，分擔我實驗時的不順與不開心，感謝不論風雨，皆能在一路上陪伴著我到最後的一分一秒，完所有的事情。最後，感謝我的家人，供給我足夠的學費，完成所有從小到大的教育。謝謝所有幫助我的人，祝福大家未來一帆風順！

# 運用奈米金粒子作為高效率的胜肽疫苗載體 並探討粒徑大小與抗體反應之影響

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## 摘要

本實驗室運用奈米金粒子作為高效率的疫苗載體，探討粒徑大小與抗體反應間的關係。首先將製備完成的口蹄疫病毒胜肽與禽流感病毒胜肽，與不同粒徑的奈米金（2 奈米、5 奈米、8 奈米、12 奈米、17 奈米、37 奈米至 50 奈米）做結合，為了確保能達到最大的鍵結量，因此我們在胜肽的酸基末端修飾一個半胱氨酸，強化鍵結能力。對照組方面，則以傳統的血氫蛋白與胜肽作結合之後，兩組接施打至老鼠體內去引發免疫反應。老鼠施打四周、六周、八周和十周後，開始採集血液，粒用免疫酵素檢測法，針對不同的胜肽與載體進行檢測。我們發現奈米金粒子在粒徑 2 奈米、5 奈米、8 奈米、12 奈米和 17 奈米時，有良好的抗體反應。其最大的抗體反應量，其粒徑範圍是在 8 奈米至 17 奈米之間，與傳統的血氫蛋白的方式相比，其抗體反應量提高了將近三倍。值得注意的是，奈米金粒子載體本身並無檢測到任何抗體反應產生，但是血氫蛋白本身卻引起相當高的抗體反應，因此干擾了其所攜帶胜肽的抗體反應。此外，我們使用離子藕荷電漿分析儀計算分佈於老鼠脾臟中的奈米金粒子含量，我們發現此種免疫性質與不同粒徑的奈米金粒子在老鼠脾臟中的含量高度相關。在此研究中，我們發現奈米金粒子不但具有集中抗體辨識的功效，還可提高抗體反應的能力，並且奈米金粒子的粒徑大小與免疫行為有高度相關，其奈米金粒子粒徑範圍從 8 奈米至 17 奈米間，可當作最理想的胜肽疫苗載體。

Assessment for the size-dependent properties of gold nanoparticles as  
vaccine carrier to elicit focused and enhanced antibody response  
against synthetic peptides

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**Abstract**

To elicit the size-dependent carrier ability of gold nanoparticles (GNPs), synthetic peptide corresponding to foot-and-mouth disease virus (FMDV) and influenza A virus subtype (H5N1) viral proteins is conjugated to GNPs with diameter 2-nm, 5-nm, 8-nm, 12-nm, 17-nm, 37-nm, and 50-nm. Extra cysteine is added to the C-terminus of the FMDV peptide (pFMDV) and H5N1 peptide (pH5N1) to ensure maximum conjugation. Immunization of peptide-keyhole limpet hemocyanin (KLH) conjugate was performed as control. Blood are withdrawn on week 4, 6, 8, and 10. Titers against peptide and carriers are obtained. For peptide-GNP immunization, specific binding against peptide is detected in the sera of mice injected with 2-nm, 5-nm, 8-nm, 12-nm and 17-nm GNP conjugates. Maximum binding occur with GNPs of sizes between 8-nm to 17-nm. The peptide -GNPs induce 2.17 ~ 3 fold antibody response

compared to peptide-KLH. In particular, all sera exhibited undetectable binding against GNP, while antisera of peptide-KLH present high levels of binding activity against KLH. Deposition of GNPs in mouse spleen was evaluated by ICP-MS. The immunogenicity of peptide is correlated to amounts of GNPs accumulated in spleen. In conclusion, we show the size-dependent immunogenic properties of peptide-GNP conjugates. GNPs ranging from 8-nm to 17-nm may serve as ideal carrier to elicit focused and enhanced antibody response against a synthetic peptide.



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