2008 年中央研究院「年輕學者研究著作獎」得獎人簡介

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得獎著作名稱：(請以申請時之格式填入)

1. Hsieh CY, Chen CA, Huang CY, Chang MC, Lee CN, Su YN, Cheng WF*, "IL-6-Encoding Tumor Antigen Generates Potent Cancer Immunotherapy Through Antigen Processing and Anti-apoptotic Pathways", *Molecular Therapy/nature publishing group*(2007), volume 15, p1890-p1897.
2. Cheng WF, Lee CN, Chang MC, Su YN, Chen CA, Hsieh CY, "Antigen-specific CD8+ T Lymphocytes Generated from a DNA Vaccine Control Tumors through the Fas-FasL Pathway", *Molecular Therapy/nature publishing group*(2005), volume 12, p960-p968.
3. Liao CW, Chen CA, Lee CN, Su YN, Chang MC, Syu MH, Hsieh CY, Cheng WF*, "Fusion protein vaccine by domains of bacterial exotoxin linked with a tumor antigen generates potent immunologic responses and antitumor effects", *Cancer Research/ American association of Cancer Research*(2005), volume 65, p9089-p9098.

得獎著作簡介: (2000 字左右)

長久以來，子宮頸癌在目前國內婦女惡性腫瘤罹患率排名第一，對國人健康影響甚鉅，而傳統手術、放射線療法或化學藥物療法等治療方式，或多或少傷害到正常的細胞。目前研究顯示，子宮頸癌的發生與人類乳突病毒(human papillomavirus, HPV)的感染有關。免疫系統能保護宿主免於受到外界如微生物或病毒等病原體的感染，有效辨識外部的侵入者或是其他外部抗原的侵入，並產生免疫反應去對抗這些外部抗原對宿主的可能刺激。正常上皮細胞在受人類乳突病毒的感染形成腫瘤細胞後，會表現出特定的人類乳突病毒的抗原。因此以人類乳突病毒為標的將可以成為治療子宮頸癌的新模式。在我們研究團隊的努力下，已經以動物模式研發出癌症疫苗和免疫療法。此種療法最大的特色，在於能夠清除全身而非僅是侷限在局部的癌細胞，此外，它只會攻擊癌細胞而不會傷害正常細

胞。

我們研發團隊所研發的子宮頸癌治療型疫苗，包括蛋白質疫苗、DNA 基因疫苗和細胞治療。舉例來說，研究人員模擬子宮頸癌轉移到肺臟的實驗，先在鼷鼠尾靜脈注射癌細胞，並於注射癌細胞後七日，再對這些鼷鼠注射所研發的疫苗，實驗結果發現未接種疫苗的鼷鼠，卅五日後兩側肺臟平均長出一百多顆大小腫瘤，而施打疫苗的實驗組則絕大多數未發現腫瘤。我们的結果顯示這些治療型疫苗可誘發「抗原特異的毒殺 T 細胞」，對罹癌鼷鼠具有治療效果，對健康的鼷鼠也有預防作用。目前蛋白質疫苗和 DNA 基因疫苗已完成動物實驗，將準備申請人體試驗中。我們實驗室所製備之疫苗與即將上市的疫苗有所不同。藥廠目前研發的子宮頸癌疫苗屬於「預防性疫苗」，在注射後能避免受到人類乳突病毒的感染。因為我們研究團隊所研發的子宮頸癌疫苗，不論是 DNA 疫苗、細胞疫苗或是蛋白質疫苗，注射後可以同時產生「體液性和細胞性免疫反應」，將兼具「預防和治療」的效果，目前細胞疫苗的免疫治療已在臺大醫院進行臨床試驗。值得期盼的是，此疫苗除了應用在子宮頸癌之外，未來也有機會應用在包括其它諸多直腸癌、食道癌、口腔癌等與人類乳突病毒有關的癌症。

評審簡評：

鄭文芳博士於 1999 年自台灣大學臨床醫學研究所取得博士學位，1998-2005 年為台大婦產部主治醫師，2005 年起擔任醫學研究部副教授。

鄭教授此次提出三篇論文(2005 年 2 篇，2007 年 1 篇)，主題皆在癌症免疫治療領域。在其中二篇中，鄭博士為通信作者(2005 Cancer Research 及 2007 Molecular Therapy)，其中一篇謝長堯教授為第一作者；鄭教授提出之第三篇論文(2005 Molecular Therapy)則他為第一作者，謝教授為通信作者。鄭教授資料經送三位學者外審，一致給與高分評價，認為鄭教授已建立獨立研究實驗室，且其研究成果很好，值得給予此「年輕學者研究著作獎」。生命組委員經詳細討論後，亦一致贊成鄭文芳博士為本屆得獎人之一。

2008 Academia Sinica Research Award for Junior Research Investigators

Name: Wen-Fang Cheng 	Education: 1985-1992 M.D., College of Medicine, National Taiwan University 1996-1999 Ph.D., Institute of Clinical Medicine, College of Medicine, National Taiwan University Employer(s)/Job Title(s): 2006 till now Associate Professor, Graduate Institute of Clinical Medicine, College of Medicine, National Taiwan University 1998 till now Obstetrician and Gynecologist, Department of Obstetrics and Gynecology, National Taiwan University Hospital 1999-2001 Post-doctor, School of Medicine, Johns Hopkins University, Baltimore, Maryland

Award publications：

1. Hsieh CY, Chen CA, Huang CY, Chang MC, Lee CN, Su YN, Cheng WF*, "IL-6-Encoding Tumor Antigen Generates Potent Cancer Immunotherapy Through Antigen Processing and Anti-apoptotic Pathways", *Molecular Therapy/nature publishing group*(2007), volume 15, p1890-p1897.
2. Cheng WF, Lee CN, Chang MC, Su YN, Chen CA, Hsieh CY, "Antigen-specific CD8+ T Lymphocytes Generated from a DNA Vaccine Control Tumors through the Fas-FasL Pathway", *Molecular Therapy/nature publishing group*(2005), volume 12, p960-p968.
3. Liao CW, Chen CA, Lee CN, Su YN, Chang MC, Syu MH, Hsieh CY, Cheng WF*, "Fusion protein vaccine by domains of bacterial exotoxin linked with a tumor antigen generates potent immunologic responses and antitumor effects", *Cancer Research/ American association of Cancer Research*(2005), volume 65, p9089-p9098.

Summary of the Award publications（around 2000 words）：

Over a long period of time, cervical cancer is the most prevalent cancer of women’s malignancies in Taiwan. Conventional treatment modalities for cervical cancer such as surgery, radiotherapy, and cytotoxic chemotherapy, though effective to some extent, have a shortcoming in common: these methods may injure normal cells. Present researches have indicated that the development of cervical cancer has

strong correlation with the infection of human papilloma virus (HPV). The immune system can protect its host from being infected by pathogens such as microorganisms or viruses of the external world, distinguish external invasions or other external antigens effectively, and take immune response to fight against probable stimulations of these external antigens. The normal epithelial cells could become cancer cells and expressed the specific HPV antigens after infected by HPV. Targeting of HPV antigen-specific immunotherapy represent an attractive approach for cervical cancer treatment. Our research team has developed several strategies in the development of cancer vaccine and immunotherapy. The main feature of immunotherapy is that it could eliminate cancer cells not only in local parts of the body, but also over the whole body. Besides, it has the distinct advantage of attacking only cancer cells without damaging normal cells.

The therapeutic vaccines of cervical cancer developed from our team include protein-based vaccine, naked DNA vaccine and cell-based therapy. For example, we first injected cancer cells via tail vein of mice to simulate the distant metastasis of cervical cancer cells to the lungs of mice. Seven days after the injection, we then started to treat the mice of lung metastasis with effective therapeutic vaccine. The results showed that mice which didn’t receive the immunization of effective therapeutic vaccine had numerous tumors grown in their lungs after 35 days, but mice that received effective therapeutic vaccine didn’t. Our results demonstrated that therapeutic vaccines developed from our team could not only stimulate antigen-sepcific T cells activation, generate a significant therapeutic effect in tumor-bearing murine, but also prevent tumor cells growth in native mice. For now, the vaccines, such as protein-based and DNA vaccine, which we developed have completed the pre-clinical trials in our studies, and we are in the process of applying the clinical trials recently. It is worth to mention that the vaccines in our laboratory are not the same as those available in the market. The vaccines from pharmaceutical companies belong to “preventing vaccines”, which only prevents the infection of human papilloma virus. On the other hand, we developed cervical cancer vaccines whether DNA vaccines, cell vaccines or protein vaccines causes humoral and cellular immune response after injection, becoming effective in prevention and treatment. At this moment, cell-based immunotherapy is ongoing in our hospital. In the future, those cancers related to human papilloma virus including colorectal cancer, esophageal cancer, penile cancer and oral cancer would be potential target diseases to be treated through this technique.