出國報告(出國類別：參加國際會議)

參加 2009 年美國癌症研究學會(AACR)年會回國報告

服務機關：三軍總醫院

姓名職稱：禚靖 上校軍醫官

派赴國家：美國

報告日期：中華民國 98 年 05 月 08 日

出國時間：自 98 年 04 月 17 日至 98 年 04 月 24 日

摘要

三軍總醫院胸腔外科軍醫禚靖於民國 98 年 04 月 17 日至 98 年 04 月 24 日參加於美國科羅拉多州(Colorado)丹佛(Denver)市舉辦之第 100 屆美國癌症研究學會(American Association for Cancer Research, AACR)年會，提報研究論文一篇，題目爲 Anticancer Effects of Suberoylanilide Hydroxamic Acid (SAHA) in Esophageal Squamous Cell Carcinoma。該會爲全世界最具規模之國際癌症研究會議，本屆主題爲科學、協同、成功 (Science, Synergy, Success)。本人於 98 年 04 月 21 日下午提報論文、爲海報展示及討論。與會期間，參與各類型之研討會、含教育(Educational Session)、與專家見面(Meet the expert), 大型專題研討會(Symposium), 小型專題研討會(Mini-symposium), 講座(Forum), 海報展示及討論(Poster presentation)會議等學術活動、內容涵蓋相當廣泛，筆者主要參加之研討會內容爲癌症附基因體研究(cancer epigenetics)、癌症幹細胞研究(cancer stem cell)、發炎及腫瘤微環境(inflammation and tumor microenvironment)、癌症轉移模型(tumor metastasis models)，癌症基因體、癌症附基因體及新藥研發等主題(cancer genomics, epigenomics and development of novel anticancer drugs)。以下筆者就這次與會之發現及所學作一詳細之心得報告。以期將來對本單位及相關同仁有所助益。

2009 年美國癌症研究學會(AACR)年會回國報告

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本文

一、目的: 參加 2009 年第 100 屆美國癌症研究學會(American Association for Cancer Research, AACR)國際會議暨海報論文研究成果報告

地點: 美國丹佛市科羅拉多州國際會議中心(Colorado Convention Center)

時間: 2009 年 4 月 18 至 4 月 22 日

海報論文報告 (2009 年 4 月 21 日 2009, 1:00 PM, Hall B-F, Experimental and Molecular Therapeutics 32, Poster Section 34),題目: Anticancer effects of suberoylanilide hydroxamic Acid (SAHA) in esophageal squamous cell carcinoma

二、過程: 4月17 日上午自台北起程飛往美國、於當日下午抵達美國科羅拉多州丹佛市。該城市幅員遼闊交通發達，爲著名之觀光景點。大眾運輸系統及公車四通八達，與會期間大家均依靠該系統爲主要交通工具，另有由大會安排之接泊巴士往不斷穿梭、往返於國際會議中心與各衛星會場及旅館，十分方便。此次會議有來自世界各地之癌症研究學者等約八千人，論文報告近三千餘篇，本會爲全世界最具學術地位之癌症研究學會之一、含癌症研究最新趨勢之探討。本人之主要興趣爲胸腔癌症之附基因學及癌症幹細胞之研究，故於會前即鎖定以上課題，積極參與各研討會、海報展示及相關之醫學再教育課程，不斷穿梭於各會場，將各演講或海報展示之內容以數位相機攝影或記筆記存檔於筆記型電腦後整理以爲日後之重要參考。與會期間，參與各類型之研討會、含教育(Educational Session)、與專家見面(Meet the expert), 大型專題研討會(Symposium), 小型專題研討會(Mini-symposium), 講座(Forum), 海報展示及討論(Poster presentation)會議等學術活動、內容涵蓋相當廣泛，筆者主要參加之研討會內容爲癌症附基因體研究(cancer epigenetics)、癌症幹細胞研究(cancer stem cell)、發炎及腫瘤微環境(inflammation and tumor microenvironment)、癌症轉移模型(tumor metastasis models)，癌症基因體、癌症附基因體及新藥研發等主題(cancer genomics, epigenomics and development of novel anticancer drugs)，會議期間與多位大師級學者如Edward Seto (大會記實圖一), H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL、Ricky W. Johnstone, Peter MacCallum Cancer Institute, East Melbourne, Australia等討論組蛋白去乙醯胺抑制劑於抑制腫瘤生長機轉，他們均熱心提供了寶貴的經驗，讓本人受益良多。他們同時也希望有機會到台灣訪問交流，若能安排來台，相信對台灣胸腔內外科學界能有相當之貢獻。本人於4月21日的海報論文報

告，過程順利引起許多有興趣之研究人員之廣泛討論，受益良多,另外也見識到相關領域的其他研究結果及進展之快速，對自己是一個警惕，與他們討論的當中受益匪淺。大會於4月22圓滿結束，筆者於4月23自美啓程返國，於4月24抵台，結束了此行豐富的學術饗宴。

以下就每日行程及學習之經過作一報告。

4 月 17 :日下午自台北起程飛往美國、當日下午抵達美國科羅拉多州丹佛市，下榻於 Cherry Creek Holiday Inn Select.4 月 18 日主要爲大會各項繼續教育課程、參加了與筆者目前研究極爲相關之 Histone Deacetylases as Targets of Cancer Therapy、Methods in Cancer Epigenetics and Epigenomics 及 Chemokines and Cancer 研討會，與多位大師級學者如 Edward Seto, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL、Ricky W. Johnstone, Peter MacCallum Cancer Institute, East Melbourne, Australia, Dr. Bhalla (大會記實圖二 at Georgia Medical Center 等討論組蛋白去乙醯胺抑制劑於抑制腫瘤生長機轉，受益良多。

4月19日:一早首先參加了與專家見面(Meet the expert)討論會題目爲Biomarker Selection of Non-Small Cell Lung Cancer Patients for Initial Therapy，由Professor Paul A. Bunn, Jr., University of Colorado Health Sciences Center, Aurora, CO主持，對肺癌腫瘤標記之臨床應用有更深之認識。接著又參加了癌症基因研究及診斷EMT(上皮間質移行)及Cancer Stem Cells(癌症幹細胞)研討會，主要在探討目前熱門的幾個分子生物學技術及應用，包括單一核酸咁多形性變異分析，基因晶片及微陣序列分析、蛋白基因學及生物資訊系統分析及癌症幹細胞等研究及先進技術及應用之介紹，期間與固態腫瘤(solid tumor)癌症幹細胞領域之大師Stanford University Michael F. Clarke教授請益，對本人日後相關研究，有相當的啓發。下午參加了腫瘤生物學(Tumor Biology)海報討論會，含 Biomarkers of Tumor Metastasis Cancer Stem Cells: Therapies and Chemoresistance, Cytokines and Chemokines in the Microenvironment, Extracellular Matrix and Proteases in Tumorigenesis, Innate Immune Response in Tumorigenesis, Metastasis Suppressor Genes等重要課題，收獲良多。

4月20日: 本人主要參加了癌症Epithelial-Mesenchymal Transitions in Cancer EMT(上皮間質移行)研討會，由UCSF Prof. Tlsty, Dr.Greg D. Longmore, Washington University, St. Louis, 及 University of Michigan Prof. Weiss等討論1.Snail regulation and EMT Pathways regulating basement membrane

transmigration in EMT. 其中有關snail基因在癌症上皮間質移行扮演之角色有深入之探討。引起許多有興趣之研究人員之廣泛討論，受益良多,另外也見識到相關領域的其他研究結果及進展之快速，對自己是一個警惕，與他們討論的當中受益匪淺。下午利用會議空檔由前國衛院院長吳成文教授帶領一群與會之國內學者及研究人員至位於 Aurora 之 University of Colorado Cancer Center 參訪(大會記實圖五)，該中心爲全美排名前五名之癌症中心，由肺癌研究先驅 Prof. Paul Bunn 及該中心主任 Prof. Byer (大會記實圖六)負責接待，瞭解該中心之運作，主要臨床試驗之發展及癌症相關研究團隊及核心實驗室，其整合及品質管制令人印象深刻。爲此行增添不少見聞，也結交了少國內外研究先進及同好。

4 月 21 日: 當日參加了 The Molecular Biology of Lung Cancer in Never Smokers: A Different Disease 研討會，對非吸煙肺癌患者之流病基因學及治療有更深一層之瞭解。另外又參加 Exploiting the Hypoxic Tumor Microenvironment for Therapeutics 研討會，此爲目前引起廣泛興趣之研究領域，亦爲筆者未來積極開拓之研究方向。下午爲筆者海報論文報告(大會記實圖三),題目爲 Anticancer effects of suberoylanilide hydroxamic Acid (SAHA) in esophageal squamous cell carcinoma,引起廣泛討論，並與相關各國學者(大會記實圖四)之報告交換意見，並討論互相合作之可能性，成果豐碩。

4 月 22 日: 爲大會最後一天，爲期半天當日參加了 Cancer Stem Cells: Advances and Challenges 研討會，對癌症幹細胞研究之發展、應用及面臨之挑戰有進一步之瞭解，予筆者目前相關研究相關之啓發。

於 4 月 23 日啓程返台，結束了豐碩的丹佛之旅。

三、心得：

1. 本屆大會所在地科羅拉多國際會議中心爲本人歷屆參加類似會議中設備最爲完善規模最大者，且議程安排緊湊流暢、會議內容充實。
2. 幾個重要疾病之基因研究突飛猛進，惟預防及治療方面仍有很大的努力空間
3. 此會議規模之大、議題之廣，實在很難一窺全貌，選擇本院重點發展與自己興趣所在之領域，儘可能吸收，可能較切合實際。
4. 應把握與世界級大師與同好研究學者認識與溝通之機會，建立學術交流管道，提升院譽及提供本院同仁與國際學者合作之機會。

5. 本院提報論文約三至五篇，相較其他研究機構(計 200 餘篇)似嫌不足，應再努力。

四、建議事項:

1. 感謝國科會經費補助與院方之支持。
2. 蒐集及整合出席國際會議所獲得之具體資料，以數位影像及文字檔存於電腦檔案並建立全院資料，供有興趣者參閱。
3. 代表院方於國際會議提報論文者，予以書面獎勵或列入年度研究績效(如醫勤獎金點數加計)，以鼓勵研究發表之風氣。

附件：論文報告摘要及證明文件如後

論文報告摘要

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Current Date/Time: 12/2/2008 4:09:23 PM

Anticancer effects of suberoylanilide hydroxamic Acid (SAHA) in esophageal squamous cell carcinoma

Short Title:
SAHA in esophageal cancer

Author Block: *Ching Tzao*, *Ban-Hen Chen*, *Ting-Yun Hsu*, *Guang-Huan Sun*, *Shi-Hwa Chiou*, *Shih-Chun Lee*. Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan, Veterans General Hospital, Taipei, Taiwan

Abstract:
Background: Histone deacetylation, one of the major histone modifications, is known to be associated with tumorigenesis and cancer progression. A histone deacetylase (HDAC) inhibitor, suberoylanilide hydroxamic acid (SAHA) has been used in clinical trials to treat cancers other than esophageal cancer. We aimed to anticancer effects of SAHA for esophageal squamous cell carcinoma (ESCC) *in vitro* and *in vivo*. **Methods:** Six ESCC cell lines, KYSE 70, 150,170, 510 (kindly provided by Dr. Yutaka Shimada at University of Toyama, Japan), CE48-T/VGH, and CE81-T/VGH were treated with SAHA (2 μm for 48 hrs). Cell viability was measured by MTT assay and cell migration was measured by trans-well migration assay, respectively. Proportions of cells in different phases of cell cycle were counted by flow cytometry. Apoptosis of ESCC cells was analyzed by Annexin-V staining kit with flow cytometry. Western blot was used to determine cell cycle regulatory proteins such as cdk1, 2 and their corresponding coupled cyclins A, B1 for G2 arrested cell lines as opposed to cdk 4 and D1 for G1 arrested cell lines. In addition, expression of G1 inhibitory tumor suppressors, p21, p53, Rb, and p27 were studied in cell lines with G1 arrest. A tumor xenograft model using nude mice inoculated with KYSE 510 was used to determine effects of SAHA (50mg/kg/day, ip, 5 days a week) *in vivo* on tumor growth along with analysis of expression of cyclin D1, p21, p53, Rb, and p27 in grafted tumors. Effects in reversing histone acetylation by SAHA was confirmed by Western blot of acetylated histone 3 (H3) and 4 (H4). **Results:** Significant inhibition in cell survival and migration was induced by SAHA in all cell lines except KYSE 170. SAHA effectively reversed acetylation of H3 and H4. G1 1 arrest was observed in CE48-T/VGH, CE81-T/VGH, KYSE 170 and 510, whereas G2 arrest was observed in KYSE 70 and 150. Protein expression of cdk 4, cyclin D1 decreased in SAHA-treated G1 arrested cell lines, whereas expression of cdk 1, 2, cyclin A and B1 decreased in G2 arrested cell lines. Expression of p21, p27, and Rb increased 24 hrs after treatment with SAHA in G1 arrested cell lines. Higher dose of SAHA at 10 μM induced significant apoptosis of KYSE 510 cells at 24 and 48 hr. SAHA significantly inhibited tumor growth *in vivo* from day 16 to day 52 after SAHA treatment with a significant decrease in expression of cyclin D1 and p21 in KYSE 510 grafted tumors. **Conclusion:** G1 arrest with concomitant down-regulation of cdk 4, cyclin D1 and up-regulation of G1 inhibitory tumor suppressors is one of the major mechanisms responsible for inhibition of tumor growth by SAHA treatment. SAHA effectively inhibited tumor growth of ESCC *in vitro* and *in vivo*. Our results suggested that SAHA may serve as a potential epigenetic treatment for ESCC while elucidating in part mechanisms responsible for its anticancer effects.

Author Disclosure Information: **C. Tzao**, None; **B. Chen**, None; **T. Hsu**, None; **G. Sun**, None; **S. Chiou**, None; **S. Lee**, None.

論文接受函

AACR 100th Annual Meeting 2009: Poster Session Abstract #1061　2009/2/4(星期三) 上午6:08
寄件者："support@abstractsonline.com" <support@abstractsonline.com>
收件者：tzao@yahoo.com

February 3, 2009

Re: AACR 100th Annual Meeting 2009 in Denver, CO
Temporary Abstract Number: 1061
Title: Anticancer effects of suberoylanilide hydroxamic Acid (SAHA) in esophageal squamous cell carcinoma

Dear Dr. Tzao:

Your above-referenced abstract has been scheduled for presentation in a Poster Session at the 2009 AACR Annual Meeting in Denver, CO and will be published in the 2009 Proceedings of the American Association for Cancer Research. Presentation information pertaining to your abstract is below:

Session ID: Experimental and Molecular Therapeutics 32
Session Date and Time: Tuesday, April 21, 2009, 1:00 PM
Location: Hall B-F, Poster Section 34
Permanent Abstract Number: 4613

Please refer to the printed Final Program (distributed onsite) or the online Annual Meeting Itinerary Planner [available in mid-March through the AACR Website at http://www.aacr.org] for the exact location of your presentation.

Instructions for Presenters in Poster Sessions can be found on the 2009 AACR Annual Meeting home page:
http://www.aacr.org/page15991.aspx

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The AACR has contracted with Marathon Multimedia to provide their Call4Posters service to Annual Meeting presenters at a discount. Accepted poster presenters can use the Call4Posters application to create, format, and print their posters on a range of high-quality paper stocks. For an additional fee, presenters can have their poster shipped directly to the Annual Meeting and pick up their posters onsite beginning the day before the meeting. Accepted poster presenters will receive detailed information about the Call4Posters service in a separate e-mail in late February 2009.

Poster Session presenters at the AACR Annual Meeting must register for the full meeting at the rate appropriate to their membership status and obtain their own hotel accommodations. Registration and housing information are included below:

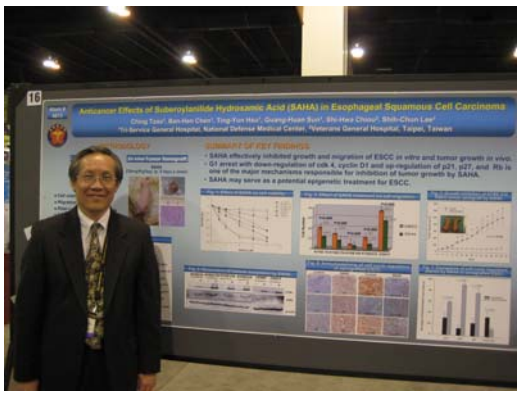
Advance Registration Deadline: March 10, 2009
Online Registration
http://www.aacr.org/home/scientists/meetings--workshops/aacr-100th-annual-meeting-2009/registration.aspx

Housing Deadline: March 11, 2009
Online Housing System
http://www.aacr.org/home/scientists/meetings--workshops/aacr-100th-annual-meeting-2009/accommodations.aspx

Online Travel Information and Reservation System
http://www.aacr.org/home/scientists/meetings--workshops/aacr-100th-annual-meeting-2009/travel.aspx

一、與 Professor Seto 合影

二、與 Professor Bhalla 合影



三、於海報前留影

四、與臺大李章銘醫師於會場合影

五、於科羅拉多大學癌症中心留影

六、與科羅拉多大學癌症中心主任 Prof. Byer 合影