

出國報告（出國類別：國際會議）

歐洲科學科技研究高階會議~  
天然物之化學生物與醫藥

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## 摘要 (200-300 字)

### **Tumor suppression and angiogenesis inhibition of protoilludane norsesquiterpenoid esters from *Armillaria mellea***

*Armillaria mellea* (Tricholomataceae) is a medicinal fungus symbiotic with Chinese medicinal herb “Tianma” (*Gastrodia elata* Blume). 17 compounds with the same sesquiterpenoid skeleton were isolated from mycelium of *Armillaria mellea*, among them, 7 compounds are novel. All 17 compounds were confirmed with anti-angiogenesis activity and strong cancer cell cytotoxic effect on human breast, lung and colon cancers, and leukemia. Among them, armillaridin showed potential effect on human non-small cell lung cancer. Armillaridin decreased the amounts of Cdk2, Cdk4, Cyclin D1 and Cyclin E that resulted in cell cycle arresting in G1 phase in H460 and A549 cells. It also induced apoptosis via activation of caspase 3 and 7 but not affected caspase 8 and 9. These effects might participate in cancer cell cytotoxicity of armillaridin. Besides, actin rearrangement and cytoskeleton alternation were visualized under confocal microscope after amillaridin treatment. Immunoblot assay revealed a suppression of Rho/cdc25-LIMK pathway by amillaridin. These results indicated that amillaridin disrupted actin rearrangement through inhibition of Rho/cdc25-LIMK pathway. Animal tests indicated that amillaridin dose-dependently inhibited *in vivo* angiogenesis and showed similar dose-dependent tumor regression in human H460 xenograft animals. Therefore, we anticipate to identify valuable leads from *Armillaria mellea* for development of new anticancer drug.

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### 一、目的:

由歐洲科學基金會(ESF)所舉辦的天然物化學及生物醫葯相關的研討會，由於各界學者的踴躍參與，今年已是第三屆舉辦這類的會議。藉由國際各國在天然物的相關化學及醫葯方面的專家齊聚一堂的機會，希望能擴展個人在中醫葯及天然物研究領域的國際觀，並將相關知識及技術帶回本所希望能有所貢獻。

### 二、參加會議經過

本次會議在義大利舉行，為期六天，來自世界各國等在天然物相關領域包括化學結構及生物活性方面的各界學者專家齊聚一堂，共同研討近年來以天然物發展所衍生出來之新葯的開發與應用。這已經是第三年由歐洲科學基金會舉辦天然物相關的國際會議，這個基金會贊助的會議每年都有固定的特色，同時舉辦的地點都選在同一地點舉辦，會議選在義大利南部的一個小鎮郊區 Acquafredda di maratea 舉辦，不少人連續參與該會議當作每年對天然物相關訊息的進修，這個會議的特色包括每天的大會演講之外，晚餐時間則安排與各界學者共進晚餐並藉機討論交換彼此經驗，持續三天的海報區互動討論讓大家可以仔細的討論所有的相關細節。由於義大利是熱衷足球的國家，在與會的第三天夜間十點大會特別從與會的壯丁中挑選一些稍具經驗的男士，臨時組成一對足球隊與當地小鎮的球隊進行一場聯誼賽，在第三天的下半年特別安排到附近的一個景點作參觀，同時有需要的參與學者該會也幫忙提供訂購回程火車票的服務。所有與會的學者態度都相當的和藹可親，整場會議就這樣成功的落幕。

在與會的機會中，與去年認識的主辦單位的委員會成員 Trond Vidar Hansen 教授討論去年一年的合作進度及未來的合作方式與文章投稿的細

節，由於研究的藥物結構是類似，因此去年對方即主動提出合作的需求，藉由他所合成的各種衍生物，配合個人在癌症及血管新生作用研究的專長，將對方寄來的一系列相關衍生物完成相關生物活性測試，目前已經在擬稿朝國際期刊投稿的目標前進，未來與這位教授的合作將繼續不會中斷，能在國際會議中找到跨國的合作議題實在事件令人振奮的事。

### 三、與會心得

The conference of “Natural Product” is routinely held for 3 times in Italy by ESF (European Science Foundation). Peoples from the whole world came to the same place to exchange information of chemistry, biology and medical activity of natural products. ESF provides a common platform for its Member Organisations in order to advance science research, explore new directions for research and facilitate cooperation and collaboration for science research since 1974. Through its activities, the ESF serves the needs of the European research community in a global context.

The conference, Natural products, Chemistry, Biology and Medicine, was held by ESF to make its efforts on research of natural products from plants, fungi, bacteria and marine products by isolation or synthesis. The issues of this conference included from chemistry to biology of natural product medicine development. The chairman professor Jef K. De Brabander is now one of the leaders in chemistry synthesis. The main topic includes isolation, structural elucidation, biology, total synthesis, chemical modification, and medicines of natural products. Understanding biological mechanisms will lead to more rapid and better-targeted discovery of clinically designed drugs. In these days of sustainability and environmental concern, chemistry assumes more crucial and demanding role than ever as the central science upon which society will rely of for solutions. The information provided me to learn more about not only properties of natural products but also their application on diseases evaluation for medicine development. Furthermore, many advanced techniques also demonstrated bioassay-based modifications on angiogenesis and cancer drugs development. I learned more and had a much clear picture of natural products properties and to design the anti-angiogenesis and anti-cancer drugs.

Since last year I attended this conference, I've got the opportunity to in cooperation with Professor Hansen. He provided me some compounds for anti-angiogenic approach and some promoter constructs and some technical model to help my research on angiogenesis and cancer. Actually, after one year research in angiogenesis inhibition assay and mechanism determination, the

manuscript is now writing for the compounds I've got since last year from Professor Hansen. I believe the manuscript will be sent out for revision for SCI journal within one month. The international cooperation still lasts up to now. I hope that someday maybe we have the opportunity to get the funding from ESF after such international team program activity.

The conference of Natural products, Chemistry, Biology and Medicine IV was announced and will be held on Sep 4-9, 2011.

### **Suggestions:**

The meeting is about natural products including chemistry, biology, total synthesis and application of medicine development. Base on the global research areas in our Institute, it's strongly suggests that other chemists and biologists can attend this meeting ("Natural Products IV" will be held on Sep 4-9, 2011) and in the future to seek for global cooperation. Besides, COST (European Cooperation in Science and Technology) was established to coordinate research activities since 1971. The funds provided by COST support the coordination costs of the research networks. More than 300 Institutions from non-COST countries now participate in COST action. Now, many countries in Asia including China, Japan, Hong-Kong and Korea *etc* participate in cooperation project with COST countries form the funding by ESF. I think this conference gives us the opportunity to have contact with COST members and raises programs for international cooperation.

### 四、帶回資料；

1. 會議摘要壹本
2. ESF (歐洲科學基金會) 舉辦之歷年會議及承辦業務簡介之光碟一片
3. About COST 2010 活動手冊一本

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