

出國報告（出國類別：開會）

第二十三屆歐洲顱顏面 外科年會與會心得報告

服務機關：臺北榮民總醫院

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摘要

歐洲顛顏面外科年會為世界二大顛顏面外科年會之一，另一則為國際口腔顎面外科會議。該會每二年舉辦一次，且顛顏面外科的濫觴源自歐洲，目前的一些經典顛顏面外科術式皆為歐洲大師發明，而且不斷推陳出新，是口腔顎面外科醫師每二年必參加的盛會。第二十三屆歐洲顛顏面外科年會今年於英國倫敦舉辦。臺灣的顛顎關節病變生物分子研究名列前茅，此次與會藉由 e-poster 與歐洲各國顛顏面外科醫師進行交流。除與歐洲各國顛顏面外科醫師進行交流外，學習顛顏面外科最新技術並導入臺灣，造福病患，且提升臺灣口腔顎面外科醫療水準。筆者二年前參加第二十二屆歐洲顛顏面外科年會，即將顛顎關節沖洗技術引進臺灣，臺北榮民總醫院成為全國施行顛顎關節沖洗術最多之醫療機構。本次會後預計引進最新顛顎關節內視鏡手術方式，配合即將採購之顛顎關節內視鏡手術組，為本院病患提供先進醫療服務。

關鍵字: 歐洲顛顏面外科年會

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一、 目的

歐洲顱顏面外科年會為世界第二大顱顏面外科年會之一，另一則為國際口腔顎面外科會議。該會每二年舉辦一次，且顱顏面外科的濫觴源自歐洲，目前的一些經典顱顏面外科術式皆為歐洲大師發明，而且不斷推陳出新，是口腔顎面外科醫師每二年必參加的盛會。第二十三屆歐洲顱顏面外科年會今年於英國倫敦舉辦。臺灣的顱顎關節病變生物分子研究名列前茅，此次與會藉由 e-poster 與歐洲各國顱顏面外科醫師進行交流。除與歐洲各國顱顏面外科醫師進行交流外，學習顱顏面外科最新技術並導入臺灣，造福病患，且提升臺灣口腔顎面外科醫療水準。

二、 過程

本次會議時間為 105 年 9 月 13 至 16 日。筆者早在二年前申請臺北榮民總醫院公費出國報告，榮幸獲得院方及高副院長（時任口腔醫學部主任）大力支持，即著手進行實驗進行及摘要寫作。本次提出之海報主題為「LINK PROTEIN AND MMP3 GENE EXPRESSION IN RAT CFA-INDUCED TMJ ARTHRITIS MODEL」（圖一），為筆者與國立陽明大學牙醫學院王鼎涵及楊牧蓁博士生在許明倫教授與高壽延教授指導下進行顱顎關節病變生物分子研究的實驗。主要目的在藉由非手術的方式來治療顱顎關節內的病變（如：OA 或 RA）。因為臺灣在顱顎關節病變生物分子研究於國際上享有盛名，此次與會藉由顱顎關節病變生物分子研究與歐洲顱顏面外科醫師交流。本次會議地點在英國倫敦舉行，由於臺灣直達之國航班機到達倫敦的時間均為夜間，筆者為首次至英國，惟恐人生地不熟，選擇於 9 月 12 日清晨搭乘國泰航空經香港轉機於當日下午三時許到達倫敦，抵達下榻飯店已近夜晚。9 月 13 日一早便前往位於西敏寺旁的伊利莎白二世會議中心（The Queen Elizabeth II Conference Center）參加會議。筆者一到達會場後即前往電子海報區確任本次投稿文章（圖二）。隨即參加自費課程（五十英磅）聆聽顱顎關節鏡手術大師奧地利 Professor Undt 對於現今顱顎關節鏡手術的新作法及想法，來驗證與筆者近年施行顱顎關節鏡手術之心得是否相異。當天直到下午四時前，分別前往三個演講會場聆聽相關議題。下午四時至五時，為 opening ceremony，除了介紹歷任理事長外，同時也安排了精彩的英國傳統的儀隊表演。與會的臺灣同好們也一起參與了這個莊嚴隆重的開幕式（圖三、四）！9 月 14 日至 9 月 16 日緊密的 oral presentation 令人目不暇給，恨不得能有分身聽遍所有報告。於 9 月 18 日搭機回台，於 9 月 19 日上午平安返抵國門。

三、心得

正如同二年前在捷克布拉格參加第二十二屆歐洲顱顏面外科年會完後一樣，對於歐洲顱顏外科的博大精深及日益求新的態度所感動。特別有感觸的一點是臺灣口腔顎面外科雖人數不及日韓，但發展國家特色、鼓勵多樣化及獎勵年輕一代走進世界舞台，卻是臺灣有立足之地所必須努力的。歐洲顱顏面外科今年的趨勢也朝向 computer aided surgery & virtual planning，針對此世界潮流，本院高壽延副院長已高瞻遠矚地規劃於二門診六樓設立顱顏面數位中心。另外組織工程、顱顎關節手術、手術缺損重建、藥物造成之顎骨壞死及睡眠呼吸中止症的治療等，在高副院長多年的經營下，臺北榮總口腔顎面外科都具備了國際級的水準！此次尚有一項重要任務，就是臺灣即將舉辦 2018 年的亞洲口腔顎面外科年會，高副院長為理事長，筆者則負責資訊方面，深感下列重點需要加強，尤其是環保減量，在此次歐洲年會上各是隨處可見。

1. 網頁

- 甲、 初發布時間：應至少在會議日期前一年半至二年即 announce.
- 乙、 更新時段 & 更新頻率：應每月或每二月更新。
- 丙、 Information inside：包含有效的資訊，頁面需簡潔
- 丁、 Optional package booking: registration (master classes, Gala dinner, etc.)、transportation, accommodation：提供來訪人員貼心的服務。
- 戊、

2. App for iOS (10 and below), Android：因應手機普及化，及減少紙本浪費

- 甲、 及時性：會議前應保持每週更新；會議期間應保持每小時更新。
- 乙、 個人化：可讓與會者先排定個人想要聽的課程，並可設定 alarm。
- 丙、 是否放入 abstract：應放入 oral presentation 及 poster 的 abstract，讓會員能預先得知演講內容。
- 丁、 Information inside：簡潔有效，操作上採用直覺

3. 報到處

- 甲、 自助報名：以 QR code 完成報名
- 乙、 名片材質：由於自助報名採列印名牌，可用自黏性貼紙，並列印餐卷等。

四、建議事項

由於報告人數眾多，每位 key note speaker 時間僅有 20 分鐘，實難領略其中的奧妙。最近二屆歐洲顱顏面外科年會於會期每天早上 7 點 30 分至 9 點均安排 Master classes，請各領域的大師就某一項手術分享他們的獨到之處，此類演講其實收穫較大。然而 Master class 每堂要另外收費 50 至 100 歐元（約新台幣 2000~4000 元），目前在院方所制定的額外支出方面並無明定，使得筆者常掙扎要不要花大錢學。茲建議院方能將屬於學術方面的非事前申請核備的支出，採實報實銷，讓補助能真正用在刀口上，用在提升接受補助學者之實力。

五、附圖

圖一

LINK PROTEIN AND MMP3 GENE EXPRESSION IN RAT CFA-INDUCED TMJ ARTHRITIS MODEL

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Aims:

Link protein is one of the components of extracellular matrix (ECM) which plays an important role to stabilize the interaction between aggrecan and hyaluronate to maintain the joint viscoelasticity. According to previous studies, link protein will be destroyed by matrix metalloproteinase 3 (MMP3) and resulting in the loss of the link protein in intervertebral disc (IVD) osteoarthritis. However, temporomandibular joint (TMJ) fibrocartilage composition is similar to IVD, but it still lack of information to discuss about the effect of link protein in TMJ arthritis animal model. Therefore, this study tried to clarify the correlation between link protein and inflammatory factors expression in rat TMJ arthritis.

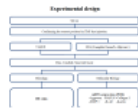
Methods: 12 Eight-week-old female Sprague-Dawley rats were divided randomly into 2 groups (n=6/group), experimental group was injected CFA that can mimic TMJ osteoarthritis at day 0. After CFA induced, experimental group was compared with control group and sacrificed at day 7. TMJ tissues were stained by H&E staining and examined *link protein* and *MMP3* gene expression by conventional PCR. *β-actin* as internal control. All data were presented as the Mean ± SD. Using Student's t test to analyze the data.

Result: In histological staining, the fibrocartilage tissue adapted to thickness in CFA group compared with control group. In gene expression, there were significant difference in *MMP3* (p<0.05) and increasing trend in *link protein* gene expression compared with control group.

Conclusions:

After 7 days CFA injection, CFA group appears higher *MMP3* gene and *link protein* gene expression compare than the control group. These results may provide some information to clarify the inflammation mechanism in TMJ arthritis.

Aim
To investigate the link protein and MMP3 gene expression in rat CFA induced TMJ arthritis model.



Materials and Methods:

In this study, we used 8 weeks old female Sprague-Dawley rats and divided randomly into 2 groups (control, and CFA). Rats only accepted one injection on day 0 and sacrificed on day 7. We collected one side of TMJ tissue to do the H&E stain. The other side was to investigate inflammatory (IL-1β and MMP3) gene expression in disc, condyle and synovial tissue by conventional PCR. *β-actin* as internal control. All data are presented as the mean ± SEM. Using one-way ANOVA and post-hoc test (Dunn's) to analyze the data.

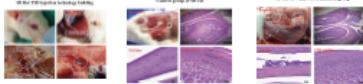


Fig1. SD Rat TMJ injection technology building. (A) Bright view and needle direction of rat TMJ injection technology. (B) To establish the TMJ arthritis model, we inject the dye into TMJ capsule to demonstrate the injected skill. After injection and cut of the temporal muscle, the dye distribution in the TMJ capsule could be observed. (C-D) After cleaning out the peripheral tissue show the TMJ anatomy position and the needle direction. The TMJ disc color is changed from white to blue and the glenoid fossa is not stained by any color.

Fig2. Control group of SD rat. (A) Bright view of SD rat. The anatomy structure could be observed easily in control group. (B) Sagittal section of rat TMJ. (C) Enlarge view of TMJ disc. Some of disc cells were distributed in the TMJ disc (black arrows). (D) Enlarge view of TMJ condyle. The subchondral bone of condyle could be divided into articular zone, proliferative zone, transition zone and hypertrophic zone.

Fig3. SD rat of 7 days CFA induced group. (A) Bright view of CFA-induced SD rat. There are granuloma formation in the injection site of CFA groups compared to control group. (B) Sagittal section of rat TMJ. The subchondral bone of CFA group present adaptive thickening in thickness during 7 days compare to the control group. (C) Enlarge view of TMJ disc. A few disc cells were distributed in the TMJ disc. (D) Enlarge view of TMJ condyle. The subchondral bone of condyle present adaptive thickening especially in transition zone.

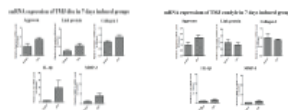


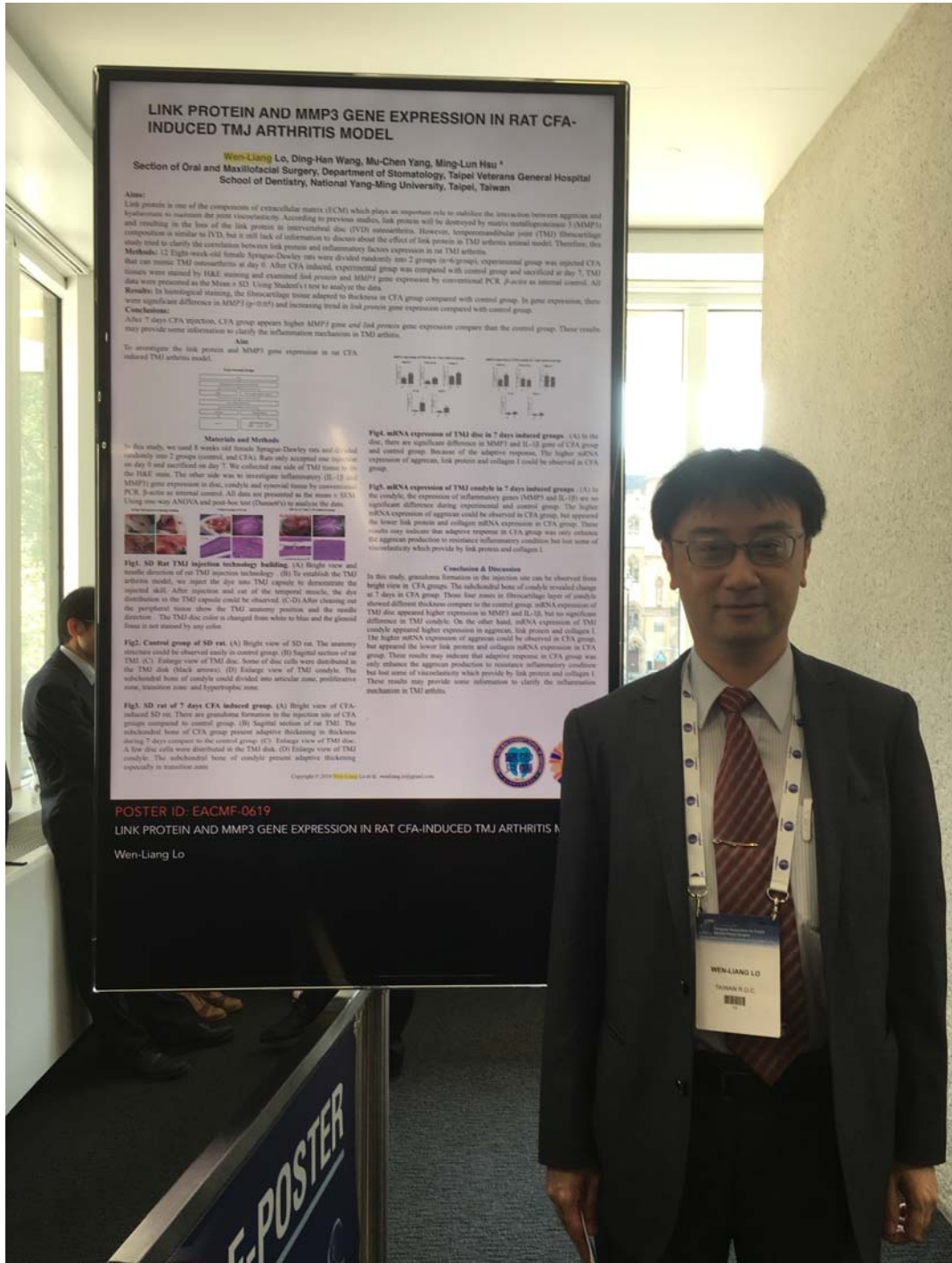
Fig4. mRNA expression of TMJ disc in 7 days induced groups. (A) In the disc, there are significant difference in *MMP3* and *IL-1β* gene of CFA group and control group. Because of the adaptive response, the higher mRNA expression of aggrecan, link protein and collagen I could be observed in CFA group.

Fig5. mRNA expression of TMJ condyle in 7 days induced groups. (A) In the condyle, the expression of inflammatory genes (*MMP3* and *IL-1β*) are no significant difference during experimental and control group. The higher mRNA expression of aggrecan could be observed in CFA group, but appeared the lower link protein and collagen mRNA expression in CFA group. These results may indicate that adaptive response in CFA group was only enhance the aggrecan production to resistance inflammatory condition but lost some of viscoelasticity which provide by link protein and collagen I.

Conclusion & Discussion

In this study, granuloma formation in the injection site can be observed from bright view in CFA groups. The subchondral bone of condyle revealed change at 7 days in CFA group. These four zones in fibrocartilage layer of condyle showed different thickness compare to the control group. mRNA expression of TMJ disc appeared higher expression in *MMP3* and *IL-1β*, but no significant difference in TMJ condyle. On the other hand, mRNA expression of TMJ condyle appeared higher expression in aggrecan, link protein and collagen I. The higher mRNA expression of aggrecan could be observed in CFA group, but appeared the lower link protein and collagen mRNA expression in CFA group. These results may indicate that adaptive response in CFA group was only enhance the aggrecan production to resistance inflammatory condition but lost some of viscoelasticity which provide by link protein and collagen I. These results may provide some information to clarify the inflammation mechanism in TMJ arthritis.





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Aims:
 Link protein is one of the components of extracellular matrix (ECM) which plays an important role to stabilize the interaction between aggrecan and hyaluronan to maintain the joint viscoelasticity. According to previous studies, link protein will be destroyed by matrix metalloproteinase 3 (MMP3) composition is similar to IV-D, but a still lack of information to discuss about the effect of link protein in TMJ arthritis animal model. Therefore, this study tried to clarify the correlation between link protein and inflammatory factors expression in rat TMJ arthritis.
Methods: 12 Eight-week-old female Sprague-Dawley rats were divided randomly into 2 groups (n=6/group), experimental group was injected CFA into one masticatory TMJ intra-articular at day 0. After CFA injection, experimental group was compared with control group and sacrificed at day 7. TMJ data were presented as the Mean ± SD. Using Student's t test to analyze the data.
Results: In histological staining, the fibrocytic tissue adapted to thickness in CFA group compared with control group. In gene expression, there were significant difference in MMP3 (p<0.05) and increasing trend in link protein gene expression compared with control group.
Conclusions:
 After 7 days CFA injection, CFA group appears higher MMP3 gene and link protein gene expression compare that the control group. These results may provide some information to clarify the inflammation mechanism in TMJ arthritis.
Key:
 To investigate the link protein and MMP3 gene expression in rat CFA-induced TMJ arthritis model.

Gene	Control Group	CFA Group
MMP3	~1.0	~2.5
Link Protein	~1.0	~1.5
Aggrecan	~1.0	~1.2
Collagen I	~1.0	~1.1

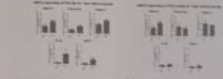


Fig. 1. mRNA expression of TMJ disc in 7 days induced groups. (A) In the disc, there are significant difference in MMP3 and Link protein gene expression in CFA group and control group. Because of the adaptive response, the higher mRNA expression of aggrecan, link protein and collagen I could be observed in CFA group.

Fig. 2. mRNA expression of TMJ condyle in 7 days induced groups. (A) In the condyle, the expression of inflammatory genes (MMP3 and IL-1β) are no significant difference during experimental and control group. The higher mRNA expression of aggrecan could be observed in CFA group, but appeared the lower link protein and collagen mRNA expression in CFA group. These results may indicate the adaptive response in CFA group was only enhance the aggrecan production to maintain inflammatory condition but lost some of viscoelasticity which provide by link protein and collagen I.

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Materials and Methods
 In this study, we used 8 weeks old female Sprague-Dawley rats and divided randomly into 2 groups (control, and CFA). Rats only accepted one injection on day 0 and sacrificed on day 7. We collected one side of TMJ tissue in the H&E stain. The other side was to investigate inflammatory (IL-1β and MMP3) gene expression in disc, condyle and synovial tissue by conventional PCR. In each animal control. All data are presented as the mean ± SEM. Using one-way ANOVA and post-hoc test (Duncan's) to analyze the data.

Fig. 1. SD Rat TMJ injection technology building. (A) Bright view and needle insertion of rat TMJ injection technology. (B) To establish the TMJ arthritis model, we inject the dye into TMJ capsule to demonstrate the injection skill. After injection and cut of the temporal muscle, the dye distribution in the TMJ capsule could be observed. (C-D) After cleaning the peripheral tissue, show the TMJ anatomy position and the needle direction. The TMJ disc color is changed from white to blue and the glanded form is not stained by any color.

Fig. 2. Control group of SD rat. (A) Bright view of SD rat. The anatomy structure could be observed easily in control group. (B) Sagittal section of rat TMJ. (C) Enlarge view of TMJ disc. Some of disc cells were distributed in the TMJ disk (black arrow). (D) Enlarge view of TMJ condyle. The subchondral bone of condyle could divided into articular zone, proliferation zone, transition zone and hypertrophic zone.

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 TAIWAN R.O.C.

圖三



圖四

