Oral presentation 3

時　間：113 年 12 月 14 日(星期六) 09：20-09：50

地　點：新竹喜來登大飯店 3 樓梅花桐花百合廳

座長/Moderator	臺中榮民總醫院 陳一銘醫師
09:20 - 10:32	**Pharmaceutical mechanism of taiwan chingguan yihau (NRICM101 清冠一號) on monocyte proliferation, inflammation, and phagocytosis in autoimmune patients** **探討清冠一號(NRICM-01)促單核球增生移行、影響吞噬作用的機轉及在自體免疫治療中的應用** Chih-Ying Changchien (張簡芝穎)[1], Yi-Hsuan Lin (林宜萱)[2], Chen Hsuan Hsu (許宸瑄)[2], Ying Chen (陳瀅)[2], Feng-Cheng Liu (劉峰誠)[1,*] [1] Division of Rheumatology, Immunology, and Allergy, Department of Internal Medicine, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan(三軍總醫院內科部風濕免疫科) [2] Department of Biology and Anatomy, National Defense Medical Center, Taipei, Taiwan (國防醫學院生物及解剖學科) *Corresponding authors: Feng-Cheng Liu, Division of Rheumatology, Immunology and Allergy, Department of Internal Medicine, Tri-Service General Hospital, National Defense Medical Center, Taipei 114, Taiwan. Email: lfc10399@yahoo.com.tw
10:32 - 10:35	Q & A
10:35 - 10:47	**Investigation of Immunomodulatory Effect of Umbilical Cord Mesenchymal Stem Cell Therapy on Systemic Lupus Erythematous Using a Murine Model** Chung-Mao Kao[1, 2], Ya-Hsuan Chao[3], Chi-Chien Lin[3*], Hsin-Hua Chen[1, 3, 4*] 高宗楸 [1, 2], 趙雅萱 [3], 林季千 [3*],陳信華 [1, 3, 4*] [1] Division of Allergy, Immunology, and Rheumatology, Department of Internal Medicine, Taichung Veterans General Hospital, Taichung, Taiwan. [2] Division of Translational Medicine, Department of Medical Research, Taichung Veterans General Hospital, Taichung, Taiwan. [3] Institute of Biomedical Science and Rong Hsing Research Center for Translational Medicine & Big Data Center, National Chung Hsing University, Taichung, Taiwan. [4] Division of General Internal Medicine, Department of Internal Medicine, Taichung Veterans General Hospital, Taichung, Taiwan. [1] 臺中榮民總醫院 內科部 過敏免疫風濕科 [2] 臺中榮民總醫院 醫學研究部 轉譯醫學研究科 [3] 國立中興大學 生命科學院 榮興轉譯醫學研究中心 [4] 臺中榮民總醫院 內科部 一般內科
10:47 - 10:50	Q & A

Pharmaceutical mechanism of taiwan chingguan yihau (NRICM101 清冠一號) on monocyte proliferation, inflammation, and phagocytosis in autoimmune patients
探討清冠一號(NRICM-01)促單核球增生移行、影響吞噬作用的機轉及在自體免疫治療中的應用

Chih-Ying Changchien (張簡芝穎)[1], Yi-Hsuan Lin (林宜萱)[2], Chen Hsuan Hsu (許宸瑄)[2], Ying Chen (陳瀅)[2], Feng-Cheng Liu (劉峰誠)[1,*]

[1] Division of Rheumatology, Immunology, and Allergy, Department of Internal Medicine, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan. (三軍總醫院內科部風濕免疫科)
[2] Department of Biology and Anatomy, National Defense Medical Center, Taipei, Taiwan (國防醫學院生物及解剖學科)
*Corresponding authors: Feng-Cheng Liu, Division of Rheumatology, Immunology and Allergy, Department of Internal Medicine, Tri-Service General Hospital, National Defense Medical Center, Taipei 114, Taiwan. Email: lfc10399@yahoo.com.tw

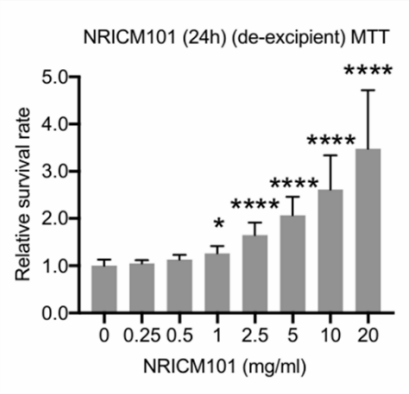
Abstract
Background: Taiwan Chingguan Yihau (NRICM101) and NRICM102 were developed by The Department of Traditional Chinese Medicine of the Ministry of Health and Welfare of Taiwan launched since 2020 to combat COVID-19 pandemic. The formula of NRICM contained mint, nepeta, mulberry leaf, parsnip, skullcap, Houttuynia cordata, northern isatis root, cogongrass, magnolia bark, and licorice that each ingredient was proved with anti-inflammatory properties. According to statics, patients with autoimmune diseases had an increased risk of COVID-19 and most of them received NRICM101 or NRICM102 as adjuvant therapy. However, the cellular effect of NRICM-01 and NRICM-02 on autoimmune disease remained obscure.

Materials: Human THP-1 cells were applied to investigate pharmaceutical effect of NRICM-01 and NRICM-02, including cell proliferation, migration, ROS production and phagocytosis. Serum obtained from patients with rheumatoid arthritis and SLE were incubated with THP-1 cells and NRICM, respectively to evaluate their anti-inflammatory strength in autoimmune disease.

Results: Both NRICM-01 and NRICM-02 significantly promoted monocyte proliferation with dose-dependent manner from 1mg/mL to 20mg/mL. NRICM-01 also increased ROS production in THP-1 cells with increased p-p65 expression, but HIF-1α downregulation. Increased monocyte migration capacity was observed in NRICM-treated group with increased integrins expression. Under NRICM-1 stimulation, THP-1 showed increased E-coli phagocytosis with p-JNK involvement. NRICM-01 stimulated THP-1 gain-in function were preserved when co-incubating serum derived from RA and SLE patients.

Conclusions:
Current bedside-to-bench studies aimed to elucidate underlying effect of NRICM-01 and NRICM-02 on autoimmune disease patients with monocytes proliferation and phagocytosis. Since taiwan chingguan yihau (清冠一號) exhibited beneficial effects on monocytes function, future application of NRICM-01 might extende to salvage autoimmune disease patient with immunocompromised status.
Keyword:, taiwan chingguan yihau (NRICM101 清冠一號), monocyte, rheumatoid arthritis, SLE, phagocytosis

A


NRICM101 (24h) (de-excipient) MTT
Relative survival rate
5.0
4.0
3.0
2.0
1.0
0.0
0 0.25 0.5 1 2.5 5 10 20
NRICM101 (mg/ml)
*
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****
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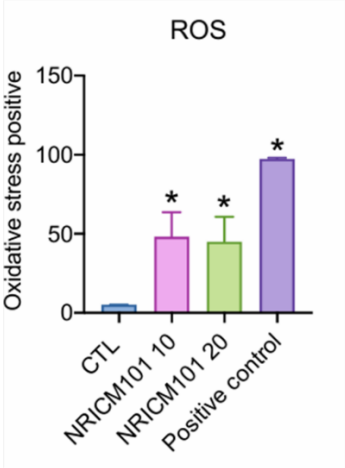
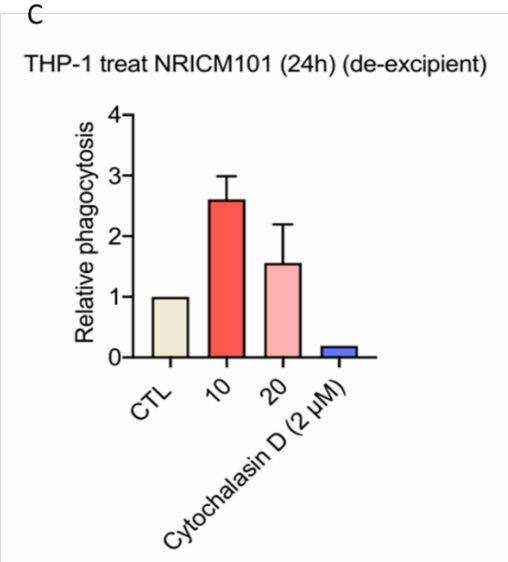
B


ROS
Oxidative stress positive
150
100
50
0
CTL
NRICM101 10
NRICM101 20
Positive control
*
*
*

C


THP-1 treat NRICM101 (24h) (de-excipient)
Relative phagocytosis
4
3
2
1
0
CTL
10
20
Cytochalasin D (2 μM)

Investigation of Immunomodulatory Effect of Umbilical Cord Mesenchymal Stem Cell Therapy on Systemic Lupus Erythematous Using a Murine Model

Chung-Mao Kao[1, 2], Ya-Hsuan Chao[3], Chi-Chien Lin[3*], Hsin-Hua Chen[1, 3, 4*]
高宗楸 [1, 2], 趙雅萱 [3], 林季千 [3*],陳信華 [1, 3, 4*]

[1] Division of Allergy, Immunology, and Rheumatology, Department of Internal Medicine, Taichung Veterans General Hospital, Taichung, Taiwan.
[2] Division of Translational Medicine, Department of Medical Research, Taichung Veterans General Hospital, Taichung, Taiwan.
[3] Institute of Biomedical Science and Rong Hsing Research Center for Translational Medicine & Big Data Center, National Chung Hsing University, Taichung, Taiwan.
[4] Division of General Internal Medicine, Department of Internal Medicine, Taichung Veterans General Hospital, Taichung, Taiwan.
[1] 臺中榮民總醫院 內科部 過敏免疫風濕科
[2] 臺中榮民總醫院 醫學研究部 轉譯醫學研究科
[3] 國立中興大學 生命科學院 榮興轉譯醫學研究中心
[4] 臺中榮民總醫院 內科部 一般內科

Abstract

Background: Systemic lupus erythematosus (SLE) is a chronic multi-systemic autoimmune disease, with many patients complicated with refractory lupus nephritis. Despite emerging approved therapies, currently available management exhibits limited effects for many patients who remain persistently active and corticosteroid-dependent, highlighting the need for efficacious immunomodulatory therapies. Allogeneic human umbilical cord mesenchymal stem cells (UC-MSCs) have been demonstrated satisfactory safety profiles, clinical remission rates and 5-year survival rates for refractory SLE patients in prior studies.

Methods: Female 8-week-old Balb/c mice were intraperitoneally administered 0.5ml of pristane or PBS for induction. After one month, mice showing significantly higher urine protein levels compared with control group were selected for further therapeutic experiments, acting as the murine model mimicking SLE. They then received one dose of intravenous allogeneic human UC-MSCs (1×10^6 cells/dose), manufactured by BIONET Therapeutics Corporation, via tail vein. The mice were sacrificed at 26 weeks (with urine protein tested every 2-4 weeks during this period), and blood, spleen, and kidneys were collected.

Results: In successfully induced SLE mice, UC-MSC therapy significantly reduced serum anti-dsDNA levels in SLE mice from 7 weeks after administration. It didn't impact blood urea nitrogen (BUN) levels, indicating no significant adverse effects on renal function (Figure 1). UC-MSCs therapy significantly reduced percentages of Treg and Th17 cells, signifying an immunomodulatory effect on T cell responses (Figure 2).

Conclusion: This study underscores the therapeutic potential of UC-MSC therapy in treating refractory SLE and provides a foundation for future human clinical trials. Pathological changes in murine kidneys will be analyzed.

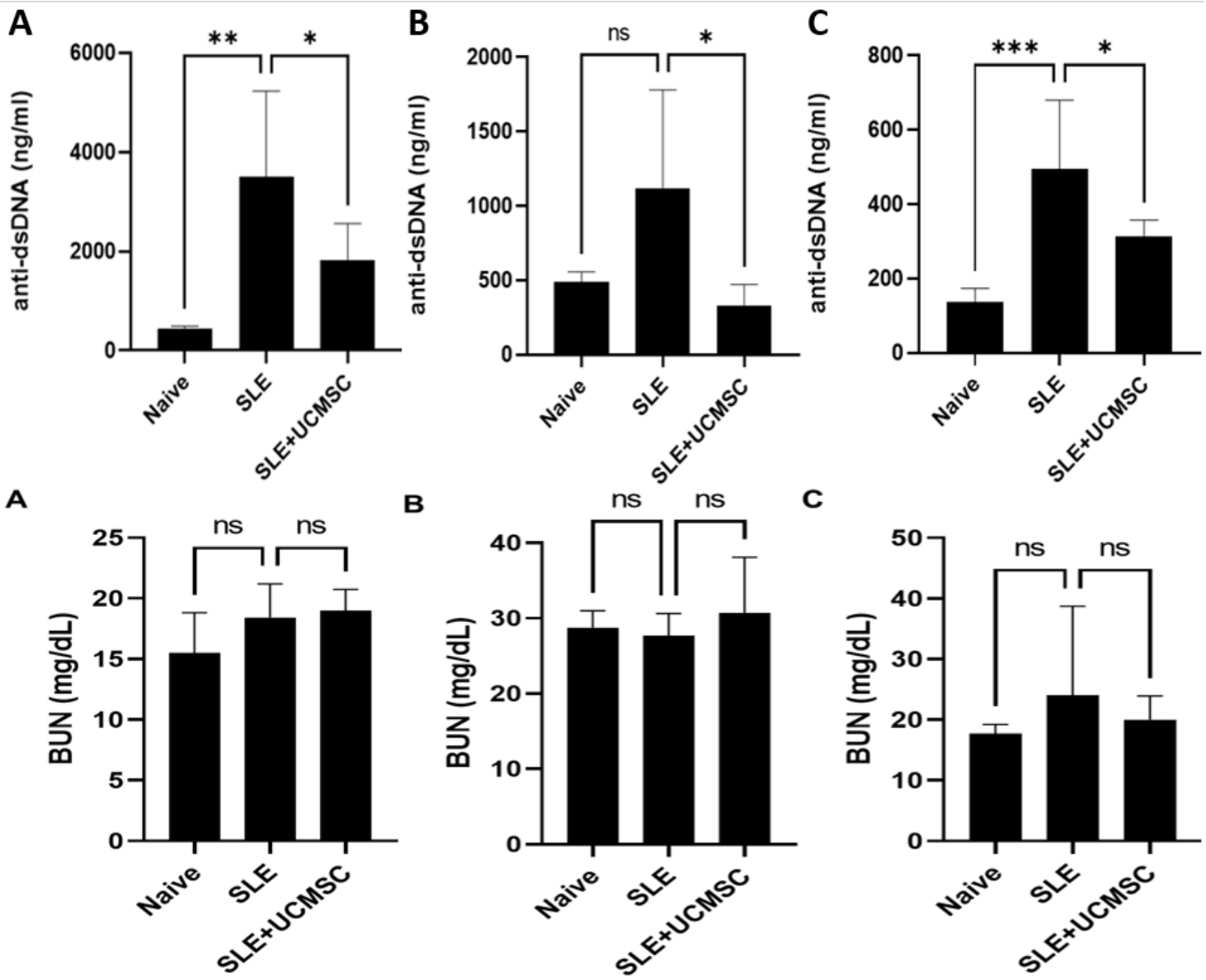


Figure 1. Serum anti-dsDNA levels and BUN levels were collected from SLE mice treated with UC-MSCs at (A) 7 weeks, (B) 15 weeks, and (C) 26 weeks. Data are expressed as mean ± standard deviation (SD), with the SLE group as the control group. One-way ANOVA statistical analysis was performed using GraphPad Prism 9.0, and the results are indicated with * representing statistical significance (*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$).

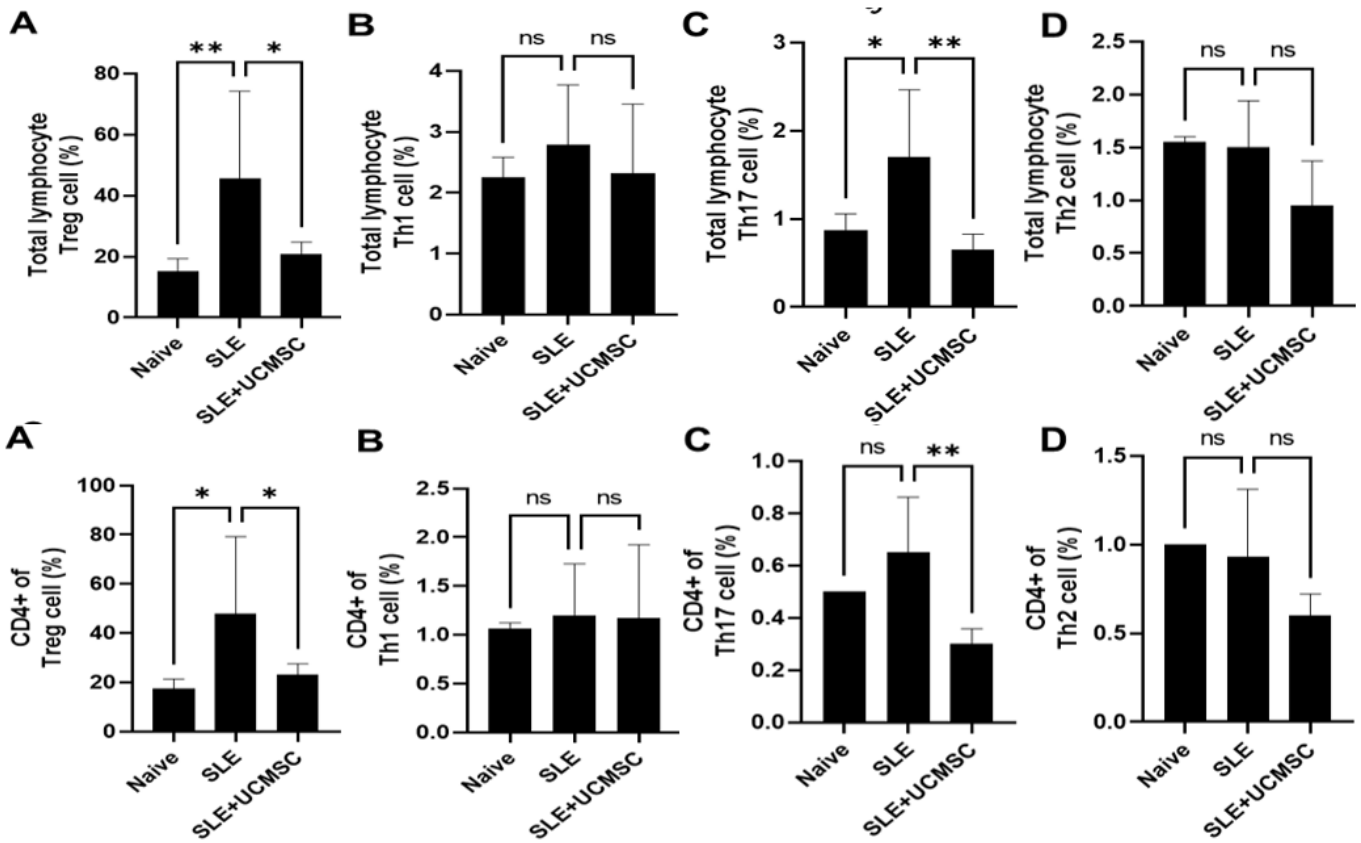


Figure 2. The expression levels of T cells and CD4+ T cells in spleen cells were analyzed after 26 weeks of UC-MSC treatment in SLE mice. (A) Treg, (B) Th1, (C) Th17, and (D) Th2 cells. Data are expressed as mean ± standard deviation (SD), with the SLE group as the control group. One-way ANOVA statistical analysis was performed using GraphPad Prism 9.0, and the results are indicated with * representing statistical significance (*$p < 0.05$, **$p < 0.01$).