

行政院國家科學委員會專題研究計畫 成果報告

T help1 細胞與 T help2 細胞及其分化過程與急性移植物對
抗宿主疾病之相關性研究

計畫類別：個別型計畫

計畫編號：NSC92-2314-B-039-004-

執行期間：92年08月01日至93年07月31日

執行單位：中國醫藥大學中醫學系

計畫主持人：葉士芃

共同主持人：邱昌芳

報告類型：精簡報告

報告附件：出席國際會議研究心得報告及發表論文

處理方式：本計畫可公開查詢

中 華 民 國 93 年 11 月 16 日

專題研究計畫成果報告繳交

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This study is still ongoing although the support was discontinued in 2004. We continue to enroll patients receiving allogeneic transplantation to this study in this year. The initial result of this study showed that the pos-transplant serum level of T helper2-cytokine, the interleukin-10, correlate well with the clinical activity of chronic graft-versus-host disease (GVHD). I submitted this result to the American Society of Hematology (ASH) and was selected to present at the 2004 annual meeting, which will be hold in this December at San Diego. Attached are the acceptance letter and the abstract to be presented, which will also be published at "Blood" journal. Despite the initial success, I will further study on the T cell subpopulation (TH1/TH2) before / during / after the onset of GVHD after collecting more specimens. I believe this novel study & possibly the novel results will be of great interest to most of the hematologists engaged in hematopoietic stem cell transplantation. I will also continue to submit the study result to Journals in this field for consideration of publication. Of course, I will also submit all the new information of this study to NSC.

Su-Peng Yeh

Division of Hematology and Oncology / Stem Cell Research Lab.
Department of Internal Medicine and Medical Research
China Medical University Hospital
China Medical University

葉士芃 中國醫藥大學附設醫院

Oct. 30, 2004

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46th ASH Annual Meeting

Department/Institution: Internal Medicine, China Medical University Hospital

Address: 2 Yu-Der Road, Taichung, 404, Taiwan

Phone: 886-4-22052121-1513 **Fax:** 886-4-22052121-1511

E-mail: d6771@www.cmuh.org.tw

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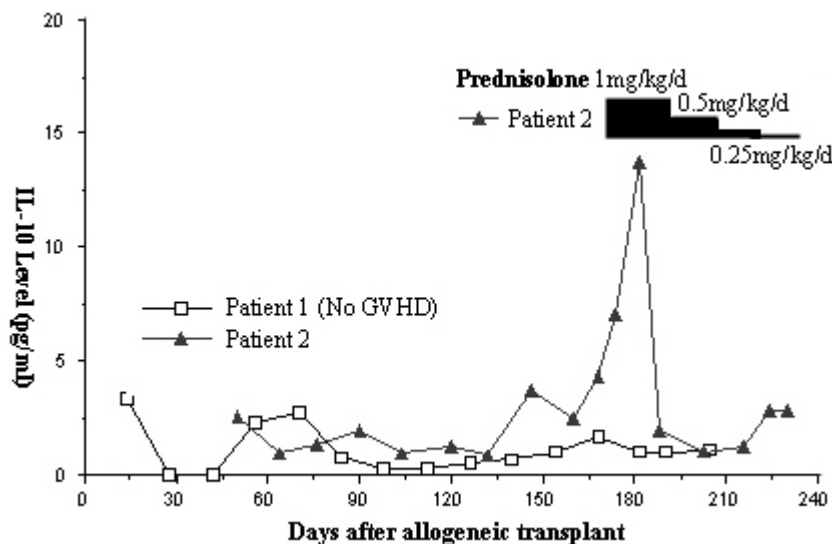
IL-10; Chronic graft-versus-host; Th1/Th2

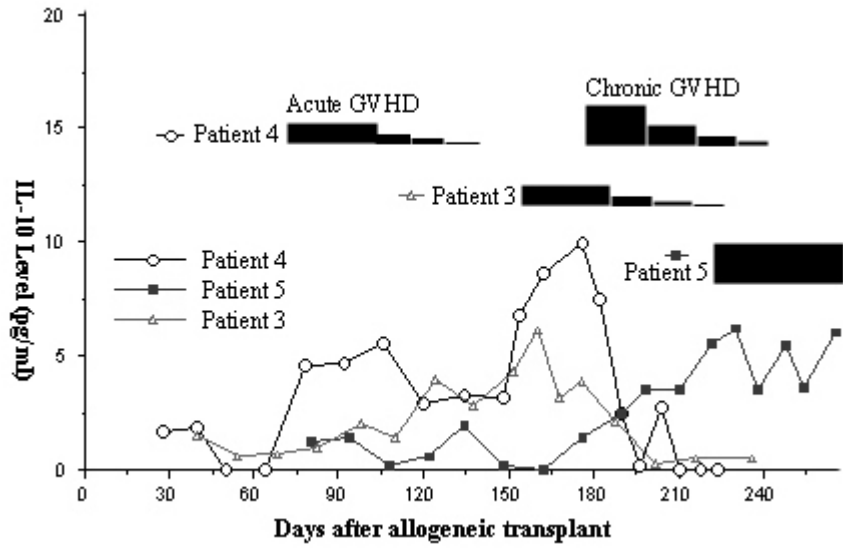
Title: Serum Level of Interleukin-10 Correlates Well With The Activity of Chronic Graft-Versus-Host Disease & The Responsiveness To Corticosteroid Treatment

Su-Peng Yeh, MD^{1,2*}, Chang-Fang Chiu, MD, PhD^{1*}, Yu-Min Liao, MD^{1*}, Wen-Jyi Lo^{2*}, Yu-Ching Liaw^{2*}, Chiao-Lin Lin^{2*}, Jan-Gowth Chang, MD^{2*} and Chung-Tsen Hsueh, MD, PhD³. ¹ Internal Medicine, China Medical University Hospital, Taichung, Taiwan, 404; ² Medical Research, China Medical University Hospital, Taichung, Taiwan, 404 and ³ Internal Medicine, University of Kansas Medical Center, Kansas City, Kansas, United States, 66160-7353.

Current evidence suggest the interaction between subset of T cells, the T help1 (Th1) and T help2 (Th2), plays an important role in the pathogenesis of GVHD. Cytokines, either produced by Th1/Th2 or other cells, are important regulators in the whole process and will define the polarization of Th1 or Th2 from naïve T cell. In this study, we used ELISA (R&D, Minneapolis, MN, US) to monitor the serum level of Interleukin-4 (IL-4), IL-10, IL-12, and interferon- γ (INF- γ) in patients receiving allogeneic transplant **weekly** from day 0 to at least day 200. From Jan. 2003, consecutive 20 patients were enrolled. The GVHD prophylaxis consisted of Cyclosporine-A and short course Methotrexate. Of the 20 patients, 2 had grade 3/4 acute GVHD (GVHD) (15.1%) and 1 had grade 3/4 chronic GVHD (CGVHD) (5.0%). The serum level of IL-4 and IL-10

(aGVHD) and 7 had extensive chronic GVHD (cGVHD). The serum levels of IL-4 and IL-12 were below the detectable level (0.13pg/ml and 0.5pg/ml respectively) in most occasions, even during the period of GVHD. Nevertheless, the serum level of IL-10 correlated well with the activity of cGVHD and we used data gathered from 5 patients to demonstrate this good correlation in figure 1 and 2. Patient 1 (open square, figure 1) had no GVHD and the IL-10 levels were below 5pg/ml during the whole period of follow-up. Patient 2 (solid triangle, figure 1) and 3 (open triangle, figure 2) had de novo cGVHD. The IL-10 level increased gradually when cGVHD developed, however, both clinical manifestations of cGVHD and serum IL-10 level decreased rapidly after the administration of Prednisolone (black bar on figure 1 and 2, with the thickness indicating the relative dosage of Prednisolone). Patient 4 (open circle, figure 2) had grade 2 aGVHD that resolved quickly after Prednisolone treatment. However, IL-10 level increased gradually after discontinuing Prednisolone and cGVHD developed subsequently. After adding Prednisolone again, cGVHD improved and IL-10 decreased to undetectable level rapidly. Patient 5 (solid square, figure 2) had steroid-refractory cGVHD. The IL-10 level kept above 5pg/ml for more than 1 month despite Prednisolone 1mg/kg/day giving at the same time and the patient eventually needed further salvage treatment (thalidomide). The serum INF- γ were undetectable in most occasions. It became detectable during period of cGVHD in patients 3, 4 and 5 but not patient 2. **In conclusion**, post-transplant serum IL-10 level correlates well with the clinical activity of cGVHD as well as the responsiveness to corticosteroid treatment. This novel finding will allow the functional evaluation of individuals' immune system after allogeneic transplant and should give insight for the adjustment of immunosuppression necessary for cGVHD control.





Certification for Human Subjects: I certify that this study abides by the rules of the appropriate internal review board and the tenets of the Helsinki protocol, if human subjects were involved.

Signature of Presenting Author:

Su-Peng Yeh



THE AMERICAN SOCIETY OF HEMATOLOGY

900 M Street, NW, Suite 200 Washington, DC 20036 ph: 202.770.0944 fax: 202.770.0545 e-mail: ASH@hematology.org

Friday, September 24, 2004

Dear Dr. Yeh:

RE: Publication Number: 1647

TITLE: Serum Level of Interleukin-10 Correlates Well with the Activity of Chronic Graft-Versus-Host Disease and the Responsiveness to Corticosteroid Treatment.

We are happy to inform you that the Program Committee has selected your abstract for poster presentation at the 2004 Annual Meeting of the American Society of Hematology as detailed below:

Session Name: Relapse, Immune Responses, and Immunotherapy after Transplantation

Date: Saturday, 12/4/2004

Presentation Time: 6:00 PM- 7:30 PM

Room: Halls D and E

Poster Board #: 801

See our Web site (www.hematology.org/meeting/abstracts.cfm) for poster instructions, including set-up, viewing, and dismantling times. In addition, learn more about ASH's poster preparation service, which gives poster presenters a convenient and inexpensive way to create posters online and have them attractively printed and shipped directly to the annual meeting.

Please plan to mount your materials on your assigned board at least one hour prior to your viewing time on the day of your scheduled presentation. It is very important that you and/or your co-authors be present at your poster throughout the presentation time listed above and be prepared to talk about your research and answer questions from attendees. Immediately after the presentation, you should dismantle your poster.

Please note that the deadline for pre-registration is November 3, 2004. After this date, on-site registration is available. Contact the ASH Meetings Department at 202-776-0544 or visit our Web site (www.hematology.org/meeting/2004/attendee/registration.cfm) if you need additional housing and registration information.

If you are not currently a member of ASH and are interested in joining the Society, please visit the ASH Web site (www.hematology.org/membership) for information about the benefits of membership and the appropriate application form, or e-mail ASH headquarters at ash@hematology.org.

Congratulations on having your abstract selected for the 2004 ASH Annual Meeting Program!

The American Society of Hematology

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2004

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Darryl L. Silliman, MD
Stanford University School of Medicine
CCPR, Room 1100
Stanford, CA 94305-5080
ph: 650.723.0500
fax: 650.723.0274
sills@leland.stanford.edu

President-Elect

David H. George, MD
University of Oklahoma Health Sciences Center
1500 N. East Drive, Room 20271
Oklahoma City, OK 73104
ph: 405.271.4200
fax: 405.271.4249
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Paul T. Pex, Jr, D
Long Beach Coastal Medical Center
Newport Beach, CA 92660
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fax: 714.435.2160
pex@lbc.com

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Nancy DeWitt, MD
New England Medical Center
Department of Hematology, MMSB422
300 Brookline Street
New Haven, CT 06510
ph: 203.785.4144
fax: 203.785.7330
nedewitt@yale.edu

Treasurer

J. Earl Smith, MD, PhD
Washington University School of Medicine
660 South Euclid Avenue, Box 8102
St. Louis, MO 63110-1002
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esmith@wustl.edu

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Editor-in-Chief

Stephen J. Scher, MD
The Scripps Research Institute
13200 La Jolla Village Road, MS D
La Jolla, CA 92037
ph: 858.754.7140
fax: 858.754.7410
scher@scripps.edu

Executive Director

William J. Leggett, PhD
The American Society of Hematology
1400 M Street, NW, Suite 200
Washington, DC 20036
ph: 202.776.0544
fax: 202.776.0540
leggett@hematology.org