18 MAY 2016

MEMORANDUM FOR ST
ATTN: SANDRA VALTIER

FROM: 59 MDW/SGVU

SUBJECT: Professional Presentation Approval

1. Your paper, entitled Correlation between SNPs in Interleukin and Cannabinoid Receptor Genes and Type 2 Diabetes Mellitus in the Military presented at/published to 2016 Military Health System Research Symposium (MHSRS), Kissimmee, FL August 2016 with MDWI 41-108, and has been assigned local file #16198.

2. Pertinent biographic information (name of author(s), title, etc.) has been entered into our computer file. Please advise us (by phone or mail) that your presentation was given. At that time, we will need the date (month, day and year) along with the location of your presentation. It is important to update this information so that we can provide quality support for you, your department, and the Medical Center commander. This information is used to document the scholarly activities of our professional staff and students, which is an essential component of Wilford Hall Ambulatory Surgical Center (WHASC) internship and residency programs.

3. Please know that if you are a Graduate Health Sciences Education student and your department has told you they cannot fund your publication, the 59th Clinical Research Division may pay for your basic journal publishing charges (to include costs for tables and black and white photos). We cannot pay for reprints. If you are 59 MDW staff member, we can forward your request for funds to the designated wing POC.

4. Congratulations, and thank you for your efforts and time. Your contributions are vital to the medical mission. We look forward to assisting you in your future publication/presentation efforts.

LINDA STEEL-GOODWIN, Col, USAF, BSC
Director, Clinical Investigations & Research Support

Warrior Medics – Mission Ready – Patient Focused
INSTRUCTIONS

USE ONLY THE MOST CURRENT 59 MDW FORM 3039 LOCATED ON AF E-PUBLISHING

1. The author must complete page two of this form:
   a. In Section 2, add the funding source for your study [e.g., 59 MDW CRD Graduate Health Sciences Education (GHSE) (SG5 O&M); SG5 R&D; Tri-Service Nursing Research Program (TSNRP); Defense Medical Research & Development Program (DMRP); NIH; Congressionally Directed Medical Research Program (CDMRP); Grants; etc.]
   b. In Section 2, there may be funding available for journal costs, if your department is not paying for figures, tables or photographs for your publication. Please state "YES" or "NO" in Section 2 of the form, if you need publication funding support.

2. Print your name, rank/grade, sign and date the form in the author's signature block or use an electronic signature.

3. Attach a copy of the 59 MDW IRB or IACUC approval letter for the research related study. If this is a technical publication/presentation, state the type (e.g. case report. OA/QI study, program evaluation study, informational report/briefing, etc.) in the "Protocol Title" box.

4. Attach a copy of your abstract, paper, poster and other supporting documentation.

5. Save and forward, via email, the processing form and all supporting documentation to your unit commander, program director or immediate supervisor for review/approval.

6. On page 2, have either your unit commander, program director or immediate supervisor:
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7. Submit your completed form and all supporting documentation to the CRD for processing (59crdpubsres@us.af.mil). If you have any questions or concerns, please contact the 59 CRD/ Publications and Presentations Section at 292-7141 for assistance.

8. The 59 CRD/Publications and Presentations Section will route the request form to clinical investigations, 502 ISG/JAC (Ethics Review) and Public Affairs (59 MDW/PA) for review and then forward you a final letter of approval or disapproval.

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NOTE: All abstracts, papers, posters, etc., should contain the following disclaimer statement:
"The views expressed are those of the [author(s)] [presenter(s)] and do not reflect the official views or policy of the Department of Defense or its Components"

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"The voluntary, fully informed consent of the subjects used in this research was obtained as required by 32 CFR 219 and DODI 3216.02_AFI 40-402."

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"The experiments reported herein were conducted according to the principles set forth in the National Institute of Health Publication No. 86-23, Guide for the Care and Use of Laboratory Animals and the Animal Welfare Act of 1966, as amended."
PROCESSING OF PROFESSIONAL MEDICAL RESEARCH/TECHNICAL PUBLICATIONS/PRESENTATIONS

1. TO: CLINICAL RESEARCH
   (Author's Name, Rank, Grade, Office Symbol)
   Sandra Valtier/ GS13/ ST

2. FROM: (Author's Name, Rank, Grade, Office Symbol)
   (Author's Name, Rank, Grade, Office Symbol)
   (Author's Name, Rank, Grade, Office Symbol)

3. GME/GHSE STUDENT: [ ] YES [ ] NO
   FWH20150054N

4. PROTOCOL NUMBER:

5. PROTOCOL TITLE: (NOTE: For each new release of medical research or technical information as a publication/presentation, a new 59 MDW Form 3039 must be submitted for review and approval.)
   Pharmacogenomic Risk Profile Application in a Clinical Setting

6. TITLE OF MATERIAL TO BE PUBLISHED OR PRESENTED:
   Correlation between SNPs in Interleukin and Cannabinoid Receptor Genes and Type 2 Diabetes Mellitus in the Military

7. FUNDING RECEIVED FOR THIS STUDY: [ ] YES [ ] NO
   FUNDING SOURCE: AFMS

8. DO YOU NEED FUNDING SUPPORT FOR PUBLICATION PURPOSES: [ ] YES [ ] NO

9. IS THIS MATERIAL CLASSIFIED? [ ] YES [ ] NO

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    2016 Military Health System Research Symposium (MHSRS), Kissimmee, FL August 2016

    [ ] 11d. PLATFORM PRESENTATION (At civilian institutions: name of meeting, state, and date of meeting.)

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13. 59 MDW PRIMARY POINT OF CONTACT (Last Name, First Name, M.I., email)
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14. DUTY PHONE/PAGER NUMBER
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15. AUTHORSHIP AND CO-AUTHOR(S) List in the order they will appear in the manuscript.

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   d. Sandra Valtier                | GS13        | CAMD/ST                     |                         |
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   f.                              |             |                             |                         |

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16. AUTHOR'S PRINTED NAME, RANK, GRADE
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18. DATE
   May 05, 2016

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21. DATE
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<tr>
<td>23. ASSIGNED PROCESSING REQUEST FILE NUMBER</td>
<td>16198</td>
</tr>
<tr>
<td>24. DATE REVIEWED</td>
<td>10 May 2016</td>
</tr>
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The author added the DoD disclaimer statement. The article is approved.

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| 38. DATE FORWARDED TO 59 MDW/SGVU | May 17, 2016 |
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Correlation between SNPs in Interleukin and Cannabinoid Receptor Genes and Type 2 Diabetes Mellitus in the Military

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Center for Advanced Molecular Detection, Science and Technology, 59 Medical Wing, US Air Force, JBSA-Lackland, San Antonio, Texas

**Background:** Type 2 diabetes mellitus (T2DM) is a prevalent metabolic disorder in the military population, as in the general population. The main diagnostic index of the condition is hyperglycemia of varying degrees. Pathologic consequences of hyperglycemia are many, and they develop at various stages during the course of the condition. Among them are atherosclerosis, glaucoma, nephropathy, and neuropathy. Certain genetic variations and environmental factors strongly influence the onset and severity of T2DM. Likewise, certain habits of lifestyle, notably poor eating and lack of physical activity, are critical players in onset and severity of the disease. Among the genetic variations that determine susceptibility to T2DM are single nucleotide polymorphisms (SNPs). Indeed the pathologic role of SNPs has emerged as a major focus of the genetics of disease. Thus, a number of SNPs that associate with T2DM or its consequent pathologies have already been identified. This work focused on analyzing 18 SNPs that have been associated with T2DM or one or more of its consequent pathologies. These SNPs occur in 9 genes: IL-1 alpha, IL-1 beta, IL-4, IL-6, IL-10, IL-18, CNR1, CNR2, and FAAH. The population studied represented active duty military personnel, veterans, or their families at the 59 Medical Wing, JBSA-Lackland.

**Methods:** A repository of genomic DNA isolated from patient blood samples, archived at the Center for Advanced Molecular Detection, 59 Medical Wing, was utilized for this study. The samples were from T2DM patients, as well as healthy individuals (controls). Of the total 866 samples, 613 were diabetes samples and 253 control. SNPs were detected by real-time PCR (TaqMan SNP genotyping assays).

**Results:** Based on 90 control and 263 diabetes samples, logistic regression analysis (95% confidence limit) revealed that two SNPs in CNR2 gene show strong correlation with T2DM. One is the single nucleotide missense variation designated rs2229579 (C/C homozygous; His316; p-value = 0.00134; odds ratio = 1.880). The other is the tandem dinucleotide variation rs35761398 (GG/GG homozygous; Arg63; p-value = 0.00884; odds ratio = 2.414). The FAAH SNP rs324420 also showed correlation with T2DM (C/C homozygous; Pro129; p-value = 0.0464; odds ratio = 1.665).

**Conclusions:** The identification of T2DM genetic markers is essential to predicting future risk and preventing the development of complex pathologies that are a significant cost to military health care. We identified three SNPs that show a positive correlation with T2DM in the subject population for this study. Two of these SNPs are in the CNR2 gene, which is largely expressed in immune system cells and is part of the inflammatory response. Further analysis of the SNP genotypes is in progress.

Opinions of the authors do not reflect the official policy of the US Government, Department of Defense, or the Department of the Air Force.