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TITLE: Phospholipids as Biomarkers for Excessive Alcohol Use

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14. ABSTRACT Our proposal is to determine the diagnostic utility of sphingomyelin (SM) and lysophosphatidylcholine (LPC) as the potential biomarkers to screen for excessive alcohol use (EAU); a rising epidemic reported to be as high as 40% among returning veterans. Drinking becomes excessive when it causes or elevates the risk for alcohol-related problems or complicates the management of other health problems. According to the NIH/NIAAA, excessive drinking is defined as men who drink more than 4 standard drinks in a day (or more than 14 per week) and women who drink more than 3 drinks in a day (or more than 7 per week). Non-civilian military personnel have been deployed in support of the war efforts in Afghanistan (Operation Enduring Freedom, OEF) and Iraq (Operation Iraqi Freedom, OIF) since September 11, 2001. These sustained combat operations have resulted in military personnel experiencing physical threat or actual injury during the deployment and difficult adjustments during post-deployment period. Negative life stress is a major contributor to the onset and exacerbation of EAU. The prevalence of EAU is alarming, and the vigilance and action to identify veterans with EAU is of importance. The consequences of under-detection of EAU, thus delayed intervention are serious because relative risk of alcohol-related health conditions such as cirrhosis, pancreatitis, and hepatocellular carcinoma, is increased with the amounts and duration of alcohol consumed per day. We hypothesize that alcohol consumption elevates a panel of serum phospholipids (sphingomyelin, and lysophosphatidylcholines) in proportion to the level of consumption in the past month.					
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INTRODUCTION:

Our proposal is to determine the diagnostic utility of sphingomyelin (SM) and lysophosphatidylcholine (LPC) as the potential biomarkers to screen for excessive alcohol use (EAU); a rising epidemic reported to be as high as 40% among returning veterans. Drinking becomes excessive when it causes or elevates the risk for alcohol-related problems or complicates the management of other health problems. According to the NIH/NIAAA, excessive drinking is defined as men who drink more than 4 standard drinks in a day (or more than 14 per week) and women who drink more than 3 drinks in a day (or more than 7 per week). Non-civilian military personnel have been deployed in support of the war efforts in Afghanistan (Operation Enduring Freedom, OEF) and Iraq (Operation Iraqi Freedom, OIF) since September 11, 2001. These sustained combat operations have resulted in military personnel experiencing physical threat or actual injury during the deployment and difficult adjustments during post-deployment period. Negative life stress is a major contributor to the onset and exacerbation of EAU. The prevalence of EAU is alarming, and the vigilance and action to identify veterans with EAU is of importance. The consequences of under-detection of EAU, thus delayed intervention are serious because relative risk of alcohol-related health conditions such as cirrhosis, pancreatitis, and hepatocellular carcinoma, is increased with the amounts and duration of alcohol consumed per day. We hypothesize that alcohol consumption elevates a panel of serum phospholipids (sphingomyelin, and lysophosphatidylcholines) in proportion to the level of consumption in the past month. Further, we hypothesize that such relationship can also be identified from a dried blood spot via a finger-stick procedure. The *central objective* of this proposal is to determine the diagnostic values of these two phospholipids as the potential biomarkers for EAU. We plan to recruit subjects to determine the relationship between the panel of serum phospholipids of interest and the amount of alcohol consumption during the past month in returning Indiana OEF/OIF veterans.

KEYWORDS: Excessive alcohol use, phospholipids, biomarkers

OVERALL PROJECT SUMMARY:

Recruitment: Since the inception of the study, we do not experience any problems with subjects' recruitment. To date, we have completed the recruitment for Part I and II. We are now working on the data entry as well as creating the data sheet for analysis. We are now in preparation for analysis of all the samples we collected which will take another 6-9 months.

KEY RESEARCH ACCOMPLISHMENTS: Nothing to report at this stage

CONCLUSION: Our project is significant to military personnel including the veterans. If successful, we expect to identify the non-invasive markers that can be used in clinical practice to screen for excessive alcohol use.

PUBLICATIONS, ABSTRACTS, AND PRESENTATIONS:

I would like to thank the DoD for support of my research. Because of the protected time that I received, I would be able to use this time to publish several papers (cited the DoD support) below.

1. Gough G, Heathers L, Puckett D, Westerhold C, Ren X, Yu Z, Crabb DW, Liangpunsakul S. The Utility of Commonly Used Laboratory Tests to Screen for Excessive Alcohol Use in Clinical Practice. *Alcohol Clin Exp Res*. 2015 Jun 25. doi: 10.1111/acer.12780. [Epub ahead of print] PubMed PMID: 26110815.
2. Liangpunsakul S, Lai X, Ross RA, Yu Z, Modlik E, Westerhold C, Heathers L, Paul R, O'Connor S, Crabb DW, Witzmann F. Novel serum biomarkers for detection of excessive alcohol use. *Alcohol Clin Exp Res*. 2015 Mar;39(3):556-65. doi: 10.1111/acer.12654. Epub 2015 Feb 19. PubMed PMID: 25704570; PubMed Central PMCID: PMC4348329.
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10. Jinjuvadia R, Liangpunsakul S; Translational Research and Evolving Alcoholic Hepatitis Treatment Consortium. Trends in Alcoholic Hepatitis-related Hospitalizations, Financial Burden, and Mortality in the United States. *J Clin Gastroenterol*. 2015 Jul;49(6):506-11. doi: 10.1097/MCG.000000000000161. PubMed PMID: 25198164; PubMed Central PMCID: PMC4276725.
11. Chayanupatkul M, Liangpunsakul S. Cirrhotic cardiomyopathy: review of pathophysiology and treatment. *Hepato Int*. 2014 Jul;8(3):308-15. doi: 10.1007/s12072-014-9531-y. PubMed PMID: 25221635; PubMed Central PMCID: PMC4160726.

INVENTIONS, PATENTS AND LICENSES: N/A

REPORTABLE OUTCOMES: Nothing to report at this time

OTHER ACHIEVEMENTS: Nothing to report

If you have any questions or concerns, please do not hesitate to contact me.

Sincerely,

A handwritten signature in black ink, appearing to read 'Suthat Liangpunsakul', followed by a horizontal line.

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