Morphine-induced suppressive effect in

• Opioids induce effects across a multitude of
development of additional novel therapeutic
of opioid replacement therapy as well as the

• easily categorized into meaningful patterns
infections.

• contributes directly to a third of all HIV

large public health problem. Addicted individuals
are susceptible to a broad array of infectious
complications and, in the U.S. alone, drug abuse
directs contribute to a third of all HIV/

• Tissue samples were mechanistically disrupted, digested with collagenase type II,
• Relative peptide abundances were transformed, and a model-based statistical
• Protein-level ANOVA identified statistical changes, and Benjamini-Hochberg
• Operated in data-dependent mode with

Statistical analysis
• Outlier exclusion was modeled using a peptide-centric approach that considers 5
• Statistical results are shown as mean ± SEM and reported as fold change typical of
• Protein-level ANOVA identified statistical changes, and Benjamini-Hochberg

Conclusions
• Morphine produces an immunosuppressive
effect in the lymph node (LN) of both NHPs,
paired by decreases in activation levels of T
• Findings across gut mucosa, CSF, and plasma
• These findings highlight the need for alternative
• A number of these proteins have been
• These findings highlight the need for alternative

References
1. Matzke MM, et al. Improved quality control processing of peptide-
... 27:2866-2872 (2011).
... procedures were performed using
... analysis was performed in parentheses below

Acknowledgements
Portions of the T32 grant (GM78726) are supported by funds from NIH National Center
for Research Resources (P41 RR019262 and P20 GM081236-11 M1) and the National Institute of Health (HG001834-11, P20 M100533-11, and P20 CO620000), and
Many thanks to the University of Washington Environmental Health and Safety
standard protocols and according to guidelines approved by the

CONTACT: Joseph Brown, Ph.D.
(509) 375-2687
joseph.brown@pnl.gov

Joseph N. Brown1, Gabriel M. Ortiz2, Thomas E. Angel1, Jon M. Jacobs1, Marina Gritsenko1, Eric Y. Chan3, Anil K. Shukla1, Therese R. W. Clauss1, Joseph M. McCune2, and Richard D. Smith1
1Pacific Northwest National Laboratory, Richland, WA; 2University of California San Francisco, San Francisco, CA; 3University of Washington, Seattle, WA

Integrated omics model schema of morphine immunosuppressive effects in NHPs

Figure 1. Proteome variation across 132 high-resolution LC-MS were co-fed to measure inter-
... isolated (C2), CSF (CSF-2), and plasma (LGD-3).

Figure 4. Samples were divided into tissues (A and B) and fluids (C and D).

Figure 3. Biopsies representing the percent depletion of cell types measured in the lymph node
... biopsies, colonic mucosal compartments.

Figure 2. Similar analysis to Figure 1, except using cell counts from the lymph node as opposed
to proteins. The number of cell types used in the analysis is below the heatmap in parentheses.

Table 1. Number A Percent of significantly expressed proteins.

General
Compartment
Lymph node
Number
Lymph node
402 (28.5)

Activated T-cells in the lymph node

Conclusions
• Morphine produces an immunosuppressive
effect in the lymph node (LN) of both NHPs,
paired by decreases in activation levels of T
• Findings across gut mucosa, CSF, and plasma
• These findings highlight the need for alternative
• A number of these proteins have been
• These findings highlight the need for alternative

Introduction
With 20 million heroin addicts estimated worldwide and countless others who abuse prescription opioids, drug addiction remains a
worldwide and countless others who abuse

Overview
• Goal: To identify the systemic changes induced by morphine in two primate species:
• Matzke MM, et al. Improved quality control processing of peptide-
... 18522 and (P41 GM103493-
... Portitions of this work were supported by funds from NIH National Center
... 3.

Experimental
Design
• Morphine administered intravenously starting at 1 mg/kg intravenously every 5 h and
dosed upwards to a maximum dose of 5 mg/kg by day 20.

Methods
Flow Cytometry
• Peripherally blood samples at days 10, 15, and 20
• While lymph node biopsy, intramuscular inoculation, biopsies, colonic mucosal

Sample preparation for proteomics
• Samples were isolated in RIPA buffer, and quantified by BCA. Samples were
denatured in 8 M urea, and quantified by BCA. Samples were
denatured in 8 M urea, and quantified by BCA. Samples were

tissue counts, and NK cells counts.

Morphine-induced suppressive effect in lymph nodes, with decreased abundance of protein mediators involved in energy
metabolism, signaling, and maintenance of cell structure.

Results
Proteome variation Inter-individual / inter-species

Cellular variation in lymph node - Inter-individual / inter-species

Integrated omics model schema of morphine immunosuppressive effects in NHPs

Figure 4. Samples were divided into tissues (A and B) and fluids (C and D).

The number of proteins considered in each analysis
resulted in extreme peptide abundance distributions (P<0.05).

Figure 3. Biopsies representing the percent depletion of cell types measured in the lymph node

Figure 2. Similar analysis to Figure 1, except using cell counts from the lymph node as opposed
to proteins. The number of cell types used in the analysis is below the heatmap in parentheses.

Table 1. Number A Percent of significantly expressed proteins.

General
Compartment
Lymph node
Number

CONCLUSIONS
• Morphine produces an immunosuppressive
effect in the lymph node (LN) of both NHPs,
paired by decreases in activation levels of T
• Findings across gut mucosa, CSF, and plasma
• These findings highlight the need for alternative
• A number of these proteins have been
• These findings highlight the need for alternative