PROJECT DESCRIPTION

The project involves enrolling clients in drug treatment programs (including medication-assisted treatment programs) who suffer from a variety of disadvantages and medical issues, including access to care, complications from infectious agents, and drug-related problems such as overdoses. The project aims to develop an interdisciplinary team of faculty co-investigators and senior drug treatment program staff to embark on a set of endeavors. Past cohort studies included systematic administered interviews of treatment program clients using an extensive structured interview developed asking about their demographics, behaviors; patterns of drug abuse, including opioids, cannabis, other classes of drugs, alcohol and tobacco; and sexual behavior. In study subsets, issues such as overdose and treatment of hepatitis C virus (HCV) and for HIV have been explored in detail. We have documented high rates of infection with hepatitis C. Beyond the epidemiology, the health policy and system implications are being explored.

Current novel findings from our past studies include the association of specific drugs such as tobacco and cannabis with lung cancer, a picture of long-term mortality due to liver failure, the epidemiology and impact of infection with HCV and HIV, occurrence of overdoses, and health issues among male and female drug users with a focus on chronic diseases such as cancer, including hepatocellular carcinoma and lung cancer. From 2016-2019 we enrolled over 300 additional drug users to examine in detail some highly relevant current issues, methadone dosage over a prolonged period of time, and their use of opioids during and out of treatment. This study is helping to provide the basis for our new initiatives.

This project complements and builds upon the several national prospective cohort studies that Dr. Weiss designed in the mid 1980’s while he was at the National Cancer Institute (NCI), which totaled about 11,084 enrollments from over about 10,000 persons nationally, including ~2,500 from NJ. He joined the NJMS faculty in 1987. These studies have substantial accumulated medical, laboratory and questionnaire data, plus a linked biospecimen repository of about 100,000 vials. The follow-up period is ~30+ years, with an extensive baseline database. These constitute the only large cohort study of adults...
with high rates of human immunodeficiency virus (HIV) and hepatitis C virus (HCV) infection within New Jersey, and furthermore included both men and women and a diverse racial/ethnic mix, from the start. In September 2012, in the largest material transfer from NIH in legacy UMDNJ history, 82,962 vials were transferred from NCI to Dr. Weiss, supplementing other specimens already held here. Linkage and personal identifying data are known to us. Collaborations have been renewed with many of the original treatment programs and with the NJ Department of Health and the NJ State Cancer Registry, with administrative approvals obtained to repeat various types of registry matching studies to ascertain long-term outcomes.

NIDA has already completed analysis of >5000 blood biospecimens from our cohort subjects, ascertaining the presence or absence of ~800,000 single nucleotide polymorphisms (SNPs, that is, genetic variants) that may affect risk for a broad array of diseases and conditions, including various chronic diseases and cancers, drug addiction, tobacco use, etc. We anticipate analyses both using GWAS approaches (as part of the NIDA Genetics Consortium, of which Dr. Weiss is an active member) as well as creating polygenic models when examining disease outcomes. About 3,000 additional subjects are anticipated to be run on the same genetics array.

Another ongoing new initiative is the study of metabolomics, including ~4000 compounds such as cannabinoid and nicotine metabolites. Specimens collected in the 1990’s are expected to complete laboratory testing in Spring 2020, with data then available for additional analyses in summer 2020.

Assessment of the accrued data is leading to the development with several Rutgers investigators of plans to utilize the biologic repository, contingent upon approval by the IRB of protocols in development or revision. NIDA’s genotyping of a large numbers of specimens is planned as the first step in a sequence of laboratory-based analyses of these biospecimens. For example, because most members of these cohorts have a history of injection drug use, the rates of HIV, HTLV-II, and hepatitis C virus (HCV) infection among them are all quite high. Thus, these data have the potential to be a rich resource for finding predictors of mortality due to these infectious agents – such as hepatocellular carcinoma, HCV-associated liver failure and HIV-associated issues. Data sharing agreements with NIDA have been approved by Rutgers.

Utilizing our linkage information and follow-up data, beginning in 2015 we matched 2,254 persons enrolled from NJ to the NJ State Cancer Registry (NJSCR), with over 185 cancers previously documented. Future matching is anticipated to once again include national databases (such as the National Death Index and the Social Security Administration database). In the near term, matching will occur to NJ statewide databases (such as the New Jersey HIV/AIDS registry) and updating the NJSCR match. Later on, we may again match to the NJ Vital Statistics database and/or the federal National Death Index Plus (NDI-Plus). Relevant analyses are ongoing.

Technology has been evolving over the decades, with laboratory analyses becoming possible on minute amounts of stored material. These tests need to be validated on our stored samples, prior to embarking on large-scale studies. Multiple laboratory-based investigators have expressed interest, and opportunities to do laboratory-based work and related analyses will be evolving.

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Indeed, Dr. Weiss was responsible for detecting and demonstrating an epidemic of HTLV-II in drug users. He also demonstrated immunologic abnormalities associated with HTLV-II, and played an integral role in the FDA’s decision to screen blood donors for HTLV-II. The long-term medical effects of HTLV-II, if any, remain to be determined. These cohorts will provide new epidemiologic information about HTLV-II as well as many other infectious agents.

Data were assembled over the last 30+ years from these cohorts using questionnaires and other data collection forms designed by Dr. Weiss and his collaborators. In the approximately three decades since these studies were initiated, advances and standardization of data elements and their design have occurred to facilitate inter-institutional laboratory studies. Such standards include PhenX (www.phenxtoolkit.org) and DataSHaper (www.datashaper.org), as well as a consortium of large prospective cohort studies that has some support from the National Cancer Institute. We shall assess the compatibility of our data collection with one or more of these standardized formats used in various other large-scale projects, and shall explore the feasibility of transforming our existing data into the most appropriate format. These steps may permit us to join other groups in large-scale data projects. We shall also provide NIH appropriate data, with due attention to confidentiality issues, per national standards. Because of our plans to match our data to the existing national databases described earlier, we will need to be mindful of those data sources’ requirements as well as of our existing data if we undertake such transformation.

The detailed specific project based upon our many initiatives and very long-term prospective cohort studies, with an appropriate timeline for a summer project, will be developed with the student based upon her/his past experience, training, and interests. Dr. Daniel M. Rosenblum, Assistant Professor, will also provide mentorship on the project, as will many collaborators from the NJSCR and the Cancer Institute of NJ and other Rutgers faculty.

**SPONSOR’S PUBLICATIONS MOST RELEVANT TO THIS RESEARCH:**

**Recent Abstracts:**
Summer 2020 Student Research Program
Project Description


Past Relevant Student Summer Projects:
Journal Publications (selected):


Summer 2020 Student Research Program
Project Description


IS THIS PROJECT SUPPORTED BY EXTRAMURAL FUNDS?
Yes or No ☒
(IF YES, PLEASE SUPPLY THE GRANTING AGENCY’S NAME)
For some of the activities performed outside of NJMS, existing grants and contracts from the National Institute on Drug Abuse (NIDA) are employed:
- NIDA grant # 1R01DA044014-01 to Eric O. Johnson, PhD, PI, at RTI International;
- NIDA contract to RUCDR Infinite Biologics.

THIS PROJECT IS: ☒Clinical ☒Laboratory ☒Behavioral ☐ Other

THIS PROJECT IS CANCER-RELATED ☒
Please explain Cancer relevance:
- A major emphasis is currently on the detailed examination of our lung cancer and liver cancer outcome data.
- The ongoing follow-up in conjunction with the NJ State Cancer Registry and matches to the NJ AIDS/HIV registry will enable us to assess risk factors for cancer and progression in these well-defined cohorts, and understand aspects of the AIDS epidemic over three decades of time.
- Hepatitis C virus (HCV) infection (which a study drawn from these cohorts was the very first to demonstrate is highly prevalent in injection drug users) is a major cause of hepatocellular carcinoma with a latency on the order of decades. Better understanding of biomarkers in HCV-infected individuals that are correlated with occurrence of hepatocellular carcinoma can lead to more effective use of medical resources to prevent this cancer. Another key outcome is end stage liver failure.
- HIV and HTLV-I infection are linked with specific types of cancers.
- Beyond immunologic abnormalities, a health impact of HTLV-II remains to be determined. This project is uniquely suited to examine this issue due to the high prevalence of HTLV-II, plus the study’s size and longevity.

THIS PROJECT IS HEART, LUNG & BLOOD-RELATED ☒
Please explain Heart, Lung, Blood relevance:
A major emphasis is currently on the detailed examination of our lung cancer outcome data. Specimens that have been collected and that could be examined for biomarkers include sera, plasma, urine, Ficoll-hypaque purified lymphocytes, and EBV-transformed cell lines, and viral isolates. Data from these studies were instrumental in the decision by the US FDA that all blood products be screened for HTLV-II. The demonstration that these retroviruses were highly prevalent in these specimens helped lead to setting the early policies in the state of NJ concerning testing for HIV, and on the FDA’s approach to test licensing. The results from this study will be relevant to U.S. screening practices of potential blood donors.

THIS PROJECT EMPLOYS RADIOISOTOPES ☒
THIS PROJECT INvolves the USE OF ANIMALS ☐
Pending ☐ Approved ☒ IACUC PROTOCOL #

THIS PROJECT INVOLVES THE USE OF HUMAN SUBJECTS ☒
Pending ☒ Approved ☒ IRB PROTOCOLS #’s Pro20150001314, Pro20160000704 (both approved), & Pro2019002287 (pending).

Page 6 of 7
Summer 2020 Student Research Program
Project Description

THIS PROJECT IS SUITABLE FOR:
UNDERGRADUATE STUDENTS ☐ ENTERING FRESHMAN ☐
SOPHMORES ☐ ALL STUDENTS ☑

THIS PROJECT IS WORK-STUDY: Yes ☑ or No ☐
THIS PROJECT WILL BE POSTED DURING ACADEMIC YEAR FOR INTERESTED VOLUNTEERS?: Yes ☑ or No ☐

WHAT WILL THE STUDENT LEARN FROM THIS EXPERIENCE?
• Receive training in confidential study procedures.
• How to design follow-up analyses in cohort studies, such as nested-case control designs.
• Strategies for efficient use of health data.
• How to approach the analysis of datasets.
• How to perform critical and systematic assessment of methodologies, and their practical applications.
• How critical assessment of findings can lead to changes in approach or implementation.
• How to understand and utilize power calculations in setting project objectives and goals that appear feasible.
• For those who include a laboratory based component, how to conduct lab analyses and assess results.
• For those who assist in our field work: receive training in conducting in-person interviews using a written questionnaire, and develop comfort working with staff and subjects in novel outpatient settings.

CRITICAL PRIOR EXPERIENCE AND SKILLS
• Prior experience in performing data analysis and in using data analysis software such as SAS, SPSS or R is REQUIRED; there is insufficient time during the summer period to newly learn and become expert in SAS programming and to perform new data analyses on the considerable new data we are continually receiving.
• Prior experience with software such as MS Excel and the Microsoft Office Suite.
• Excellent written and communication skill is REQUIRED.
• Human subjects protection training and certification through the Rutgers-specified CITI course for Social, Behavioral, and Epidemiologic Research Investigators. (See orra.rutgers.edu/citi for details.) Certification will be REQUIRED at least 6 weeks prior to starting, to give adequate time to be added to our current IRB protocol.

USEFUL ADDITIONAL RELEVANT PRIOR EXPERIENCE AND SKILLS
(Note: Only some of these skills are requisite for a specific project. However, some skill(s) are important to enable getting a jump-start.)
• In conjunction with another, new study - prior fieldwork experience in urban areas, including client interviewing and/or administration.
• Prior experience working on a research team.
• If interested in a lab-associated component: prior relevant lab experience.
• Car and driver’s license (for projects involving access to community sites).