Cohort Studies of Drug Users and Related Groups

HYPOTHESES:
1) Our new studies begun in summer 2016 will reveal community-level dynamics relevant to public policies.
2) Our long-term cohorts are uniquely suited to examining the dynamics of the HIV and HCV epidemics among adult drug users.
3) Baseline data, such as medical and behavioral factors and biomarkers, as well as new biomarker data, are predictive of specific health and vital status outcomes.

PROJECT DESCRIPTION (Include design, methodology, data collection, techniques, data analysis to be employed and evaluation and interpretation methodology)

Clients enrolled in drug treatment programs suffer from a variety of disadvantages and medical issues, including access to care, complications from infectious agents, and drug-related problems such as overdoses. In 2016 we enlisted a team of faculty co-investigators and senior drug treatment program staff to embark on a new set of endeavors. Current program clients are being interviewed at NJ drug treatment programs using an extensive structured interview we developed asking about their demographics, behaviors, and attitudes, with a particular focus on hepatitis C infection and the availability and barriers to treatment for hepatitis C, as well as issues related to drug overdoses. We have documented low rates of treatment for hepatitis C, in the face of continuing high rates of infection. Beyond the epidemiology, the health policy and system implications are being explored.

The above project complements and builds upon 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 10,066 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 over 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. Beginning in 2016, collaborations were renewed with many of the original treatment programs and with the NJ Department of Health and the NJ State Cancer Registry. Preliminary, detailed sample size calculations incorporating estimates of various outcome measures have already been performed. Planning for the judicious use of these repository samples and data sets has begun.

The National Institute on Drug Abuse (NIDA) has offered to analyze biospecimens from our subjects, ascertaining the presence or absence of hundreds of thousands of 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, which Dr. Weiss has joined) as well as polygenic models when examining disease outcomes. We continue to explore what factors to study among the stored human biospecimens, such as from sera, urine, and purified viable lymphocytes.

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. NIDA’s offer to genotype large numbers of specimens will constitute 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.

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 found. Future matching will include national databases (such as the National Death Index and the Social Security Administration database), and other state-wide databases (such as the New Jersey HIV/AIDS, Hepatitis C and tuberculosis registries). We are in the process of moving ahead with matching to several NJDOH state-wide databases (such as the New Jersey HIV and AIDS registries and tuberculosis registry) and later on may again match to the NJ Vital Statistics database. Relevant analyses are ongoing.

Current novel findings from our studies include a picture of long-term mortality due to liver failure, the epidemiology and impact of infection with HCV and HIV, and health issues among male and female drug users with a focus on chronic diseases such as cancer, including hepatocellular carcinoma and lung cancer.

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.

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.

The detailed specific project based upon these 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 may 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 2018 Student Research Program
Project Description


Past Student Summer Projects:
- Kabaria S (NJMS 2019). Follow-up of Long-Term Prospective Cohort Studies of Injection Drug Users and Related Groups.
- Connor JA (NJMS 2019). Follow-up of Long-Term Prospective Cohort Studies of Injection Drug Users and Related Groups.

Journal Publications (selected):
- Briggs NC, Battjes RJ, Cantor KP, Blattner WA, Yelin FM, Wilson S, Ritz AL, Weiss SH, Goedert JJ. Seroprevalence of human T cell lymphotropic virus type II infection, with or without human
Summer 2018 Student Research Program
Project Description


IS THIS PROJECT SUPPORTED BY EXTRAMURAL FUNDS?
Yes ☒ or No ☐

(IF YES, PLEASE SUPPLY THE GRANTING AGENCY'S NAME)

Although the project is not currently supported by extramural funds, extramural support for some of the infrastructure supporting a project exists.

THIS PROJECT IS: ☒Clinical ☒Laboratory ☒Behavioral ☐Other
THIS PROJECT IS CANCER-RELATED
Please explain Cancer relevance:
- The ongoing follow-up in conjunction with the NJ State Cancer Registry will enable us to assess risk factors for cancer and progression in these well-defined cohorts.
- 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.
- 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:
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  □  IRB PROTOCOLS #’s Pro20150001314, Pro20160000704

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

THIS PROJECT IS WORK-STUDY:  Yes  □  or  No  □

WHAT WILL THE STUDENT LEARN FROM THIS EXPERIENCE?
- 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.

USEFUL 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.)
- Prior experience with data analysis and data analysis software such as MS Excel and SAS.
- Prior fieldwork experience in urban areas, including client interviewing and/or administration.
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- Excellent written and communication skills.
- Prior experience working on a research team.
- If interested in a lab-associated component: prior relevant lab experience.
- 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.)
- Car and driver’s license (for projects involving access to community sites).