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14. ABSTRACT This research project will build upon the Long Island Breast Cancer Study Project (LIBCSP), a large population-based, case-control study of the environment and breast cancer. Participants completed an in-person interviewer-administered interview, donated blood and urine samples and had home environment samples (dust, soil and water) collected. For this study, 200 cases and 200 controls who donated urine samples will be selected and their urine samples will be analyzed for a panel of EE biomarkers. In addition, these same women will be screened for polymorphisms in both the estrogen receptor alpha and beta genes. Breast cancer risk in relation to the combination of these multiple EE exposures and gene-environment interaction will be investigated using sophisticated statistical methods such as hierarchical regression models and factor analysis. Additionally, a pilot investigation of the correlation between EE levels in house dust and urinary biomarker levels will be conducted. Currently, samples for this study have been selected and the laboratory analyses are underway. Results of the proposed research project will be of enormous public health relevance since they may advance our knowledge of modifiable breast cancer risk factors and newly identified EEs, thereby providing information that is essential for primary prevention.					
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Introduction

The primary aim of the multidisciplinary postdoctoral award is to position Dr. Teitelbaum as an independent research scientist specializing in the environmental and molecular epidemiology of combined effects of multiple exposures. The research aims – relating multiple environmental estrogen exposure to breast cancer risk – will be examined in the Long Island Breast Cancer Study Project, a large population-based case-control study of breast cancer and the environment.

Specific Aims:

- To investigate whether women with higher combined exposure levels to multiple environmental estrogens are at increased risk of breast cancer.
- To investigate the possibility that women who carry adverse alleles in the estrogen receptor alpha and beta genes and have higher combined exposure levels to multiple environmental estrogens are at higher risk of breast cancer than women without these alleles.
- To evaluate the relationship between household dust and urinary levels of environmental estrogens.

Body

Below I have detailed the training and research that has been completed over the past year according to the tasks outlined in the Statement of Work.

Task 1. To undertake the proposed training program (Months 1-36):

- a. Complete graduate coursework in biostatistics, genetics, and pharmacology
 - Completed The Jackson Laboratory Annual Short Course In Medical And Experimental Mammalian Genetics, July 2005.
 - Over the next year, I plan to attend courses in advanced statistical methods such as a graduate course on Structural Equation Methods and SAS short courses on various advanced statistical analyses.
 - I participated in a course on the biology of cancer given by the faculty in the MSSM Cancer Center.
- b. Conduct several epidemiologic analyses of multiple environmental exposures
 - Author and co-author on multiple publications (see Reportable Outcomes)
 - Continue to participate in departmental environmental and biometry journal clubs, attend monthly meetings of departmental projects, attend weekly Cancer Center seminars and Mount Sinai grand rounds on endocrinology, breast pathology, and oncology.
 - Attended and presented at the departmental biometry and environmental epidemiology journal clubs.
 - Attended monthly meeting of the NIEHS Center for Children's Environmental Health
 - Attended Cancer Center seminars and grand rounds when topics were relevant to my research and training goals
- c. Become a member of and alternately attend annual meetings of the International Society of Exposure Analysis (ISEA)/International Society for Environmental Epidemiology (ISEE) and Eastern North American Region of the International Biometric Society (ENAR).
 - Current member of:
 - o International Society for Environmental Epidemiology
 - o Eastern North American Region of the International Biometric Society
 - o American Association for Cancer Research (AACR) and Molecular Epidemiology Working Group of AACR
 - o Society for Epidemiologic Research
 - Attended professional scientific meetings:
 - o DOD Era of Hope Meeting and presented a poster on this funded project “Gene-Environment Interaction and Breast Cancer on Long Island, NY”
 - o International Society of Environmental Epidemiology (ISEE) and presented a poster on “Temporal variability in urinary phthalate metabolites, phenols and phytoestrogens among children ”
 - o Emerging Topics in Breast Cancer and the Environment
 - o Cornell University’s Breast Cancer and Environment Research Factors Forum

- d. Complete an internship in the lab conducting genetic screening to gain an appreciation for laboratory work commonly performed in molecular epidemiology studies.
 - Completed the New England Biolabs course in Molecular Biology and PCR, June 2005. This is an intensive two-week course that provided required training through theoretical and practical lab work training.
- f. Regularly meet with my mentors and advisors to oversee my progress and research development.
 - Met both formally and informally with Dr. Wolff each week to review progress, discuss issues related to conducting research and professional development.
 - Met with other mentors and advisors on an “as needed” basis depending on the specific research issue requiring discussion

Task 2. To conduct a case-control study of combined environmental estrogen exposure, the estrogen receptor alpha and estrogen receptor beta genes and breast cancer (Months 1-30):

- a. Conduct sample selection for urinary biomarkers (200 cases and 200 controls) and dust analysis (50 cases and 50 controls)
 - Study subjects have been chosen in consultation with Dr. Sylvan Wallenstein for both analyses.
 - Additional funding has been obtained to increase urinary biomarker sample size.
- b. Conduct urinary biomarker environmental estrogen assays.
 - Several in-person meetings, phone conferences and email communication with collaborators from the CDC (where biomarker assays will be conducted) have been held.
 - Due to the physical relocation of the CDC laboratory there is an extensive backlog for performing these analyses. Thus there has been a delay in getting this task underway. The head of the lab estimates that the samples from this study will not be able to begin before the end of the summer. Communication with the CDC lab will continue throughout this period to monitor their progress.
- c. Conduct screening for estrogen receptor alpha and estrogen receptor beta genetic polymorphisms.
 - Identification of the appropriate polymorphisms has been conducted and arrangements for the transfer of DNA samples to the lab have been made
- d. Conduct house dust environmental estrogen analyses.
 - All selected dust samples were located in repository freezers.
 - Processing/analyses of the samples is underway
- e. Conduct quality control and verification of data.
 - To be conducted in Years 2 and 3

Task 3. To conduct data analysis, manuscript preparation and dissemination of research results at conferences (Months 31-36)

- To be conducted in Year 3

Key Research Accomplishments

- Designed and oversaw field operations of a methodological study to assess the inter- and intra-person variability of urinary metabolites of the environmental estrogens, including bisphenol A, phthalates and pyrethroid pesticides.
 - o The collection of serial urine samples was completed.
 - o The CDC has completed sample analysis and has delivered the biomarker analyte results.
 - o Using this data, an abstract has been submitted for presentation at the 2006 Annual meeting of the International Society of Environmental Epidemiology.
 - o The first of several manuscripts based on this data is in preparation.

Reportable Outcomes

- Publications
 - Teitelbaum, SL, Calafat, AM, Britton, JA, Silva, MJ, Ye, X, Kuklenyik, Z, Reidy, JA, Brenner, BL, Galvez, MP, Wolff, MS. Temporal variability in urinary phthalate metabolites, phenols and

phytoestrogens among children. (abstract submitted to International Society of Environmental Epidemiology 2005).

Teitelbaum SL, Gammon MD, Britton JA, Neugut AI, Levin B, Stellman SD. Reported residential pesticide use and breast cancer risk on Long Island, NY. (revised manuscript submitted to American Journal of Epidemiology – awaiting acceptance decision)

Teitelbaum SL, Calafat AM, Britton JA, Silva MJ, Ye X, Kuklenyik Z, Reidy JA, Brenner BL, Galvez MP, Wolff MS. Temporal variability in urinary phthalate metabolites, phenols and phytoestrogens among children. Epidemiology. 2005. Abstract 16(5):S41 (manuscript in preparation).

Teitelbaum SL, Gammon MD, Britton JA, Neugut AI, Levin B, Stellman SD, Wolff MS. Characteristics and patterns of residential pesticide use on Long Island, NY. International Society of Environmental Epidemiology. (in preparation for submission to Environmental Health Perspectives)

Teitelbaum SL, et al. Environmental chemicals in household dust and breast cancer risk on Long Island, NY. (in preparation)

Teitelbaum SL, et al. The combined effect of multiple environmental exposures on pregnancy outcome in the World Trade Center Pregnancy cohort. (in preparation)

Teitelbaum SL, et al. Interaction of PCB exposure with Cyp1A1 genetic polymorphisms and breast cancer risk on Long Island, NY. (in preparation)

- Principal Investigator of NIEHS funded Mentored Scientist Career Development Award.
- Co-Investigator on Project 2 of NIEHS/EPA funded “Breast Cancer and the Environment Research Center” (MS Wolff, PI).
- New investigator award in our department’s NIEHS/EPA funded Children’s Environmental Health Center.
- Invited abstract reviewer for 3rd annual Breast Cancer and the Environment Research Symposia.

Conclusions

I have made significant progress towards becoming an independent research scientist specializing in the environmental and molecular epidemiology of combined effects of multiple exposures. I have extended my multiple exposure study opportunities by obtaining 2 additional federally funded initiatives and increased my ability to conduct multiple exposure epidemiologic analyses through the training I have completed. The work accomplished during the second year of this grant has built a strong foundation for completing the proposed research in the remaining years of this project.

The research I have conducted thus far is directly related to the goals of my postdoctoral award. All of these urinary metabolites measured in the temporal variability study will be measured in the urine samples of the case-control study analyses that will be conducted in future years of this award. The results will provide invaluable information for the data analysis of the case-control study and contribute to our understanding of how these biomarkers can be best used in epidemiologic studies.

References

None

Appendices

None