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The Women's Environmental Cancer and Radiation Epidemiology (WECARE) Study

Principal Investigator

Jonine Bernstein, PhD

What is the WECARE Study?

The WECARE Study is a large international multi-center, population-based case-control study nested within a cohort of over 52,500 female breast cancer survivors. In this study, 708 women with asynchronous contralateral breast cancer (CBC) serve as cases, and 1397 women with unilateral breast cancer (UBC), individually matched to the cases on age, diagnosis date, latency, and race serve as controls. All participants were recruited through 5 population-based registries in the US and Denmark. Using a multi-faceted approach, this international study examines the interaction of radiation exposure and genetic predisposition in breast cancer, especially radiation-induced contralateral breast cancer (CBC). Currently, we are carrying out studies of: candidate genes BRCA1, BRCA2, CHEK2, and ATM; candidate gene pathways of DNA damage response involved in radiation-induced double strand break repair—ATM, CHEK2, P53 binding protein (53BPI), and MDC1, Mre11, Rad50, and Nbs1 (e.g., MRN nuclease complex); function

and mechanism studies of the ATM gene; pharmacogenetics of key drug metabolizing genes; and statistical methods for estimating the cancer risk of rare genetic variants. The global hypothesis across these studies is that women who carry certain types of mutations will be more susceptible to radiogenic breast cancer than non-carriers. The most recent expansion, the WECARE:GWAS Study, was funded to conduct the first multi-stage genome-wide association (GWA) studies of bilateral breast cancer with a built in replication population. We have already completed the genotyping to discover novel common SNPs associated with CBC and radiation exposure. For validation, we are currently in the field recruiting an additional 800 CBC cases and 800 UBC controls from the US, Denmark, and Canada. Various replication and fine-mapping phases are planned as well.

Who Is Conducting this Study?

This study involves a large international group of scientists, with significant experience in specialties such as molecular genetics, radiation epidemiology/dosimetry and quantitative epidemiologic methods. Collaborating sites include:

Memorial Sloan Kettering Cancer Center: Jonine Bernstein PhD, Colin Begg PhD, Marinela Capanu PhD, Irene Orlow PhD, Ken Offit MD, Xiaolin Liang, MD, Anne Reiner MPH, Meghan Woods

City of Hope: Leslie Bernstein PhD (sub PI), Laura Donnelly-Allen

Danish Cancer Society: Jørgen Olsen MD DMSc (Sub PI), Michael Andersson MD, Lisbeth Bertelsen MSc, Per Guldbergj PhD, Lene Mellemkjær PhD

Fred Hutchinson Cancer Research Center: Kathleen Malone PhD (Sub PI), Noemi Epstein

International Epidemiology Institute/Vanderbilt University: John D. Boice Jr. ScD (Sub PI)

Lund University: Åke Borg PhD (Sub PI),Theresa Sandberg PhD

Mount Sinai School of Medicine: Barry Rosenstein PhD (Sub PI), David Atencio PhD

National Cancer Institute: Daniela Seminara PhD MPH

New York University: Roy Shore PhD, DrPH.(Sub PI)

Northern California Cancer Center: Esther John PhD (Sub PI), Ellen Chang ScD

Norwegian Radium Hospital: Anne-Lise Børresen-Dale PhD (Sub PI), Laila Jansen

Samuel Lunenfeld Research Institute: Julia Knight PhD (Sub PI), Anna Chiarelli PhD

Stanford University: Alice Whittemore PhD

Translational Genomics Research Institute (T-Gen): David Duggan PhD (Sub PI)

University of California Irvine: Hoda Anton-Culver PhD (Sub PI), Joan Largent PhD MPH

University of California Los Angeles: Richard Gatti MD

University of Iowa: Charles Lynch MD, PhD (Sub PI), Jeanne DeWall MA

University of Southern California: Robert Haile DrPH (Sub PI), Graham Casey PhD, Bryan Langholz PhD, Daniel Stram PhD, Duncan Thomas PhD, Anh Diep, Shanyan Xue MD, Nianmin Zhou,MD, Yong Liu MD, Evgenia Ter-Karapetova, Andre Hernandez;

University of Southern Maine: W. Douglas Thompson PhD (Sub PI)

University of Texas, MD Anderson Cancer Center: Marilyn Stovall PhD (Sub PI), Susan Smith MPH, Thomas Buchhlz MD

University of Virginia: Patrick Concannon PhD (Sub PI), Sharon Teraoka PhD, Eric Olson PhD

Study Objective

To examine the interaction of radiation exposure and genetic susceptibility in the etiology of second primary breast cancer

Study Hypothesis

The global hypothesis across all of the WECARE Studies is that women who are carriers of certain genetic mutations will be more susceptible to radiation-induced breast cancer than are non-carriers.

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