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MEDIA AVAILABILITY: NHLBI Awards 12 Women's Health Initiative Contracts to Study Genetic and Biological Markers of Common Diseases Affecting Postmenopausal Women

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The Women's Health Initiative (WHI) embarks on its next phase of research with 12 new contracts awarded last week by the National Heart, Lung, and Blood Institute of the National Institutes of Health. The studies will help explain the postmenopausal hormone therapy and other clinical trial findings and will investigate the impact of genetic and biological markers on common diseases affecting postmenopausal women. The WHI was a major 15-year research program designed to address the most frequent causes of death, disability and poor quality of life in postmenopausal women -- cardiovascular disease, cancer, and osteoporosis.

The new 2-year research projects will apply innovative technologies to study factors affecting the major diseases in postmenopausal women. Investigators will conduct their research using blood, DNA and other biological samples and clinical data from the 161, 808 postmenopausal women who participated in one or more of the three WHI clinical trials or in the observational study. The total cost of all of the awards is $18, 679, 000.

The studies, institutions, and principal investigators are (alphabetically by institution):

- Adipokines and Risk of Obesity-Related Diseases, Albert Einstein College of Medicine, Bronx, NY, Gloria Ho, Ph.D., M.P.H. The research team will examine the

association of adipokines (physiologically active proteins from body fat cells) with cancer and stroke risk, and the role of these proteins in the association between obesity and the risk of cancer and stroke.

- Physical Activity, Obesity, Inflammation, and CHD in a Multi-Ethnic Cohort of Women, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, I-Min Lee, MBBS, ScD. Dr. Lee and colleagues seek to clarify the mechanisms underlying the reduced risk of CHD conferred by physical activity and lower body fat, beyond their effects on traditional risk factors. Using data from the WHI Observational Study, the team will examine associations between physical activity and inflammatory markers and whether these associations vary by a person's weight. They will also look at joint associations between physical activity combined with weight/obesity status and risk of CHD. The role of inflammatory markers in mediating the associations of physical activity and weight with CHD risk will be studied and compared with the role of traditional risk factors such as blood pressure and cholesterol levels.
- Endogenous Estradiol and the Effects of Estrogen Therapy on Major Outcomes of WHI, California Pacific Medical Center, San Francisco, Steven R Cummings, M.D. The investigators will study how baseline levels of the estrogen molecule, estradiol, and of sex hormone binding globulin (SHBG), a protein that binds to testosterone and estradiol, relate to treatment effects of hormone therapy on coronary heart disease (CHD), stroke, blood clots, fractures, breast cancer, dementia, and mild cognitive impairment. The team will test for interaction of baseline hormone levels with treatment effects of hormone therapy.
- Identification and Validation of Circulating Biomarkers for the Early Detection of Breast Cancer in Pre-Clinical Specimens, Fred Hutchinson Cancer Research Center, Seattle, WA, Christopher Li, M.D., Ph.D. Using three different proteomics techniques, the investigators hope to identify proteins associated with breast cancer as well as biomarkers that could potentially be used for early detection of breast cancer.
- Proteomics and the Health Effects of Postmenopausal Hormone Therapy, Fred Hutchinson Cancer Research Center, Seattle, WA, Ross Prentice, Ph.D. Dr. Prentice and his research team will study over 1,000 proteins, in order to identify a small number of proteins potentially associated with CHD, stroke, breast cancer, colon cancer, or hip fractures in participants in the WHI Observational Study. Together with other ongoing studies in the hormone trials, this work may lead to the identification of markers of future disease, and how these markers relate to the effects of hormone therapy.
- High-Dimensional Genotype in Relation to Breast Cancer and WHI Clinical Trial Interventions, Fred Hutchinson Cancer Research Center, Seattle, WA, Ross Prentice, Ph.D. This genome-wide association study will examine genetic variations associated with breast tumor characteristics. Since the studies are being done in women participating in the hormone therapy, calcium-vitamin D, and low fat diet trials and the investigators will have access to blood hormone and vitamin D levels in

many of these WHI participants, they hope to explore biologic pathways by relating treatments, blood levels, and genes to breast cancer.

- Genome-wide Association Study to Identify Genetic Components of Hip Fracture, Ohio State University, Columbus, OH, Rebecca Jackson, M.D. Dr. Jackson and colleagues will seek to identify common genetic variants that affect the risk for hip fracture in postmenopausal women participating in the WHI Clinical Trial and the Observational Study. This will be the first genome-wide association study of hip fractures. Due to advances in technology, the entire genome can now be scanned; in the first stage of this research project, the scientists will study 500,000 genetic variants, and those that look promising will be specifically investigated in the two subsequent stages.
- Predictive Value of Nutrient Biomarkers for Coronary Heart Disease Death, Tufts University, Boston, MA, Alice Lichtenstein, D.Sc. Dr. Lichtenstein and colleagues will determine the value of selected nutrient biomarker plasma concentrations (trans fatty acids, very long chain omega-3 fatty acids, phylloquinone, dihydrophylloquinone) in women who participated in the WHI Observational Study and died of CHD. The predictive value of these data relative to self-reported food intake will also be assessed. The results of this work will be of value in defining optimal approaches to evaluating the impact of dietary patterns on CHD risk in large groups of individuals.
- Ancestry Association Analyses of WHI Traits, University of California, Davis, CA, Michael Seldin, M.D., Ph.D. The investigators will examine the contribution of ancestry informative markers (AIMS) in DNA samples to differences in risk of CHD, stroke, breast cancer, and hip fractures in Blacks and Hispanics. They will also analyze genetic factors related to ancestry or country of origin affecting hip fracture and bone mineral density in Whites, and bone mineral density in Blacks. The results will be a valuable resource to assist other researchers who wish to combine data of minority groups with that of Whites.
- Biochemical Antecedents of Fracture in Minority Women, University of Pittsburgh, Pittsburgh, PA, Jane Cauley, Dr.P.H. This study will examine risk markers for fracture in groups of minority and white women. This study will be the first comprehensive investigation of biochemical factors leading to fracture in minority women. The results promise to explain differences in fracture rates and to help target prevention strategies.
- Hormone Therapy, Estrogen Metabolism and Risk of Breast Cancer or Hip Fracture in the WHI Hormone Trial, University of Pittsburgh, Pittsburgh, PA, Lewis Kuller, M.D., Dr.P.H. The goal of this study is to determine whether differences in estrogen metabolism in untreated women and women on estrogen or estrogen plus progestin determine risk of hip fracture and breast cancer. The research team will measure levels of two estrogen metabolites and evaluate their role as biomarkers of breast cancer and hip fracture. They will study whether estrogen metabolism differs by whether or not the estrogen is opposed by a progestin and if how a woman metabolizes estrogen on hormone therapy relates to the risk of hip fracture.

- Interaction Effects of Genes in the Inflammatory Pathway and Dietary, Supplement, and Medication Exposures on General Cancer Risk, Wake Forest University School of Medicine, Winston-Salem, NC, Jianfeng Xu, M.D., Dr. P.H. The study seeks to identify genetic variants in genes involved in inflammation and immunity which are associated with the risk of cancer (breast, colon and rectum, and lung) in European Americans and African Americans. The research team will test associations between dietary, supplement and non steroidal anti-inflammatory use (NSAID) with inflammatory markers and risk of overall cancer. They will then study interaction effects of genetic variants with dietary, supplement, and NSAID exposure on cancer risk.

The NHLBI intends to fund a second round of studies using biological specimens from the WHI in 2008.

Dr. Jacques Rossouw, WHI project officer, is available to comment on these awards and the NHLBI's interest in maximizing the scientific yield from this landmark study.

To schedule interviews with Dr. Rossouw, contact the NHLBI Communications Office at 301-496-4236. To interview Dr. Ho, call Karen Gardner, 718-430-3101, Albert Einstein College of Medicine, 718-430-3101; to interview Dr. I-Min Lee, call Jessica Podlaski, Brigham and Women's Hospital, 617-534-1603; to interview Dr. Cummings, call Kevin McCormack, California Pacific Medical Center, 415-600-2984; to interview Dr. Li or Dr. Prentice, call Kristen Woodward, Fred Hutchinson Cancer Research Center, 206-667-5095; to interview Dr. Jackson, call Michelle Gailiun, Ohio State University Medical Center, 614-293-3737; to interview Dr. Lichtenstein, call Siobhan Gallagher, Tufts University, 617-636-6586; to interview Dr. Seldin, call Carole Gan, UC – Davis Health System Public Affairs Office, 916-734-9047; to interview Dr. Cauley and Dr. Kuller, call Jim Swyers, University of Pittsburgh Medical Center, 412-586-9773; to interview Dr. Xu, call Karen Richardson, Wake Forest University Baptist Medical Center, 336-716-4453.

Part of the National Institutes of Health, the National Heart, Lung, and Blood Institute (NHLBI) plans, conducts, and supports research related to the causes, prevention, diagnosis, and treatment of heart, blood vessel, lung, and blood diseases; and sleep disorders. The Institute also administers national health education campaigns on women and heart disease, healthy weight for children, and other topics. NHLBI press releases and other materials are available online at: www.nhlbi.nih.gov.

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