ARIC MANUSCRIPT PROPOSAL #690

PC Reviewed: 08/25/99	**Status: Approved**	**Priority: 2**
SC Reviewed: _____	**Status: _____**	**Priority: _____**

1.a. Full Title:

Polymorphic Genes of Estrogen and Carcinogen Metabolism and the Risk of Breast Cancer

b. Abbreviated Title (Length 26):

Polymorphism and Breast Cancer

2. Writing Group (list individual with lead responsibility first):

Bharat Thyagarajan, Pam J. Mink, Kristin Anderson, Aaron Folsom, Myron Gross

Contact Information for Lead Author: Bharat Thyagarajan and Myron D. Gross, Ph.D.
Address: Division of Epidemiology
School of Public Health
University of Minnesota
Suite 300
1300 South 2nd Street
Minneapolis, MN 55454-1015

Phone: 612-624-5417 Fax: 612-625-8950

Electronic Mail Address: gross@epi.umn.edu

3. Timeline:

Case Ascertainment and Control Selection 9/99
Laboratory Analysis 10-11/99
Data Analysis 12/99
Manuscript Preparation 1-2/00

4. Rationale:

CYP19 and CYP1B1 are polymorphic genes with a role in estrogen and carcinogen metabolism. Estrogen metabolism, carcinogen activation and endogenous exposure may be influenced by the form of these genes which in turn may influence breast carcinogenesis. CYP1B1 has a polymorphism in exon 3 at nucleotide position 432 which results in a valine to leucine amino acid change. The leu form of CYP1B1 has been associated with estrogen and progesterone receptor status, and an

increased risk of breast cancer in one previous study (Cancer Research 1998;58(22):5038-41). A tetrad nucleotide repeat allele of CYP19 in intron 4 (171bp) has been associated with an increased risk of breast cancer in one previous study (British Journal of Cancer 1999;79:456-63). Individuals with one or both of the noted polymorphisms may have an increased risk of breast cancer.

5. Main Hypothesis:

Women with the M1 allele of CYP1B1 and/or the CYP19 allele with a 171 tetrad nucleotide repeat in intro 4 are at an increased risk of breast cancer.

6. Data (variables, time window, source, inclusions/exclusions):

Study Design: Nested case-control with a 2:1 match.
Analysis: conditional logistic regression
Genotyping of CYP1B1 and Cy19 will be done using stored DNA.

We have funds to support the analysis and no funds are requested from ARIC.

Breast cancer cases are identified as part of the ARIC Ancillary Cancer Study.

Additional variables will be obtained from visit 1 data and include age, race, study center, menopausal status, ages at menarche and menopause, waist-to-hip ratio, body mass index, weight at age 25, exogenous hormone use.

Information from the AHMA form will include age at firth birth, location history, family history of breast cancer, mammography.

Inclusions: Females ages >35 years.
Exclusions: Previous history of cancer.