1.a. **Full Title**: Mapping leanness genes in African American women from the Atherosclerosis Risk in Communities Study

b. **Abbreviated Title (Length 26 characters)**: Mapping leanness genes

2. **Writing Group (list individual with lead responsibility first)**:
   - **First**: Amy Heck
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   - **Other Writing Group Members**: Mary Hart, Deanna Hoelscher, Linda Kao, Aaron Folsom, Christie Ballantyne, Jim Pankow

3. **Timeline**:
   - Genotyping of the Illumina Linkage III mapping panel has been completed in an age-matched sample of lean (BMI less than or equal to 25 kg/m²) and morbidly obese (BMI greater than or equal to 35 kg/m²) African American women from the ARIC study. Analysis of the genetic mapping data is targeted for completion by December 2004 and a final paper will be completed by April 2004.

4. **Rationale**:
   - Despite the observation that a majority of the adult population is now considered overweight, a small proportion of mature individuals are of normal weight, and of particular interest are mature individuals who have maintained a normal weight into late adulthood without excessive caloric restriction or physical activity. The regulation of body mass and composition has been shown to have a substantial genetic component, and as such, there may be genetic mechanisms that enable these mature, lean individuals to avoid obesity despite an abundance of palatable food and lack of opportunity for exercise. Numerous candidate genes have been proposed for body size, with no single gene explaining common forms of obesity or associated with leanness in adults. Genetic linkage analysis is one strategy that has been successfully used to identify gene regions that may contain causative or susceptibility genes for disease. Association mapping using single nucleotide polymorphisms (SNPs) has been proposed as a powerful tool for identifying genes in well-defined case and control groups. We have genotyped lean (n=92) and obese (n=92) case/control groups of African American women (age 45-56 yrs) as a screening tool to identify chromosomal regions containing genes that may be associated with morbid obesity or leanness.
5. **Main Hypothesis/Study Questions:**

We will conduct high-density genome-wide association analysis, with the goal of identifying putative regions that may contain genes predisposing or protecting against obesity in mature African American women.

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

African American women will be used for these analysis. Genotype data for over 4,600 SNP markers with an average density of .78 cM has been completed in the case/control groups described above. Analyses for this type of data are emerging, and we will use the strategy of Lee (Genet Epidemiol 27:1-13, 2004) which involves a matched case/control design with genomic control to account for potential population substructure.

7.a. Will the data be used for non-CVD analysis in this manuscript?  **X** Yes  ____ No

b. If Yes, is the author aware that the file ICTDER02 must be used to exclude persons with a value RES_OTH = “CVD Research” for non-DNA analysis, and for DNA analysis RES_DNA = “CVD Research” would be used?  **X** Yes  ____ No

(This file ICTDER02 has been distributed to ARIC PIs, and contains the responses to consent updates related to stored sample use for research.)

8.a. Will the DNA data be used in this manuscript?  **X** Yes  ____ No

8.b. If yes, is the author aware that either DNA data distributed by the Coordinating Center must be used, or the file ICTDER02 must be used to exclude those with value RES_DNA = “No use/storage DNA”?  **X** Yes  ____ No

9. The lead author of this manuscript proposal has reviewed the list of existing ARIC Study manuscript proposals and has found no overlap between this proposal and previously approved manuscript proposals either published or still in active status. ARIC Investigators have access to the publications lists under the Study Members Area of the web site at: http://www.cscc.unc.edu/ARIC/search.php

  **X**  Yes  ______  No

10. What are the most related manuscript proposals in ARIC (authors are encouraged to contact lead authors of these proposals for comments on the new proposal or collaboration)?

None

11. Manuscript preparation is expected to be completed in one to three years. If a manuscript is not submitted for ARIC review at the end of the 3-years from the date of the approval, the manuscript proposal will expire.