NIH Award from the National Institute of Diabetes and Digestive and Kidney Diseases

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- Project: Epidemiologic Studies of Type 2 Diabetes in Normal Weight Adults
- Start Date: July 27, 2009
- Total Award Amount: $228,750

How the results of this project will benefit society:
Type 2 diabetes (T2DM) is a serious chronic medical condition. Approximately 15 percent of persons with T2DM are normal weight according to body mass index measurements (BMI<25 kg/m2). Findings from this study extend beyond the small proportion of normal weight persons with T2DM to provide a better understanding of risk factors other than overweight for T2DM and the cardiovascular consequences of T2DM.

The problem the project is trying to solve:
Using common measurements across studies and long-term follow up for illness and death, we will test whether established baseline clinical and demographic characteristics and candidate genes are more common in participants who are normal weight vs. overweight/obese at the time of incident T2DM and whether rates of illness and death from cardiovascular diseases differ between the two groups. By investigating the presence of an interaction between obesity and established genes for T2DM (PPARG, KCNJ11 and TCF7L2) in association with T2DM, we can begin to unravel the mechanisms by which these candidate genes are associated with T2DM.

How this project will work:
The metabolically obese normal weight (MONW) phenotype is a clustering of obesity-related metabolic disorders (e.g., T2DM, hypertriglyceridemia, hypertension) in persons with normal body mass index (BMI). T2DM in normal weight persons is an intriguing and understudied representation of the MONW phenotype that affects between 5-15 percent of persons with T2DM. We propose to pool together data from multiple existing longitudinal cohort studies to conduct an epidemiologic study of demographic and clinical characteristics, behavioral factors, and candidate genes associated with the development of T2DM in normal weight participants. Using longitudinal follow-up for clinical events in each of the studies, we will compare the rates of cardiovascular complications between normal weight and overweight/obese persons who experienced incident T2DM. The resulting pooled dataset will include a large, diverse (e.g., race/ethnic, gender, and age) sample of persons who can be classified at the time of incident T2DM as normal weight (BMI<25 kg/m2) or overweight/obese (BMI>25 kg/m2). Preliminary studies and published reports suggest that more than 2600 cases of incident T2DM, and the largest sample of normal weight persons with incident T2DM to date (~10 percent of total with T2DM), will be available to carry out the following aims: (1) compare the prevalence or mean levels of baseline demographic and clinical characteristics between normal weight and overweight/obese participants with incident T2DM; (2) test whether the relation between genotype and incident T2DM is modified by weight status at the time T2DM is identified; (3) compare the cardiovascular morbidity and mortality rates between normal weight and overweight/obese persons with incident T2DM. The successful completion of these studies can be expected to identify demographic and clinical characteristics associated with a higher likelihood of having T2DM despite being normal weight, and to determine whether three previously identified novel risk factors for T2DM (i.e., inflammation, autonomic nervous system function, and depressive symptoms) are predictors of disease in the absence of obesity.

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