NIH Award from the Eunice Kennedy Shriver National Institute of Child Health and Human Development

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- **Project:** Genome-Wide Association Scan of Polycystic Ovary Syndrome Phenotypes
- **Start Date:** August 15, 2009
- **Total Award Amount:** $2,393,203

How the results of this project will benefit society:
Polycystic ovary syndrome (PCOS) is the most common endocrine disorder of premenopausal women, affecting ~7 percent of this population. It is a leading cause of infertility, type 2 diabetes and metabolic syndrome that cost the U.S. healthcare system at least $4 billion annually. Identifying susceptibility genes should result in improved treatment for and prevention of PCOS.

The problem the project is trying to solve:
PCOS has major reproductive and metabolic morbidities across the lifespan, including markedly increased prevalence rates of obesity, type 2 diabetes (T2D), metabolic syndrome (MBS), and other cardiovascular disease (CVD) risk factors. It has been estimated that ~25 percent of premenopausal women with T2D have PCOS, making it perhaps the most common T2D subtype. The features of PCOS cluster within families providing evidence that genetic variation contributes to their pathogenesis. Indeed, male as well as female first-degree relatives have reproductive and metabolic phenotypes. Further, the cardinal reproductive feature of the syndrome, hyperandrogenemia, appears to play a direct role in the etiology of the associated metabolic abnormalities. Thus, although PCOS overlaps with obesity and T2D, its unique phenotypic features raise the fundamental question: Is PCOS a genetically distinct disorder or do the same obesity/T2D susceptibility genes interact with additional genetic or environmental factors resulting in the PCOS phenotype?

How this project will work:
Genome-wide association studies (GWAS) should provide more power than linkage mapping studies for localizing PCOS susceptibility genes. We have assembled an investigative team that has extensive experience in phenotyping PCOS and in the genetic analysis of complex diseases including GWAS. We have a large cohort of extensively and consistently phenotyped PCOS cases and will employ GWAS to identify PCOS susceptibility alleles in ~1,200 PCOS cases and ~3,600 unselected population-based female controls. These control cohorts have phenotypes such as BMI available. Promising variants will be further investigated using replication studies of the 1536 most promising SNPs in an independent cohort of ~1,800 PCOS cases and ~5,400 unselected female controls.

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