Diabetes-related work in the WHI: Progress report and ideas for 2010-15

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Diabesity

- **Rationale**
  - Descriptive epidemiology – “epidemic of our time”
  - Current understanding of pathophysiology as a unifying phenotype
  - Unique potential of WHI to study diabetes’ determinants and complications

- **Activities to Date (including ongoing)**
  - Outcome papers for the E+P, E alone, and DM trials
  - Biochemical and genetic markers for clinical diabetes
  - Clinical risk prediction model
  - CORE studies
    - WHI SHARe/GWAS/PAGE/GARNET/WISP
    - The basic biomarkers proposal for women in SHARe and case/cohort of HT women

- **Future**
  - Ancillary studies
  - Core studies/consortia
  - Manuscripts
Activities to Dates: Competed Manuscripts

A. Outcome papers for the E+P, E alone, and DM trials (3 papers)
   3. Tinker LF et al. Low-fat dietary pattern and risk of treated diabetes mellitus in postmenopausal women: the women’s health initiative randomized controlled dietary modification trial. *Arch Intern Med 2008*

B. Biochemical and genetic markers (~12 papers)
   • Liu S et al. Markers of Inflammation As Predictors of Type 2 Diabetes Mellitus. *Arch Intern Med 2007*
   • Song Y et al. Circulating Levels of Endothelial Adhesion Molecules and Type 2 Diabetes in An Ethnically Diverse Cohort of Women, *Diabetes 2007*
   • Song Y et al. Insulin Sensitivity and Insulin Secretion Determined by the Homeostasis Model Assessment [HOMA] Predict Risk of Type 2 Diabetes Mellitus. *Diabetes Care 2007*
   • FTO and obesity/diabetes…Obesity 2009
Ongoing work related to diabetes in the WHI

- Many paper proposals
  - Diet

- CORE studies
  - WHI SHARE/GWAS/PAGE/GARNET/WISP
  - The basic biomarkers proposal for women in SHARE and case/cohort of HT women

- Ancillary studies funded by NIDDK
  - Telomere length and related genes (AS254)
  - Sex steroids/SHBG/cytokines (AS238)
Ideas for 2010-2015

Future

Ancillary studies

- Forming a cohort of diabetics
- Evaluation of genetic and biochemical predictors for diabetic complications (Brain, cognitive functions, CVD, cancers etc)
- Evaluation of intervention/prevention strategies for diabetic complications (Brain, cognitive functions, CVD, cancers etc)
- Investigation of gene-diet interaction for diabetes and its complications
- Comparisons of prevalence and incidence of diabetes and its complications across ethnicities
- Evaluation of adverse effects of drugs among diabetics.

Core studies/consortia

Manuscripts
Proposed vascular pathogenesis related to diets and genes

Genes $\rightarrow$ Diets (e.g., high GL/insulin demand) $\rightarrow$ Obesity $\rightarrow$ Insulin resistance $\rightarrow$ Hyperglycemia $\rightarrow$ Hyperinsulinemia

- Dyslipidemia: $+\text{TG}$, $-\text{HDL}$
- Hypertension: $\text{Na}^+$ retention; SNS$^+$, Contractility$^+$
- Hemodynamic changes: inflammation, impaired fibrinolysis and thrombosis

Relative insulin deficiency $\downarrow$
- Glycation of LDL $\downarrow$
- Beta-cell mass; $\downarrow$
- Amyloid deposit $\uparrow$
- Glycation of LDL $\uparrow$
- Sorbitol $\uparrow$
- NO/vasodilatory response $\downarrow$

Coronary Heart Disease