**Dr. Henry Ginsberg**

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The ACCORD trial tested whether 1) intensive glucose control reduces cardiovascular disease (CVD) events more than standard glucose control, 2) intensive blood pressure control reduces CVD events more than standard blood pressure control, 3) treatment of dyslipidemia with simvastatin plus fenofibrate reduce CVD events more than treatment with simvastatin alone in people with type 2 diabetes mellitus (ACCORD Lipid). In ACCORD Lipid, although simvastatin plus fenofibrate did not significantly reduce CVD events compared to simvastatin alone, prespecified analyses demonstrated heterogeneity in response to fenofibrate by gender, race, and baseline lipid values with men, whites, and those with significant dyslipidemia appearing to have fewer CVD events. To better understand this heterogeneity, we propose to identify non-lipid biomarkers predictive of fenofibrate response. These include apoB, apoCIII, apoAI, apoAII, lipoprotein size and particle number, VLDL composition, including lipidomic profiling of VLDL TG fatty acids, fibrinogen, CRP, and homocysteine. Specifically we will 1) determine the ability of these biomarkers to predict the occurrence of CVD in a sub-cohort of ACCORD Lipid participants 2) assess the ability of fenofibrate to favorably modify these biomarkers and 3) determine the ability of these biomarkers to predict favorable responses to fenofibrate in the subgroups that demonstrated heterogeneity. We will focus our study on a case-cohort of 1800 individuals from the entire study cohort. However, as noted, we will also conduct analyses on three subgroups in which there appeared to be heterogeneity regarding the effects of fenofibrate treatment on CVD: men vs. women, whites vs non-whites, and dyslipidemics vs non-dyslipidemics.

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