**KIF6, LPA, TAS2R50, and VAMP8 Genetic Variation, Low Density Lipoprotein Cholesterol Lowering Response to Pravastatin, and Heart Disease Risk Reduction**

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**Background:** Specific single nucleotide polymorphisms (SNPs) at the KIF6 (kinesin-like protein 6, rs20455 or 719Arg), LPA (lipoprotein(a), rs3798220), TAS2R50 (taste receptor type 2, member 50, rs1376251) and VAMP8 (vesicle-associated membrane protein 8, rs1010) have previously been associated with low density lipoprotein (LDL) cholesterol lowering response to statins, cardiovascular disease (CVD) at baseline, or CVD events on trial.

**Methods:** We examined SNPs at the KIF6 (rs20455 or 719Arg), LPA (rs3798220), TAS2R50 (rs1376251) and VAMP8 (rs1010) in 5411 participants in PROSPER (PROspective Study of Pravastatin in the Elderly at Risk) (mean age 75.3 years), who had been randomized to pravastatin 40 mg/day or placebo and were followed for a mean of 3.2 years.

**Results:** No SNP was related to vascular disease at baseline. Only the KIF6 SNP was related to LDL cholesterol lowering with homozygous Arg 719 subjects being significantly less responsive than other groups (p=0.025, -34.2 vs. -36.1%). With regard to the primary CVD trial endpoint, we observed a significant relationship for both KIF6 Arg719 homozygotes (p=0.03, HR0.47) and the TAS2R50 AA genotype (p=0.03, HR1.76) only in women on pravastatin.

**Conclusions:** KIF6 rs20455 and TAS2R50 rs1376251 genotypes are not useful for predicting statin induced cardiovascular risk reduction in men, and predicts CVD risk reduction only in women in this elderly population. Genotyping with regards to KIF6 and TAS2R50 would affect about 13% and 9%, respectively of the women population and in our view would only be useful in elderly women either with established CVD or at high risk for CVD.