Abstract 1921: The L162V Polymorphism of the PPARA Gene is Associated With Stage C of Heart Failure

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Background: In human heart failure (HF) peroxisome proliferator–activated receptor alpha (PPAR alpha) is downregulated and consequently, the expression of genes involved in fatty acid oxidation repressed. The L162V (rs1800206) is a functional polymorphism of the human PPAR alpha gene (PPARA). In the present study we have investigated whether this polymorphism is associated with the development of stage C of HF.

Methods and Results: We analyzed the distribution of the L162V polymorphism in genomic DNA extracted from peripheral blood cells of 233 patients in stage A, 208 patients in stage B, 93 patients in stage C and 63 subjects in stage 0 of HF. The mRNA expression of the PPAR alpha target gene long–chain 3–hydroxyacyl–CoA dehydrogenase (LCHAD) was measured in myocardial biopsies of a subgroup of stages B and C patients. We performed functional studies of the L162V polymorphism in cultured HL–1 cardiomyocytes. The V162 allele was more frequent (P<0.05) in stage C patients than in stages 0, A and B subjects. Patients with the V162 allele exhibited decreased (P<0.05) myocardial LCHAD mRNA expression as compared to L162 homozygote patients. In addition, stage C patients exhibited lower myocardial LCHAD mRNA expression than stage B patients. PPAR alpha transcriptional activity and LCHAD mRNA expression were decreased (P<0.05) in cardiomyocytes transfected with the V162 compared to the L162 polymorphic PPAR alpha cDNA.

Conclusions: These findings suggest that the V162 allele of the human PPARA gene can be a new risk factor in the development of overt HF, likely via depressed cardiac PPAR alpha activity.