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NEUROMUSCULAR SIDE EFFECTS OF STATINS LINKED TO PAIN PERCEPTION BY PHYSIOGENOMICS TECHNOLOGY AT GENOMAS

Finding enhances the resolution of DNA-Guided Medicine to diagnose and prevent statin side effects for each individual patient

(Hartford, CT) -- Research by Genomas and collaborators at Hartford Hospital, University of California San Francisco and Yale has demonstrated a strong association between myalgia (muscle pain) arising during statin treatment and variability in genes related to pain perception. The research has been published in the September issue of the leading neurological journal *Muscle and Nerve*, published by Wiley InterScience. The findings suggest that serotonergic neurotransmitter receptor function may contribute to the muscle pain induced by statins in some patients inheriting specific variants of the receptor genes.

Statins effectively reduce coronary disease risk and are currently the most prescribed drugs in the USA. The main side effects are various neuromuscular ailments ranging from mild pain to disabling weakness. Until now, most of the neuromuscular effects of statins had been ascribed to muscular complications of treatment, as diagnosed by muscle biopsies, and suggested by the group’s prior finding of vascular smooth muscle involvement. The new study results relate muscle pain during statin therapy to genes of the serotonergic receptor system, a family of genes expressed primarily in the nervous system. The findings raise the possibility that statins may affect neural processes involved in the detection of pain, its processing, and responses to pain. The genes are the *HTR3B* and *HTR7* genes, which encode the 5a-hydroxytryptamine receptors type 3B and 7 that respond to the neurotransmitter serotonin. These results suggest that gene polymorphisms producing individual differences in pain perception may have an important role in the susceptibility of patients to neuromuscular side effects induced by the statins.

Paul D. Thompson, M.D., Chief of Cardiology, and Director of Preventive Cardiology at the Henry Low heart Center of Hartford Hospital and co-author of the study commented: "Growing evidence indicates that genetics determine who does and does not have muscle complaints with statins. These new results suggest a possible neural component, but we will need additional studies to prove this connection."

Gualberto Ruano, M.D., Ph.D., President, Genomas, stated: "The newly discovered link between statins and the serotonin receptor system is a powerful demonstration of the capabilities of our physiogenomics technology. These findings add to our expanding intellectual property portfolio to be deployed into PhyzioType™ Systems for statin safety and DNA-guided cardiovascular medicine. The findings enhance the resolution of our PhyzioType System to predict and differentiate clinical symptoms of disabling statin neuromuscular effects and to improve patient safety.”

MORE
**SCIENTIFIC BACKGROUND**

Physiogenomics – a medical application of sensitivity analysis – utilizes as input the variability of genes, measured by single nucleotide polymorphisms (SNPs) and determines how the SNP frequency among individuals relates to the variability in physiological characteristics, the phenotype. Using this approach, genetic associations to a phenotype are used to suggest physiological mechanisms underlying it.

Myalgia, or muscle pain, is one of the myriad symptoms grouped under myopathy. Myalgia is potentially debilitating and can cut into patient compliance to statin therapy, yet its origins have been hard to pinpoint. To search for physiologic factors possibly influencing muscle pain due to statins, the team examined the relationship between genes involved in pain detection and processing and a myalgia score in 195 hypercholesterolemic patients receiving either atorvastatin, simvastatin, or pravastatin at Hartford Hospital in Connecticut, USA. Patients were classified as having no myalgia, probable myalgia, or definite myalgia, and assigned a myalgia score of 0, 0.5, or 1, respectively. Physiogenomic analysis and a cross section of myalgia scores in these patients suggested that genetic variants in two neurotransmitter receptor genes, \textit{HTR3B} and \textit{HTR7}, are highly significantly associated with myalgia score in patients on statin therapy. Individual differences in pain perception and nociception related to these specific serotonergic gene variants may affect the development of myalgia in statin-treated patients.

**ABOUT GENOMAS**

Genomas®, Inc. is a biomedical company advancing DNA-guided medicine and personalized health. The company develops revolutionary PhyzioType™ systems for DNA-guided diagnosis and prevention of metabolic disorders induced by drugs in cardiovascular and psychiatric medicine. PhyzioType™ systems provide physicians with the unprecedented capability to select for each patient the safest drug treatment. Genomas is located in Hartford, CT on the campus of Hartford Hospital. For more information please access www.genomas.net

**ABOUT THE HENRY LOW HEART CENTER AT HARTFORD HOSPITAL**

The Henry Low Heart Center at Hartford Hospital provides the region’s best cardiac health options. It offers an array of comprehensive services and sophisticated techniques in a setting of highly personalized care. The Center is named for Dr. Henry Low, a pioneering cardiac surgeon who performed the first successful heart transplant operation in Connecticut in 1984. Within the Henry Low Heart Center are Laboratories for Cardiac Catheterization, Nuclear Cardiology, Electrophysiology; Clinics for Preventive Cardiology and Cardiac Rehabilitation; Cardiovascular Surgery, a Heart Transplant program, as well as separate Centers for Congestive Heart Disease, Chest Pain, and Heart Rhythm Disturbance. For more information please access www.hartfordhospital.org

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