Dissecting Inflammation to Understand Chronic Disease in Type 2 Diabetes

LA JOLLA, Calif., June 24, 2021 (SEND2PRESS NEWSWIRE) — Scientists are pursuing novel strategy to understand the source of inflammation in chronic diseases at the molecular level. They're discovering that inside cells, early genes regulate inflammatory networks before disease happens. Dr. Marcelo Freire, associate professor of genomic medicine and infectious diseases at The J. Craig Venter Institute, is among the scientists conducting this provocative research and he's the lead and senior author of a recent study, "Transcriptomics of type 2 diabetic and healthy human neutrophils."

Type 2 diabetes (T2D) is a chronic inflammatory disease affecting approximately 415 million people worldwide, and its prevalence is rising in adults, increasing the risk of developing co-morbidities such as inflammatory lesions on limbs, eyes and periodontal tissues. In fact, patients with diabetes are more prone to develop severe forms of COVID-19. Recently neutrophils have also been associated with inflammatory pathways in Sars-CoV-2 infections.

Thus, demonstrating that diabetics fail to respond to microbial/viral and

metabolic challenges due to deficiencies on immune cells. However, clinicians are unable to accurately predict which patients will develop chronic inflammatory and associated co-morbidities.

“Unravelling immune and lipid mechanisms of diabetes can advance our understanding of the disease,” Freire says. “We found that aberrant inflammation is a molecular source of chronic disease in type 2 diabetes and that’s reversible.”

In laboratory studies, researchers identified two pathways that dysregulate inflammation in type 2 diabetes. By employing a global analysis of RNA (transcriptomics) from innate immune cells, they discovered novel immune and lipid-related genes that are chronically suppressed.

Though chronic diseases such as type 2 diabetes have excellent therapeutic modalities that focus on blood sugar levels and insulin, none currently control the disease-associated chronic inflammation.

In this study, human neutrophils (the most abundant leukocytes in the blood) were evaluated via transcriptomics for the first time. This new survey of human neutrophils provides access to the scientific community about regulatory signatures and mechanistic information of in health versus disease.

“Collaborative efforts have been established to expand the knowledge in our lab and others to expand the field of neutrophils and investigate the source of inflammation to other organs,” Freire says.

Inflammatory networks derived from neutrophils can become informative in terms of early diagnostics of diabetics and future development of therapeutics.

For this work, the researchers treated human cells ex vivo with a novel fatty acid, resolvin E1 (RvE1), known for its pro-resolution functions. The application of this exogenous therapeutic showed that type 2 diabetics are not irreversibly damaged and that the treatments that reduce chronic inflammation may rescue the phenotype. Because Freire’s team has expertise in inflammation and the receptor-ligand axis, they were able to assay human cells with tailored amount of RvE1 to further advance precision medicine.

In addition to conducting RNA sequencing (transcriptomics) and analysis of full neutrophil transcriptomes, the team used cell culture to enhance concentrations of RvE1 for both healthy and diabetic neutrophils The scientists tested control treatments to account for placebo stimulation of cells, but genes that were deficient or saturated in diabetic subjects only changed after specific concentrations of RvE1 were added, demonstrating that chronically inflamed cells are responsive

“There’s much more research ahead, but the findings around unresolved inflammation should be a starting point to develop novel biomarkers for chronic disease severity and treatment,” Dr. Sarah Kleinstein, first author of the study, says.

Freire agrees that the research is just in the beginning and future plans include furthering their understanding of diabetic heterogeneity and diagnostic/therapeutic development.

“We aim to find a better solution to monitor and treat chronic inflammation,” Freire says.

Read an accelerated article preview of the study in BMC Immunology here: https://bmcimmunol.biomedcentral.com/articles/10.1186/s12865-021-00428-6

About the J. Craig Venture Institute

The J. Craig Venter Institute (JCVI) is a world leader in genomic research with 160 scientists and staff who are bold innovators fearlessly pursuing revolutionary ideas. It’s registered as a 501(c)(3) nonprofit organization and has a long track-record of creativity and an interdisciplinary approach to genomics. It’s committed to accelerating foundational scientific research to drive advances in human health and environmental sustainability.

For more information about JCVI: https://www.jcvi.org/