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New oxidative pathway of demethylation: Diabetes hyperglycemic effect in global DNA methylation and hydroxymethylation

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Type 2 Diabetes Mellitus (T2DM) is characterized by hyperglycemia and increased oxidative stress that could lead to chronic micro and macro-vascular complications. We hypothesized that part of the target organ damage is mediated by involving the epigenetic mechanism of DNA demethylation. It is currently believed that this process is catalyzed by the TET enzyme family; however, we explore another pathway mediated by high cellular oxidative environment, like the one present in diabetes. We measured glycated hemoglobin (HbA1C %) and global DNA methylation and hydroxymethylation in peripheral blood cells in 79 subjects: 19 well-controlled and 25 poorly controlled patients with T2DM, and 35 healthy controls. We also analyzed microarrays of DNA methylation and gene expression of other important tissues in the context of diabetes from the GEO database repository. According to the results, levels of DNA methylation and DNA hydroxymethylation were increased in poorly controlled patients compared to well controlled and healthy individuals ($p=0.0039$ for 5 mC, and $p=0.0034$ for 5 hmC). The analysis of methylation microarrays of the same tissue was concordant since levels of 5 mC were increased in T2DM blood as compared to controls. However, the levels of DNA methylation and hydroxymethylation in peripheral blood cells were contrary to the ones observed in other tissues such as pancreas, adipose tissue and skeletal muscle. Analysis of gene expression associated with DNA demethylation indicates that the TET-mediated enzymatic demethylation pathway is not sufficient to explain the changes found, and therefore there is a new and non-enzymatic pathway mediated by oxidative stress.

Biography

Diana Carolina Polania Villanueva has completed her Master's degree in Biological Sciences at Universidad de Los Andes. She is pursuing her PhD in Biology at the same university. She is currently conducting a research on the characterization of the DNA demethylation pathway using as biological models Diabetes and Cancer. Her research fields include Epigenetics, Genetics of Human Coagulopathies such as Hemophilia and von Willebrand disease, and Molecular Epidemiology of Cancer.

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