Abstract

Global DNA Methylation (GDM), an epigenomic modification has been linked to the development of Cardiovascular Disease and its risk factors. The research focus is to identify the relationship between cardiovascular fitness measurements and epigenetic alterations specific to chronic disease states in adult subjects. Twenty-six adult human subjects were required to complete a physical activity and diet questionnaire. Each individual donated a small blood sample (600 μL) in order for us to analyze the Global DNA Methylation (GMD). Then, their body composition was estimated by using the Dual-Energy X-ray Absorptiometry (DEXA Scan) machine. The Pearson’s “r” value was used to reveal the correlation between GDM and various variables, while t-tests were used to assess if any differences exists between high and low value groups for each variable. The Body Mass Index was significantly correlated (p-value; r value=0.331, -0.556) with GDM in females only. Individuals with high folate intake had significantly greater GDM than the low folate group (high=3.1±1.2%, low=2.3±0.7%, p=0.034) as determined by the diet questionnaire. No significant correlations or differences were found in males. The results conclude that as BMI increases, GDM decreases in females. In attempts to further investigate the relationships between GDM and these variables, auxiliary research needs to be conducted with larger subject pools containing additional sedentary participants.

Introduction

Epigenomics is the field of study of heritable alterations in gene expression potential that are not caused by changes in the actual DNA sequence (Waterland, R. A., 2009). These alterations to the genome result in differences to the future outcome or expression of the genetic information. Today there are three main mechanisms that contribute to epigenomic alterations: 1) DNA methylation, considered the primary mechanism, 2) histone modification, and 3) autoregulatory proteins that add in modification (Waterland, R. A., 2009). The levels of DNA methylation and the cardiovascular disease (CVD) association has been studied in many populations. Stenvinkel et al. (2007) and Lund et al. (2004) used a similar approach as Stevinkel. The GDM results were consistent with Stevinkel et al (2007).

Review of the Literature

In 2007, Stevinkel et al, came up with a similar approach as Lund et al. (2004) but their work was done on human subjects. Stevinkel et al identified the link between DNA methylation and cardiovascular disease development in chronic kidney disease (CKD) patients who have a higher risk of cardiovascular disease, and a control group. The control and the CKD group were monitored for the elevated global DNA methylation levels (by collecting blood samples) and the symptoms of cardiovascular diseases (by analyzing the inflammation and oxidative stress biomarkers) for a period of 36 months. The results revealed that the patients with CKD and inflammation had higher levels of methylation (p<0.001) and those who did not have inflammation had results similar to those in the control group. This study helps in concluding that patients that were developing cardiovascular diseases presented elevated levels of methylation or hypermethylation (Stenvinkel et al., 2007).

Another study came out three years later showing important aspects in regards to the levels of methylation in a population based study. Kim et al (2010) used a similar approach as Stevinkel. The levels of DNA methylation and the cardiovascular disease level were assessed in 286 males and females out of a 63257 population based cohort in Singapore over a five year period. At the beginning of the study, 101 subjects were identified with cardiovascular disease. Then, at the second meeting, another 52 subjects were developing cardiovascular diseases presented elevated levels of methylation or inflammation (Kimm et al., 2010)

Results

The Table 2.1 below shows the results.

Table 2.1 Summary of DNA Methylation and Disease Research

<table>
<thead>
<tr>
<th>Article</th>
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<td>Prevalence of atherosclerosis</td>
<td>GDM</td>
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<td>Stenvinkel et al. (2007) &amp; females</td>
<td>n=191 males</td>
<td>GDM</td>
<td>Inflammation measured by IL-6 and E</td>
<td>GDM in patients with inflammation</td>
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<tr>
<td>Kim et al. (2010) &amp; females</td>
<td>n=286 males</td>
<td>GDM</td>
<td>CVD</td>
<td>GDM in CVD patients</td>
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Conclusion/Further Research

A larger and more diverse sample set would provide for more conclusive results. A 2.7% GDM was obtained from this study (which is similar to the findings shown by McGuinness et al. (2012). The GDM ranges from 0.35 to 91% (Bromberg, Berschky, & Agam, 2009). As this study shows, there is not much consistency between the DNA isolation and GDM quantification, which makes the comparison between studies very misleading. An inverse relationship between BMI and GDM is present in females, but not in males. Subjects who reported higher levels of physical activity in their diets have increased levels of GDM than those who do not. A relationship between cardiovascular fitness via VO2max measurement, and GDM was not found. There is a need of more studies and for our case there is a need of a larger sample size because DNA methylation is an important biomarker in detecting the cardiovascular disease risk and its prevention.

References


Methodology

Subjects: Apparently healthy subjects (18-44 years old) primarily from the UNLV community

Instrumentation:
- Dual Energy X-ray Absorptiometry (DEXA)
- MOXUS Metabolic Cart
- Wizard Genomic DNA Purification Kit
- Methylink Global DNA Methylation Kit

Procedures:
- Informed Consent and Health Questionnaire
- Physical activity and diet questionnaire
- DEXA Scan
- VO2Max Test

Statistical Analysis
- Pearson Product-moment correlation coefficient (“r”) for GDM and VO2Max
- t-tests were used to assess if any differences exists between high and low value groups
- “r” value was used to reveal the correlation between GDM and various variables

Body Composition

- Neutral density
- Nucleosome
- Histone modification

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References