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Relationship of Global DNA Methylation with Cardiovascular Fitness and Body Composition

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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 evaluated by using the Dual-Energy X-ray Absorptiometry (DEXA Scan) machinery. 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; 0.031, -.556) with GDM in females only. Individuals with high folate intake had sig-nificantly 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 signifi¬cant correlations or differences were found in males. The results conclude that as BMI increases, GDM decreases in females. In attempts to further investigate the relation¬ships 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 measure, 2) histone modification, and 3) autoregulatory proteins that add in modification (Waterland, R. A., 2009).

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 kindney 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 of the remaining 185 were identified with cardiovascular disease. All the subjects with cardiovascular disease (n=153) and the ones without it (n=133) from the beginning of the observation had their DNA methylation levels analyzed. Although, the results obtained did not indicate significant difference for this population, the results were further analyzed after the samples were divided by gender. A higher level of global DNA methylation ($p<0.05$) was identified in the males with cardiovascular diseases versus those who did not have cardiovascular diseases. However, in females the results were not significantly different. These results were consistent with Stenvinkel et al (2007).

The Table 2.1 below shows the results.

Table 2.1 Summary of DNA Methylation and Disease Research

Article	Subjects	Dependent Variable	Independent Variable/s	Results
Lund et al. (2004)	n=27 mice	GDM	Prevalence of atherosclerosis	GDM
Stenvinkel et al. (2007)	n=191 males & females	GDM	Inflammation measured by IL-6 and C	GDM in patients with inflammation
Kim et al. (2010)	n=286 males & females	GDM	CVD	GDM in CVD patients

GDM – Global DNA Methylation, CVD – Cardiovascular Disease

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
- Methylamp Global DNA Methylation Kit

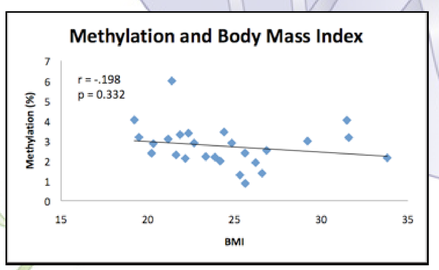
Procedures:

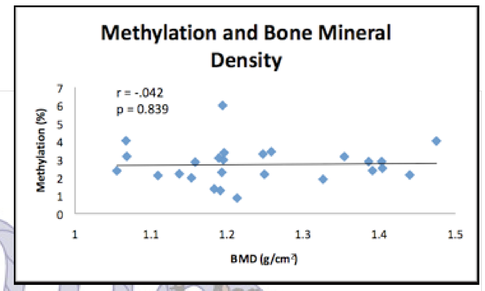
- Informed Consent and Health Questionnaire
- Physical activity and diet questionnaire
- DEXA Scan
- VO2Max Test

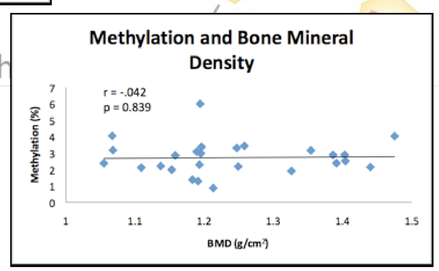
Statistical Analysis

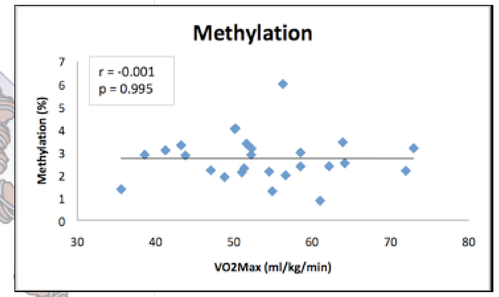
- Pearson Product-moment correlation coefficient ("r") for GDM and VO2Max as well as GDM and percent body fat.

Results









Conclusion/Further Research

A larger and more diverse sample with sedentary or less physically fit subjects would be necessary 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 0.85 to 91% (Bromberg, Bersudsky, & Agam, 2009). As this range 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 GDM and BMI is present in females, but not in males. Subjects who reported higher levels of folate 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.

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