The quest for 5th base – tracing environmental factors through time

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Introduction

In recent years, epigenetics has exploded into one of the most exciting and rapidly expanding fields in biology. Epigenetic regulation refers to biological mechanisms in which DNA, RNA, and proteins are chemically or structurally modified, *without* changing their primary sequence. Animal studies have shown that these regulations are influenced by transient environmental factors that can generate persistent changes for a life-long phenotypic consequence. Epigenetic regulatory mechanisms include for example DNA methylation and hydroxymethylation, histone modification, chromatin remodeling, and RNA methylation. Here, DNA methylation remains one of the most extensively studied areas of epigenetic research.

An interesting study was done in 2008 where a finite population who were prenatally exposed to starvation during the so called Dutch Hunger Winter in 1944-1945. This was in the western part of The Netherlands, during a well-defined period of time, where German food embargo resulted in equal daily food rations for every individual. Given also that food rations were documented, and healthcare and registries was still operational, these individuals who were prenatally exposed to this starvation could be traced. The study was focused on the imprinted gene IGF2 (insulin-like growth factor II), a key factor in human growth and development, and diseases like diabetes. Since methylation mark in IGF2 gene is stable up to middle age making the gene a good candidate for these studies.

For the 60 individuals who were conceived during the starvation period, the amount of methylation in regions within the IGF2 gene was significantly less compared to their siblings that were unexposed to the starvation. The lowest methylation was found in 43 of the starvation-exposed individuals out of the 60 sibling pairs (72%). Furthermore, the hypomethylation phenomenon was found to be time-specific. Individuals who were born in or shortly after the starvation period had no differences in IGF2 methylation compared to their unexposed siblings. This study was the first example to show an association between early conceptional exposure and DNA methylation in humans.

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Another interesting study was done on transgenerational effects for a population in the Överkalix parish in the northern of Sweden. During the 19th century and the first years of the 20th century the study area was isolated and the crops were often scarce. This provided a unique opportunity to study the association between food intake and risk for cardiovascular disease in future generations. The authors reasoned that exposure to either poor diet or plenty of food during a child's slow growth period (SGP, 8-12 years of age) could have transgenerational effects.

Interestingly, grandchildren to a paternal grandfather who was exposed to shortage of food supply during his SGP, were protected from cardiovascular death. This association was also the case for protection diabetes as the cause of death. In contrast, if the paternal grandfather was exposed to a surplus of food during his SGP, the grandchild had a four-fold risk for death caused by diabetes mellitus.

DNA methylation can be studied either globally in the genome or down to a basepair resolution. Bisulfite conversion, also known as bisulfite treatment, is used to deaminate non-methylated cytosine to produce uracil in DNA. Methylated cytosines (5-methylcytosines) are protected from the conversion to uracil, allowing the use of sequencing to determine their locations at single-nucleotide resolution. Bisulfite is considered the "gold standard" for downstream applications to assess DNA methylation status.

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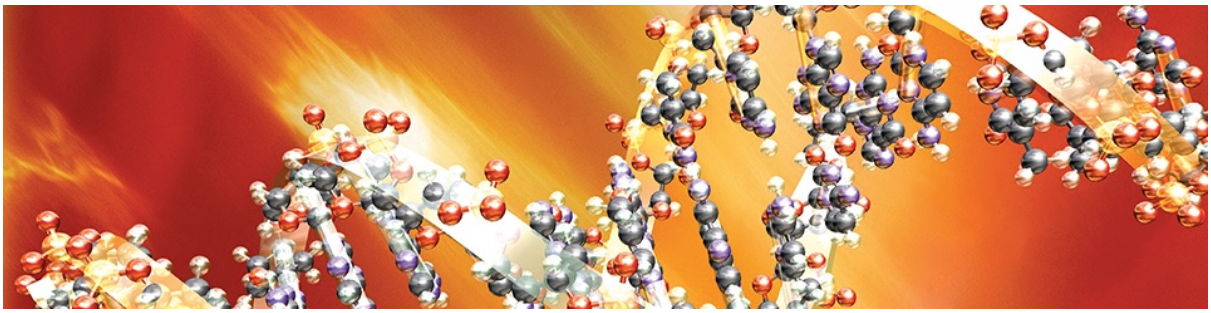

References

Bastiaan T. Heijmans et al., (2008) Persistent epigenetic differences associated with prenatal exposure to famine in humans, Proc Natl Acad Sci U S A, 105:44, 17046-17049.

Kaati G, Bygren LO, and Edvinsson S, (2002) Cardiovascular and diabetes mortality determined by nutrition during parents' and grandparents' slow growth period, Eur. J. Human Genetics, 10 682-688.

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