

Chicken consumption predisposes to diabetes through epigenetic modification by miRNAs: an in-silico prediction

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ABSTRACT

Diabetes is among the most worldwide occurring metabolic disorders. It has created a substantial socioeconomic burden because of no targeted therapy available to date. Epigenetic modifications are playing a significant role in its cause and cure. The food we eat can lead to epigenetic changes, which further can alter the expression of different genes. In the current research, we postulate that meat consumers might have a high risk of diabetes due to miRNA's ability to instigate epigenetic modifications of genes involved in diabetes. We performed bioinformatics analysis in which first we retrieved chicken miRNAs data from miRbase. Then we checked the interaction with target genes IGF2BP2, HNF1B, and TCF7L2 of obtained miRNAs utilizing miRanda and TargetScan databases. The interaction score obtained indicated good interaction between them. Based on the predicted miRNA-mRNA interactions score, we drew a miRNA network using miRNet software. The results obtained from this in-silico analysis suggest that chicken consumption may predispose diabetes through miRNAs associated with epigenetic modifications of the gene involved in diabetes. The outcome of this study can be further explored in cell-based, animal-based, and human-based studies.

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Introduction

Diabetes is one of the most prevalent chronic diseases. The affected population is still growing, and it is estimated that 4–5 million people will develop diabetes by 2030 (Guariguata et al., 2014; Cho et al., 2019). A combination of genetic, epigenetic, environmental, and lifestyle factors, such as diet, are responsible for the onset and development of T2DM (Ortega et al., 2017). Although we have not completely elucidated the

pathophysiology of T2DM so far, it is the case that the disease has a major genetic component. So far, vital genes associated with GWAS of different populations include IGF2BP2, SLC30A8, TCF7L2, HNF1B, HHEX, KCNQ11, CDKN2A/B, HMGA2, and NOTCH2-ADAM30 are involved as a major factor in the pathology of T2D (Pradhan et al., 2016). Higher concordance rates are found among monozygotic (96%) than dizygotic (DZ) twins in some not all twin studies, which has been compelling evidence of a significant genetic component in T2DM (Poulsen et al., 1999, 2009). Moreover, 40% of first-degree relatives of T2DM patients may develop diabetes, whereas the incident rate is only 6% in the general population (Kobberling, 1982). MicroRNAs (miRNAs) an epigenetic regulator, are noncoding RNAs of ~ 22 nucleotides that regulate gene expression post-transcriptionally by binding to the 3' untranslated region of messenger RNA (mRNAs), resulting in inhibition of translation or mRNA degradation (Hashimoto and Tanaka, 2017). miRNA shows participation in the β cell biology, insulin resistance, type I and type II diabetes mellitus, and its various complication in the whole anatomy and physiology of the human being (Tiwari et al., 2018).

Dietary nutrition plays an important role in the pathogenesis of T2DM, making the identification and analysis of nutrient-gene interactions a necessary step in the understanding of this chronic disease. Nutrigenomics, the area of nutrition that uses molecular tools to elucidate the influence of nutrients over the genome, proteome, and metabolome, provides a genetic understanding of how common dietary components lead to up and/or down-regulation of the gene (s) and changes in protein expression levels (Rana et al., 2016). Although several studies have confirmed a

strong association between meat consumption and susceptibility to T2DM and other metabolic disorders, including obesity, atherosclerosis, and even cancer (Vang et al., 2008; Aune et al., 2009; Pan et al., 2011), it has not yet been described as a diabetes risk factor.

In this study, we hypothesized that miRNAs present in chicken meat might regulate genes associated with diabetes. To confirm this hypothesis, we performed bioinformatics analysis in which first we retrieved chicken miRNAs data from miRbase, and then we checked the target genes of obtained miRNAs utilizing miRanda and TargetScan databases. Based on the predicted miRNA-mRNA interactions score, we drew a miRNA network utilizing miRNet software. The results obtained from this in silicon analysis suggest that chicken consumption may predispose diabetes through miRNAs associated with epigenetic modifications of the gene involved in diabetes. Hence this study gives insight into the future finding of these associations in cell-based assays, animal, and human models.

Materials and Methods

We used three different web-based bioinformatic algorithms to predict the miRNAs that target three different genes involved in diabetes. The programs are:

miRbase (<http://www.mirbase.org/>)

miRanda (<http://mirdb.org/>)

TargetScan7.2
(http://www.targetscan.org/vert_72/)

miRNet (<https://www.mirnet.ca/>)

The data of miRNAs present in *Gallus gallus* (Chicken) was retrieved from miRbase, and their regulation of three different genes, IGF2BP2, HNF1B, TCF7L2, was predicted based on interaction scores from two software miRanda & Targetscan7.2. Further interaction diagram was obtained from software miRNet.

Results and Discussion

As per the OECD meat consumption data, 14.20285 Kg/capita poultry, 12.31853 kg/capita pig, 6.508807 kg/capita beef, 1.715142 kg/capita sheep are consumed in 2018 and estimated to rise in coming decades. Several studies have confirmed the strong association between meat consumption and susceptibility to T2DM and other metabolic disorders (Vang et al., 2008; Aune et al., 2009; Pan et al., 2011).

Genetic components have been shown to be a prime predisposing factor for T2DM. The IGF2BP2 gene is located on chromosome 3q27.2 within a region linked to type 1 diabetes (T1D), type 2 diabetes (T2D), and diabetic nephropathy (DN) (Gu et al., 2012). IGF2BP2 has been found to be associated with decreased insulin secretion, which plays a role in T2DM. rs4402960 and rs1470579 of IGF2BP2 gene associated with T2DM susceptibility by comprehensive genetic association research (Rao et al., 2016). The gene encoding for transcription factor 7-like 2 (TCF7L2) is the strongest T2DM candidate gene discovered to date (Chen et al., 2018). The TCF7L2 gene is located on chromosome 10q25 in a region of replicated linkage to type 2 diabetes (Damcott et al., 2006). The TCF7L2 variant rs7903146 appears to affect the risk of T2DM, at least in part, by modifying the effect of incretins on insulin secretion (Villareal et al., 2010). Molecular defects of

hepatocyte nuclear factor 1B (HNF1B) are associated with a multiorgan disease, including diabetes (maturity-onset diabetes of the young 5) and kidney abnormalities (Dubois-Laforgue et al., 2017). In this study, we found the 3'UTR SNP (rs2229295) in the HNF1B gene was associated with the susceptibility of T2DM (Goda et al., 2015).

Hence, in this study, two bioinformatics tools, miRanda and TargetScan were used to determine the interaction between miRNAs present in chicken and IGF2BP2, HNF1B, and TCF7L2 based on miRanda score and context score++ percentile, respectively. The results predicted a strong association between them (Table 1). This interaction study indicated that the consumption of meat, especially chicken, would cause epigenetic modification of the genes involved in diabetes through the miRNAs present in chicken meat. Accordingly, prediabetics and those who have diabetes should avoid consuming chicken.

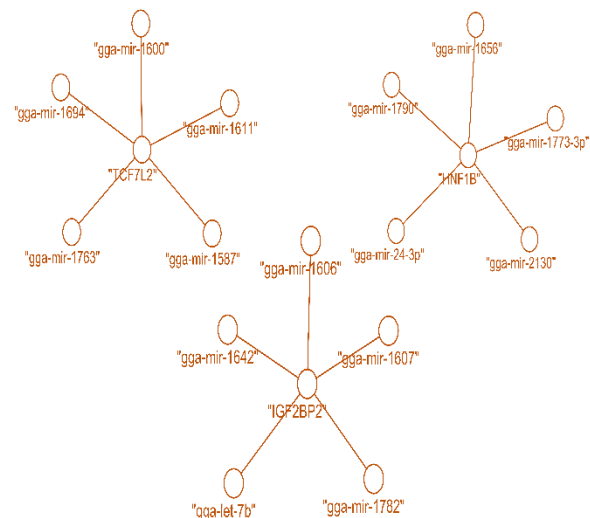


Figure: miRNA networking of chicken miRNAs and genes involved in diabetes. Network plotted and visualized utilizing miRNet.

Table 1: mRNA-miRNAs interaction table with corresponding interaction score

Gene	miRNAs	miRanda score	TargetScan score
<i>IGF2BP2</i>	gga-mir-1606	174	70
	gga-mir-1607	165	66
	gga-mir-1642	169	64
	gga-mir-1782	177	35
	gga-let-7b	178	95
<i>HNF1B</i>	gga-mir-24-3p	181	95
	gga-mir-1656	174	94
	gga-mir-1773-3p	167	85
	gga-mir-1790	165	92
	gga-mir-2130	167	68
<i>TCF7L2</i>	gga-mir-1600	155	94
	gga-mir-1611	181	80
	gga-mir-1694	173	74
	gga-mir-1763	169	48
	gga-mir-1587	168	44

gga: Gallus gallus (chicken)

Conclusion

Several miRNAs are present in chicken, and other meat may make a consumer susceptible to diabetes, as these miRNAs may epigenetically modify numerous genes associated with diabetes. Future research on cells, animals, and humans are needed to confirm further this finding that will be having clinical implication

Limitation of study

The current work is a preliminary study conducted employing the online available in silicon algorithms and databases. Thereby, the findings of this study are not confirmatory; hence, further in-vitro, in-vivo, and clinical studies are needed to confirm and validate the above findings.

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Conflict of interest

Declared none by the authors

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