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قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها

علي هذه الأقراص المدمجة قد أعدت دون أية تغيرات

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تحفظ هذه الأقراص المدمجة بعيدا عن الغبار

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The Clinical Utility of Transcription Factor 7-Like-2 (TCF7L2) Gene Polymorphism rs 12255372 in Type 2 Diabetes Mellitus.

Thesis

For partial fulfilment of master degree in clinical pathology

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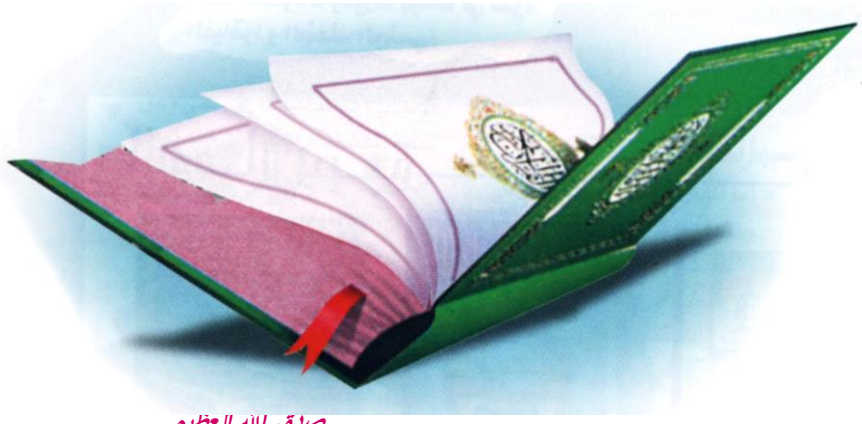
بسم الله الرحمن الرحيم

وَقُلِ اعْمَلُوا فَسَيَرَى اللَّهُ
عَمَلَكُمْ وَرَسُولُهُ وَالْمُؤْمِنُونَ



صدق الله العظيم

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Manar Hassan Farouk

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List of Abbreviations

A	: Adenine.
ADA	: American Diabetes Association.
APC	: Adenomatous Polyposis Coli.
AR	: Androgen Receptor.
BMI	: Body Mass Index.
CBP	: Catenin Binding Protein.
CE	: Cholesterol Esterase.
CK-1α	: Casein Kinase 1α.
CO	: Cholesterol Oxidase.
CTNNB1	: β-catenin gene.
DCCT	: Diabetes Control and Complications Trial.
DHPLC	: Denaturing High-Performance Liquid Chromatography.
DM	: Diabetes Mellitus.
DNA	: Deoxyribonucleic acid.
FAM	: Fluorescein amidites.
FPG	: Fasting Plasma Glucose.
Fzd	: Frizzled Proteins.
G	: Guanine.
GDM	: Gestational Diabetes Mellitus.
GIP	: Glucose-Dependent Insulin Tropic Peptide.

GLP-1 : Glucagon like Peptide-1.

GSK-3β : Glycogen Synthase Kinase-3β.

GWAS : Genome-Wide Association Studies.

HDL-C : High Density Lipoprotein Cholesterol.

HMG : High Mobility Group.

HS : Highly-Significant Difference.

IDF : International Diabetes Federation.

IFG : Impaired Fasting Glucose.

IGT : Impaired Glucose Tolerance.

IQR : Inter Quartile Range.

LDL-C : Low Density Lipoprotein-Cholesterol.

LEF : Lymphoid Enhancing Factor.

LRP5/6 : Low- density lipoprotein receptor-related proteins5 and 6.

MGB : Minor Groove Binder.

MODY : Maturity-onset Diabetes of the young.

NFQ : Non-fluorescent Quencher.

NGS : Next Generation Sequencing.

NGSP : National Glycohemoglobin Standardization Program.

NS : Non-Significant difference.

PEG : Poly Ethylene Glycol.

PKC : protein kinase c.

POD	: Peroxidase.
qPCR	: Quantitative Polymerase Chain Reaction.
RFLP	: Restriction Fragment Length Polymorphism.
ROS	: Reactive Oxygen Species.
S	: Significant Difference.
SNPs	: Single Nucleotide Polymorphisms.
SPSS	: Statistical Package for Social Science.
T	: Thiamine.
T1D	: Type 1Diabetes.
T2D	: Type 2 Diabetes.
TC	: Total Cholesterol.
T-CF	: T-cell factor.
TCF	: Transcription Factors.
TCF7L2	: Transcription Factor 7-like 2.
TG	: Triglyceride.
Tm	: Temperature.
VIC	: Victoria green fluorescent.
VLDL	: Very Low Density Lipoprotein.
β-cat	: β-catenin.
ΔHbA1c	: The difference between recent HbA1c (after 3-months therapy) and baseline HbA1c.
2-h PG	: Two-hours Plasma Glucose.

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INTRODUCTION

Diabetes mellitus (DM) is a group of metabolic disorders characterized by hyperglycemia resulting from defect of insulin secretion and/or increased cellular resistance to insulin ***(Yabe et al., 2015).***

The prevalence of DM is expected to increase by 55% in 2035 to reach 592 million of adults affected worldwide. Most of people with diabetes live in low and middle-income countries and those will experience the greatest increase in those cases of diabetes over the next 22 years ***(Guariguata et al., 2014).*** Therefore, it is crucial to understand the mechanisms that contribute to the pathogenesis of DM.

The metabolic disturbances of DM and chronic hyperglycemia lead to long term tissue and organ damage involving eyes, kidneys, neurons and vascular system**.** The vast majority of cases of diabetes fall into two broad etiopathogenetic categories of which 90% have type 2 diabetes mellitus (T2D) and no more than 10% have type 1 diabetes ***(Inzucchi et al., 2015; Chawla et al., 2016).***

In T2D, the much more common category, there is combination of resistance to insulin action and an inadequate compensatory insulin secretory response. It has been assumed that the underlying environmental factors may cause T2D only in the existence of genetic susceptibility ***(De SOuza et al., 2013; Cersosimo et al., 2018).***