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**Association of *CNTNAP2* gene Variants with Palestinian
Autism Patients**

Muhanad Said Suleiman Al-Qiq

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**Association of *CNTNAP2* gene Variants with Palestinian
Autism Patients**

Prepared by:

Muhanad Said Suleiman Al-Qiq

B.SC in Pharmacy Al-Quds University Palestine

Supervised by:

Dr.Hisham Darwish

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Biochemistry and Molecular Biology Department

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Association of *CNTNAP2* gene Variants with Palestinian Autism Patients

Prepared by: Muhanad Said Suleiman Al-Qiq

Registration Number: 21412369

Supervisor: Dr.Hisham Darwish

Master thesis submitted and accepted, Date: 26/10/2018

The names and signatures of the examining committee members are as Follows.

1-Head of Committee: Dr Hisham Darwish Signature

2-Internal Examiner: Dr Kifaya Azmi Signature

3-External Examiner: Dr Muhanad Khdeir Signature



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Dedication

To my family...

To my friends...

To my Teachers...

To all the people who supported me

Muhanad Said Suleiman Al-Qiq

Declaration:

I certify that this thesis submitted for the degree of master degree in Biochemistry and molecular biology is the results of my own research work, except where otherwise acknowledged. The results in this study has not been submitted for any other degree or publication in other universities or institution

Signed:

Muhanad Said Suleiman Al-Qiq

Date: 26/10/2018

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Abstract

Autism is a neuro developmental disorder that involve various defects with vary severity such as lack of communication, social behavior or speech development. So far, the cause of autisms is still unknown; however, it is thought that genetic background might play a major role in the disorder. Various variants within the CNTNAP2 gene were linked to autism in many populations. Our objective focused on investigating the association of selected polymorphisms in the CNTNAP2 gene with Autism and its clinical symptoms.

A case control study was conducted between 45 autism patients and 145 healthy individuals. Using PCR-RFLP technology and direct DNA sequencing regarding to specific studied single nucleotide polymorphisms within the gene. The correlation between the genotype distribution and allele frequency between autism patients and healthy individuals and the clinical symptoms of the disease was analyzed using Pearson chi squared test (SPSS 22).

No significant association could be detected between the rs 2710102 and rs 7794745 variants between the autism patients and control subjects .significant correlation was evident between specific genotype interaction between the two SNP sites and the disease. Specific genotype association between one specific SNP variant in rs 2710102 and the ability for self-expression was evident.

Table of contents:

| Item | Page |
|--|-------------|
| Dedication | |
| Declaration..... | I |
| Acknowledgment..... | II |
| Abstract..... | III |
| Table of content..... | IV |
| List of tables | VII |
| List of figures..... | VIII |
| List of abbreviation | IX |
| | |
| Chapter One: introduction..... | 1 |
| 1.1. Background | 1 |
| 1.2. Diagnosis..... | 2 |
| 1.3. Epidemiology..... | 3 |
| 1.4. Economic burden..... | 5 |
| 1.5. Risk factors..... | 5 |
| 1.5.1 Maternal and paternal age..... | 5 |
| 1.5.2 Offspring sex..... | 6 |
| 1.5.3. Prenatal and neonatal environment..... | 6 |
| 1.5.6 Vitamins level..... | 7 |
| 1.6. Morphological features and minor anomalies..... | 7 |
| 1.7. Role of Genetics..... | 9 |
| 1.8. Role of Epigenetic..... | 10 |
| 1.9. Mortalities..... | 10 |
| 1.10. Treatment..... | 11 |
| 1.10.1 Psychosocial treatment | 11 |

| | |
|---|-----------|
| 1.10.2 Dietary treatment..... | 11 |
| 1.10.3 Pharmacological treatment..... | 12 |
| 1.11. Literature review..... | 12 |
| 1.11.1 CNTANP2 gene..... | 13 |
| 1.11.2 Molecular interaction in CNTANP2 gene leading to different neurological disorders..... | 15 |
| 1.11.3 Functional mutation in CNTANP2 gene in different neurological disorders..... | 17 |
| 1.11.4 Effect of CNTANP2 variants on brain structure in autism or related disorder..... | 19 |
| 1.11.5 Effect of CNTANP2 gene variants on different neurological disorders..... | 19 |
| 1.11.6 Effect of CNTANP2 gene variants on Autism in different populations..... | 20 |
| 1.12 Study objectives..... | 23 |
| Chapter Two: Methodology..... | 24 |
| 2.1 Study design..... | 24 |
| 2.2. Study Subjects and blood sampling..... | 24 |
| 2.3. Study Area..... | 24 |
| 2.4. Methods of the study..... | 25 |
| 2.4.1 DNA extraction..... | 25 |
| 2.4.2 PCR Amplification..... | 26 |
| 2.4.3 Restriction Fragment Length Polymorphism (RFLP)..... | 28 |
| 2.4.4 Sequencing Analysis..... | 29 |
| 2.4.5 Statistical Analysis..... | 29 |
| 2.4.6 Ethical Consideration..... | 29 |
| Chapter Three: Result..... | 30 |
| 3.1 Patients records..... | 30 |
| 3.2 DNA quality | 32 |
| 3.3 PCR amplified gene fragments | 33 |
| 3.4 PCR-RFLP analysis | 34 |
| 3.5 Direct DNA sequencing..... | 36 |

| | |
|--|-----------|
| 3.6 Statistical correlation of the indicated genotypes for rs 2710102 and rs 7794745 sites with the disease | 37 |
| 3.7 Correlation between the genotypes of the rs 2710102 and rs 7794745 haplotypes with various clinical expression of the diseases..... | 40 |
| Chapter Four: Discussion..... | 42 |
| 4.1 Conclusion..... | 45 |
| 4.2 Recommendations..... | 45 |

List of tables:

| Table No. | Title of the table | Page No. |
|------------------|--|-----------------|
| Table 1 | Concentration and purity of representative DNA samples..... | 26 |
| Table 2 | Sequence of the primers needed to amplify the DNA fragment containing the two indicated SNP..... | 27 |
| Table 3 | The indicated restriction enzymes for every studied variant and the cut position..... | 28 |
| Table 4 | Patients medical records involved in the study..... | 31 |
| Table 5 | Correlation of the indicated genotype between control and case with The disease status | 38 |
| Table 6 | Correlation of combined individual genotypes of the indicated haplotypes with the Disease status..... | 38 |
| Table 7 | Distribution of various genotypes rs 2710102 and rs 7794745 between males and females subjects..... | 39 |
| Table 8 | Correlation between haplotypes combination rs 2710102 and rs 7794745 in control and Autism patients..... | 40 |
| Table 9 | correlation between haplotypes and patients major altered behavior | 41 |

List of figures:

| Figure No. | Content | Page No. |
|-------------------|--|-----------------|
| Figure 1 | Diagram summarizing prevalence study in autism from studies older than 1980 to 2010, designated at 5 years intervals.....4 | 4 |
| Figure 2 | Autisms effect on brain 8 | 8 |
| Figure 3 | location of the CNTNAP2 gene.....13 | 13 |
| Figure 4 | Caspr2 protein localization..... 14 | 14 |
| Figure 5 | Domains of CNTNAP2 gene product CASPR2..... 16 | 16 |
| Figure 6 | The location of the variants within CNTNAP2 gene..... 21 | 21 |
| Figure 7 | Quality of genomic DNA prepared from patients and control32 | 32 |
| Figure 8 | Gel electrophoreses showing PCR amplified DNA fragments containing the rs7794745 and rs 2710102 SNPs33 | 33 |
| Figure 9 | Gel electrophoresis showing RFLP analysis for selected control samples....34 | 34 |
| Figure 10 | Gel electrophoresis showing RFLP analysis for selected patient's samples..35 | 35 |
| Figure 11 | Representative sequencing and alignment result of selected DNA samples regarding the rs 2710102 and rs 7794745 variants.....37 | 37 |

List of Abbreviations:

| Abbreviation | Term |
|---------------------|---|
| ASA | American psychiatric association |
| ASD | Autism spectrum disorder |
| ABA | Applied behavioral analysis |
| GWA | Genome wide association study |
| <i>CNTANP2</i> | Contactin associated protein gene |
| SNP | Single nucleotide polymorphism |
| DSM | Diagnostic and Statistical Manual of Mental Disorders |
| CNTNAP2 | Contactin associated protein gene |
| STOX1A | Storkhead box A1 |
| TCF4 | Transcription factor 4 |
| FOXP1 | Forkhead box P1 |
| FOXP2 | Forkhead box P2 |

Chapter One

Introduction

1.1. Background

Autism came originally from a Greek word means “self”. A physician named Eugen Bleuler first used the autism term in 1911 referring to symptoms in schizophrenia. Later, in 1944 and 1943 two American psychiatrics Leo Kanner and Hans Asperger took the pioneering step in redefying autism as individual disease with varying onset of psychological symptoms, being what is called Asperger syndrome is the milder case ("Autismus Hamburg - Was ist Autismus", 2018).

Recently Autism spectrum disorder ASD is defined according to American Psychiatric Association by deficits in social communication and social interaction on many levels, such as deficits in social interchange, nonverbal communicative behaviors used for social interaction, and skills in developing, maintaining, and understanding relationships (American Psychiatric Association, 2013). Most of autism patients fail to achieve independency in adult life. In fact, minor percentage lived on their own or had constant jobs. The most patients needed help from their families and failed to be independent (Howlin, Goode, Hutton & Rutter, 2004). About 15-47% of patients achieved improvement in symptoms upon development, however at 2 years of age the symptoms begin to appear again and lose the improvement in speech and social skills. (Stefanatos, 2008) For many years, Autism and other closely related neurodevelopmental disorder, which are also considered subtypes of Autism such as Asperger syndrome, Rett syndrome, childhood disintegrative disorder, and pervasive developmental disorders, were diagnosed individually as a single condition according to the Diagnostic and Statistical Manual of Mental Disorders (DSM IV). In the last edition of the DSM , all of these subtypes are included under one classification known as Autism spectrum disorder (ASD) and the indicated subtypes are no longer diagnosed separately as individual disorder but under one condition named ASD with varying severity (American Psychiatric Association, 2013).

1.2. Diagnosis:

According to DSM 5, ASD diagnosed according to the following criteria:

A. Permanent lack of ability in social communication and interaction that include:

1. Difficulties in social and emotional contact such as, showing no interest in expressing feeling or interest or emotions. Also showing malfunction in responding to social interaction.
2. Difficulties in nonverbal communication like failure to maintain eye contact or proper body language.
3. Difficulties in forming and comprehending relationship, like showing no interest in making friends.

B. Restrained and repetitive form of behaviors, showing interest or activities as specified by at least two of the followings:

1. Repetitive motor movement like stereotyped playing style or using of objects or pattern of speech
2. Persistent attachment to certain routine or forms of verbal or non-verbal behavior Like eating the same food or taking the same route every day and showing extreme rage for small changes and modifications
3. Intense and abnormal concentration in certain interests in unusual objects and showing strong attachment
4. Showing hyper or hypo reactivity in sensory input or abnormal reaction to sensory changes in environment, like abnormal response to sound, temperature or pain

C. Symptoms must exist in early childhood and become fully visible later until social demands overwhelm the limited capability

D. Symptoms cause clinically significant deficits in social functioning.

العلاقة بين المتغيرين الجينيين (rs7794745 rs2710102) في جين ال *CNTNAP2* مع مرضى التوحد الفلسطينيين

اعداد: مهند سعيد سليمان الفيق

اشراف: د. هشام درويش

الملخص:

التوحد هو اضطراب النمو العصبي الذي ينطوي على عيوب مختلفة مع شدة متفاوتة مثل عدم التواصل والسلوك الاجتماعي أو تطوير الكلام. حتى الآن، ما زال سبب التوحد مجهولاً، ومع ذلك يعتقد أن الخلفية الوراثية للإصابة بالتوحد قد تلعب دوراً كبيراً في هذا الاضطراب

ارتبطت المتغيرات الجينية في جين *CNTNAP2* مع الإصابة بالتوحد في العديد من الدراسات السابقة التي تناولت شعوب أخرى. وبالتالي كنا مهتمين للتحري عن مدى ارتباط المتغيرات الجينية (rs7794745) و(rs2710102) في جين *CNTNAP2* مع مرض التوحد في المرضى الفلسطينيين.

أجريت الدراسة بين عامي 2016 و2018. شملت الدراسة 45 من مرضى التوحد و145 من الأفراد الأصحاء. تم استخدام تقنية (PCR-RFLP) لتحديد المتغيرات الجينية لدى المرض والأصحاء وقد تم جمع البيانات الطبية للمرض من الجمعيات والمراكز المختصة.

لمقارنة التوزيع الوراثي في المتغيرات الجينية في مجموعة التوحد والمجموعة صحية وأيضاً لمقارنة البيانات الطبية للمرضى تم استخدام برنامج ال SPSS

لم يعثر على أي ارتباط مهم في المتغيرات 2710102 و7794745 والتوحد داخل المرضى الفلسطينيين لكن عن طريق التفاعل ما بين المتغيرات قد نكون توصلنا الى ارتباط قوي مع مرض التوحد