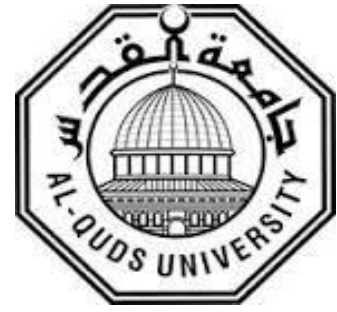


**Deanship of Graduated Studies**  
**Al-Quds University**



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

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**M.Sc. Thesis**

**Jerusalem - Palestine**

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

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

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**Jerusalem- Palestine**

**1440 - 2018**

## **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.

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## List of Abbreviations:

<b>Abbreviation</b>	<b>Term</b>
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	Diagnositic and Statistical Manual of Mental Disorders
CNTNAP2	Contactin associated protein gene
STOX1A	Storkhead box A1
TCF4	Transcription factor 4
FOXP1	Foorkhead box P1
FOXP2	Foorkhead box P2

# Chapter One

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## 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