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The genetics of autism spectrum disorder

Submission date	Recruitment status	[ ] Prospectively registered
25/10/2022	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
31/10/2022	Completed	[X] Results
Last Edited	**Condition category**	[ ] Individual participant data
30/09/2025	Mental and Behavioural Disorders	

Plain English summary of protocol

Background and study aims
Autism or autism spectrum disorders are complex developmental disorders that have dramatically increased in prevalence over the past few decades. They are characterised by varying degrees of impairments in social interaction and communication, and the exhibition of stereotypic (repetitive) behaviours. Identification of individuals at higher autism risks is of great importance as this would enable the early use of interventions/therapies that address the symptoms of this disorder, which may be beneficial to patients with autism given the known benefits of early treatment on reducing autistic symptoms. The search for any new genetic markers associated with autism development would help in such identification. Such a search may also help identify new drug targets for autism treatment. There is therefore a need to identify any new genetic variations that are present in autistic individuals. This study aims to use a combination of optical mapping and Nanopore sequencing technology to identify genetic variants among a group of individuals with autism.

Who can participate?
Individuals diagnosed with autism (aged 2 years or above) and their relatives.

What does the study involve?
After providing informed consent, the participants with autism and their family members will have 5-10 ml of blood drawn for genetic analyses. The mother or guardian will also be asked to complete a questionnaire collecting demographic information, the personal and family history of autism, any possible exposure to stress, medication, infections and other complications during pregnancy/birth, and the observable autism-related symptoms among the participants.

What are the possible benefits and risks of participating?
Participants may benefit from the acquisition of knowledge of the potential variants that may be present in autistic children. In addition, parents with children who might have a higher risk of autism (e.g. having already an older sibling diagnosed with dyslexia) would have the benefit of knowing the possible genetic factors associated with autism, enabling them to understand the genetic variations that they should be looking for through genetic testing in assessing the autism risk of their further children. The risk of participating in this study would be the potential discomfort and distress caused by blood sample collection. There may also be a low risk of infection.

Where is the study run from?
1. The Chinese University of Hong Kong (Hong Kong)
2. The Prince of Wales Hospital (Hong Kong)

When is the study starting and how long is it expected to run for?
June 2022 to September 2025

Who is funding the study?
The Nethersole School of Nursing, The Chinese University of Hong Kong (Hong Kong)

Who is the main contact?
Prof Sek Ying Chair, sychair@cuhk.edu.hk

Contact information

Type(s)
Principal investigator

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Additional identifiers

Protocol serial number
1

Study information

Scientific Title
To find endophenotypes of patients with autism spectrum disorder by phenotype and genotype correlation

Study objectives
There are risk alleles that increase the susceptibility of autism in Hong Kong Chinese children and these risk alleles might be different from those reported in other populations.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 08/09/2022, the Joint Chinese University of Hong Kong – New Territories East Cluster Clinical Research Ethics Committee (Joint CUHK-NTEC Clinical Research Ethics Committee, 8/F, Lui Che Woo Clinical Sciences Building, Prince of Wales Hospital, Shatin, Hong Kong; +852 (0) 3505 3935; crec@cuhk.edu.hk), ref: 2022.425

Study design
Single-centre prospective cohort study

Primary study design
Observational

Study type(s)
Other

Health condition(s) or problem(s) studied
Autism spectrum disorder

Interventions
Current interventions as of 03/11/2023:

Upon the provision of informed consent, the participants with autism and their family members will have 5-10 ml of blood drawn for genetic analyses. The mother or guardian will also be asked to complete a questionnaire collecting demographic information and the personal and family history of autism, any possible exposure to stress, medication, infections and other complications during pregnancy/birth, and the observable autism-related symptoms among the participants.

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Previous interventions:

Upon the provision of informed consent, the children and their family members will have 5-10 ml of blood drawn for genetic analyses. The mother or guardian will also be asked to complete a questionnaire collecting demographic information and the personal and family history of autism.

Intervention Type
Other

Primary outcome(s)
Current primary outcome measure as of 03/11/2023:

Measured at a single timepoint:
1. Success rate for systematic recruitment and ascertainment of autistic subjects who had no positive findings in previous genomic studies for the genotype and phenotype study of Hong Kong Chinese children using optical mapping. This will be measured by records of the number of individuals approached, the number of individuals recruited to the study, and the number of approached individuals who refused to participate in the study. These records will be taken during participant recruitment.
2. Structural variants in genes that are associated with autism, assessed via genetic analyses of the DNA extracted from the participants' blood samples.

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Previous primary outcome measure:

Measured at a single timepoint:
1. Success rate for systematic recruitment and ascertainment of autistic subjects who had no positive findings in previous genomic studies for the genotype and phenotype study of Hong Kong Chinese children using optical mapping. This will be measured by records of the number of individuals approached, the number of individuals recruited to the study, and the number of approached individuals who refused to participate in the study. These records will be taken during participant recruitment.
2. Structural variants in genes that are associated with autism in children, assessed via genetic analyses of the DNA extracted from the participants' blood samples

Key secondary outcome(s))
Endophenotypes in carriers of autism susceptibility risk alleles, assessed via clinical records at a single timepoint

Completion date
30/09/2025

Eligibility

Key inclusion criteria
Current inclusion criteria as of 03/11/2023:

1. Reported by the parents to be autistic or autism spectrum disorder (ASD) with confirmation from health care professional workers. The probands must have received a valid and reliable assessment and must meet cutoffs for autism spectrum or autism. (e.g. the newest Autism Diagnostic Observation Schedule [ADOS] algorithms to be used for Modules 1 - 3 and the original cutoff algorithms to be used for Module 4; or a clinical “Best Estimate Diagnosis,” of Autistic Disorder, Asperger’s Disorder, or Pervasive Developmental Disorder-Not Otherwise Specified [PDD-NOS], according to the Diagnostic and Statistical Manual of Mental Disorders [DSM-IV-TR]).
2. Age: The proband must be aged 2 or above when the phenotype measures are administered, any first and second-degree relatives and their parents (autistic or not) will also be recruited in anticipation that these samples will be valuable resources for further understanding of the genetic factors that might contribute to the phenotype.
3. Being ethnic Chinese

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2. Age: The proband must be between 2 to 18 years of age when the phenotype measures are administered, any first and second-degree relatives and their parents (autistic or not) will also be recruited in anticipation that these samples will be valuable resources for further understanding of the genetic factors that might contribute to the phenotype.
3. Being ethnic Chinese

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
All

Lower age limit
2 years

Sex
All

Total final enrolment
26

Key exclusion criteria

Current exclusion criteria as of 03/11/2023:

1. With significant injury, abnormality, or disease having effects upon the brain, extensive complications during birth or pregnancy (careful screening will be carried out for those who stayed in the hospital for more than 3 days after birth)
2. With sensory or motor deficits that preclude the effective use of the diagnostic tools
3. Other known genetic disorder: e.g. Down's syndrome, or Fragile X syndrome
4. Those diagnosed with a known genetic disorder, and those with a psychiatric disorder requiring medication

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Previous exclusion criteria:

1. With significant injury, abnormality, or disease having effects upon the brain, extensive complications during birth or pregnancy (careful screening will be carried out for those who stayed in the hospital for more than 3 days after birth)
2. With sensory or motor deficits that preclude the effective use of the diagnostic tools
3. With significant nutritional and psychological deprivation
4. Other known genetic disorder: e.g. Down's syndrome, or Fragile X syndrome
5. Those diagnosed with a known genetic disorder, and those with a psychiatric disorder requiring medication

Date of first enrolment
25/10/2022

Date of final enrolment
30/09/2024

Locations

Countries of recruitment
Hong Kong

Study participating centre
The Prince of Wales Hospital
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Shatin
The New Territories
Hong Kong
Hong Kong
N/A

Sponsor information

Organisation

Chinese University of Hong Kong

ROR
https://ror.org/00t33hh48

Funder(s)

Funder type
University/education

Funder Name
Chinese University of Hong Kong

Alternative Name(s)
The Chinese University of Hong Kong, , , Hēunggóng Jūngmàhn Daaihhohk, CUHK,

Funding Body Type
Government organisation

Funding Body Subtype
Universities (academic only)

Location
Hong Kong

Results and Publications

Individual participant data (IPD) sharing plan
The data collected and analysed during the study will be presented in the results section of a future publication, after necessary de-identification.

IPD sharing plan summary
Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		29/05/2025	30/09/2025	Yes	No