

Multicenter study on the genetic screening and diagnosis of deafness in China

Submission date 27/05/2020	Recruitment status No longer recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 16/06/2020	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
Last Edited 11/06/2020	Condition category Genetic Diseases	<input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year

Plain English summary of protocol

Background and study aims

According to the data of the national survey in 2006, there are about 27.8 million hearing and speech-disabled people in China, and about 700,000-800,000 hearing-impaired children under 7 years old. One in every 500 newborns has bilateral permanent deafness. Before the age of 5, the incidence of deafness increases to 2.7%, and to 3.5% in adolescence. Research shows that more than 60% of pre-lingual deafness is caused by genetic factors, and the rest is caused by environment or other unknown genetic factors.

As the first genetic hearing loss molecular diagnosis center in China, the genetic deafness molecular diagnosis center of PLA General Hospital has been established for 15 years. A series of achievements have been made in the research of the causes of deafness, discovery of new genes, the molecular epidemiology of deafness in the Chinese population, clinical gene diagnosis and prenatal diagnosis.

The emergence of next-generation sequencing has achieved high throughput and low cost, which brings a broad prospect for the field of gene diagnosis. At present, many gene testing institutions in China have carried out deafness gene testing services, mainly for the most common 3-4 hotspot mutation chips of deafness gene in Chinese population, and 129-167 deafness gene sequencing services. According to the research results of the researchers' center, four common gene mutations can explain about 40% of the causes of deafness, while the detection rate can rise to about 50% - 55% when the detection range is extended to more than 129 deafness genes by high-throughput sequencing technology. Although the improvement of diagnosis rate makes more deaf families or high-risk families obtain genetic consultation and prevention guidance, the promotion and implementation of deafness gene diagnosis and prenatal diagnosis in China still face a series of problems. The testing quality level of testing institutions is uneven, with a lack of standards. The testing report has not yet formed a standard, and the interpretation of variants is not clear. Testing institutions and clinical doctors give inaccurate genetic consultations. There is a lack of a referral and consultation system and process for difficult cases, and a lack of a biological database for deafness in China. The above deficiencies have greatly affected the summary of deafness molecular big data, the guidance of deafness family reproduction and the accurate treatment evaluation of deaf patients.

Therefore, the PLA general hospital takes the lead in launching the clinical multicenter research project of deafness gene diagnosis, cooperating with domestic deafness gene testing institutions such as the medical institutions of major provinces and autonomous regions,

MyGenostics Inc.; GrandOmics Inc.; WuXi NextCODE Inc.; Capital Genomics Inc. This multicenter study aims to draw a gene map of Chinese people by collecting 10,000 genetic samples; develop clinical consensus/guidelines for the diagnosis of genetic deafness; standardize deafness gene test, report interpretation and genetic consultation; and upgrade the deafness gene test panel.

Who can participate?

Patients with congenital hearing loss or late-onset hearing loss and their families, or patients with acquired sensorineural hearing loss and their families, and hearing normal individuals with a family history of deafness.

What does the study involve?

Patients will take hearing tests, a CT scan and, if necessary, a general examination (thyroid ultrasound, kidney ultrasound, electrocardiogram, chest, abdomen, limbs X-ray, cranial MRI, etc). The researchers collect patients' and their family's medical record information, and collect their blood samples. The genetic testing institution completes the gene test and preliminary data analysis, and the original data will be sent to the designated cloud platform of multicenter for verification and further analysis. The test report will be issued by the testing institution, and approved by the PLA General Hospital and/or qualified sub-centre experts. The PLA General Hospital and the clinical experts of the sending unit will jointly provide patients with genetic consultation. For the cases with suspected pathogenic mutations, the testing institution will provide follow-up research programs. For the cases with no or suspected pathogenic mutation, the leading units of multiple centers will analyze the data again, and discuss the follow-up research plan through regular case discussion and academic activities.

What are the possible benefits and risks of participating?

Taking part in this study can help patients to reduce the risk of deafness in their offspring. It should be noted that this study can not completely exclude the risk of deafness in the next generation, such as pregnancy infection, other environmental factors or rare unknown deafness caused by genetic defects. If the report result is negative, senior experts will re-analyze the report, except for false negatives. If it is positive, it will be verified free of charge, except for false positives. Difficult and complex cases will be provided with priority referral and consultation channels.

Where is the study run from?

Genetic Deafness Molecular Diagnosis Center, PLA General Hospital, Beijing, China

When is the study starting and how long is it expected to run for?

September 2018 to August 2022

Who is funding the study?

Investigator initiated and funded

Who is the main contact?

Prof. Pu Dai

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Contact information

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Additional identifiers

Clinical Trials Information System (CTIS)

Nil known

ClinicalTrials.gov (NCT)

Nil known

Protocol serial number

Study information

Scientific Title

Clinical demonstration for three-level prevention intervention of birth defect on monogenic disease (deafness)

Study objectives

The main purpose of this multicenter study is to draw a gene map of Chinese people by collecting 10,000 genetic deafness samples and develop clinical consensus/guidelines for the diagnosis of genetic deafness.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Approved 26/7/2018, ethical review board of PLA General Hospital (Fuxing Road 28, Beijing, China; +86 (0)10 66937166; 301irb@sina.com), ref: S2018-088-01

Study design

Multicenter observational epidemiological study

Primary study design

Observational

Study type(s)

Screening

Health condition(s) or problem(s) studied

Genetic deafness

Interventions

The patients and their families will provide blood samples. Next-generation sequencing and Sanger sequencing will be carried out on the samples. The testing institution will analyze preliminary data. The PLA General Hospital and the clinical experts of the sending unit will jointly provide patients with genetic consultation. For the cases with suspected pathogenic mutations, the testing institution will provide follow-up research programs. For the cases with no or suspected pathogenic mutation, the leading units of multiple centers will analyze the data again, and discuss the follow-up research plan.

Intervention Type

Other

Primary outcome(s)

1. Number of cases in the database of genetic deafness patients in China at 5 years
2. Gene map of genetic deafness patients in China measured using the coverage of pathogenic variant on genetic deafness in the public database at 5 years

Key secondary outcome(s)

1. Genetic deafness panel measured using coverage and accuracy of pathogenic variant on genetic deafness in the public database at 5 years
2. Guidelines of screening and diagnosis for genetic deafness patients in China measured using the published journal articles at 5 years

Completion date

31/08/2022

Eligibility

Key inclusion criteria

1. Congenital hearing loss or late-onset hearing loss and their families
2. Patients with congenital malformation of auditory organ and their families
3. Acquired sensorineural hearing loss patients and their families
4. Hearing normal individuals with a family history of deafness

Participant type(s)

Mixed

Healthy volunteers allowed

No

Age group

All

Sex

All

Key exclusion criteria

1. The patients and their families who refused to participate in the program after receiving the education by doctors
2. The patients with deafness caused by non-genetic factors were definitely diagnosed

Date of first enrolment

09/01/2018

Date of final enrolment

31/08/2022

Locations

Countries of recruitment

China

Study participating centre

Chinese PLA General Hospital
Fuxing Road 28, Haidian District
Beijing

China
100853

Study participating centre

China Rehabilitation Research Center for Hearing and Speech Impairment

A 8 Huixinli, Chaoyang District

Beijing

China

100029

Study participating centre

The General Hospital of the PLA Rocket Force

16 xinjiekouwei st, Xicheng District, Beijing

Beijing

China

100088

Study participating centre

Beijing Children's Hospital of Capital Medical University

56 Nanlishi Road, Xicheng District

Beijing

China

100045

Study participating centre

China-Japan Friendship Hospital

Yinghuayuan East st, Chaoyang District

Beijing

China

100029

Study participating centre

Beijing Tongren Hospital of Capital Medical University

1 Dongjiaomin Lane, Dongcheng District

Beijing

China

100730

Study participating centre

Peking University First Hospital

8 Xishiku St, Xicheng District
Beijing
China
100034

Study participating centre

Bo Gao Peking University Third Hospital

49 Huayuan North Road, Haidian District
Beijing
China
100191

Study participating centre

Peking Union Medical College Hospital

41 Damucang Hutong, Xicheng District
Beijing
China
100032

Study participating centre

Beijing Friendship Hospital of Capital Medical University

95 Yong'an Road, Xicheng District
Beijing
China
100050

Study participating centre

Shanghai Ninth People's Hospital

No. 639, Manufacturing Bureau Road, Huangpu District
Shanghai
China
200011

Study participating centre

Fujian Medical University ShengLi Clinical College, Fujian Provincial Hospital

134 East Street
Fuzhou
China
350001

Study participating centre

Union Hospital Tongji Medical College Huazhong University of Science and Technology

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Wuhan

China

430022

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The First Affiliated Hospital of UTSCAnhui Provincial Hospital

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Hefei

China

230001

Study participating centre

XiangYa Hospital CentralSouth University

87 Xiangya Road

Changsha

China

410008

Study participating centre

Nanfang Hospital

1838 North Guangzhou Avenue

Guangzhou

China

510515

Study participating centre

Maternal and Child Health Care Hospital of Guangdong Province

521 Xingnan Avenue, Panyu District

Guangzhou

China

511400

Study participating centre

Tianjin First Central Hospital

24 Fukang Road, Nankai District

Tianjin

China
300192

Study participating centre

Precision medicine research center of Zhengzhou University / precision medicine application center of the Second Affiliated Hospital of Zhengzhou University

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China
450000

Study participating centre

Henan Provincial People's Hospital, Department of Otolaryngology Head and Neck

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China
450003

Study participating centre

Hebei Medical University Second Hospital

215 Heping West Road
Shijiazhuang
China
050000

Study participating centre

Maternal and Child Health Care Hospital of Tangshan

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Tangshan
China
63017

Study participating centre

Children's Hospital of Hebei Province

133 Jianhua South Street, Yuhua District
Shijiazhuang
China
050030

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Jinan
China
250022

Study participating centre
Jinan Maternal and Child Care Hospital
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Jinan
China
250000

Study participating centre
Children's Hospital of Nanjing Medical University
72 Guangzhou road, Gulou District
Nanjing
China
210000

Study participating centre
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20 Zhengdong Road
Zhenjiang
China
212001

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The Affiliated Hospital of Guizhou Medical University
28 Guiyi street
Guiyang
China
550004

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First Affiliated Hospital of Kunming Medical University
295 Xichang Road
Kunming
China
650032

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730030

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Xian
China
710032

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230000

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Hefei
China
230013

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Hefei
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230601

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Jilin University Second Hospital
218 Ziqiang street, Nanguan District

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China
130041

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The Fourth Affiliated Hospital of China Medical University
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Shenyang
China
110032

Study participating centre
Yanbian University Hospital
Juzi Street 1327
Yanji
China
100191

Study participating centre
Shenyang Women's and Children's Hospital
No. 87, Danan street, Shenhe District
Shenyang
China
110011

Study participating centre
The First Affiliated Hospital of China Medical University
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Shenyang
China
110001

Study participating centre
The Children's Hospital, Zhejiang University School of Medicine
57 Zhugan lane
Hangzhou
China
310003

Study participating centre
Maternal and Child Health Hospital of Liuzhou
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545001

Study participating centre
The People's Hospital of Guangxi Zhuang Autonomous Region Department of Otolaryngology
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Nanning City
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Study participating centre
Second Hospital of Shanxi Medical University
No. 382, Wuyi Road
Taiyuan City
China
030001

Study participating centre
Xinjiang Viger Municipal People's Hospital
No.91, Tianchi Road, Tianshan District
Urumqi City
China
830001

Study participating centre
Qinghai Provincial People's Hospital
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Xining
China
810007

Study participating centre
General Hospital of Ningxia Medical University
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750004

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330006

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630038

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315031

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Ningbo
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310006

Study participating centre

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310006

Study participating centre

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450007

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510080

Study participating centre
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730050

Study participating centre
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100080

Study participating centre
Shenyang No.4 People's Hospital
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Sponsor information

Organisation
Chinese PLA General Hospital

ROR

<https://ror.org/04gw3ra78>

Funder(s)

Funder type

Other

Funder Name

National key research and development project (2016YFC1000700)

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are/will be available upon request from Prof. Pu Dai (daipu301@vip.sina.com), Prof. Yongyi Yuan (yyymzh@163.com) and Dr Bo Gao (imjd@163.com). The next-generation sequencing data for genetic deafness can be shared with groups who would like to participate in the trial during the research, and all data will be submitted to the public database (e.g ClinVar) in 3 years after the the end of the trial.

IPD sharing plan summary

Data sharing statement to be made available at a later date