Safety and validity evaluation of HIV immune gene CCR5 gene editing in human embryos

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Registration number:	ChiCTR1800019378
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Registration Status:	Retrospective registration
Public title:	Safety and validity evaluation of HIV immune gene CCR5 gene editing in human embryos
English Acronym:	
Scientific title:	Evaluation of the safety and efficacy of gene editing with human embryo CCR5 gene
The registration number of the Partner Registry or other register:	

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Applicant postcode:		Study leader's postcode:	
Applicant's institution:	Southern University of Science and Technology		

Approved by ethic committee:	Yes		
Approved No. of ethic committee:	20170307	Approved file of Ethical Committee:	查看附件View
Name of the ethic committee:	Medical Ethics Committee of Shenzhen HOME Women's and Children's Hospital		
Date of approved by ethic committee:	2017-03-07		
Contact Name of the ethic committee:	Huang Huafeng		
Contact Address of the ethic committee:	12018 Shenlan Road, Nanshan, Shenzhen, Guangdong, China		
Contact phone of the ethic committee:		Contact email of the ethic committee:	

Primary sponsor:	South University of Science and Technology of China
Primary sponsor's address:	1088 Xueyuan Road, Nanshan, Shenzhen, Guangdong, China

Secondary sponsor:

Country:	China	Province:	Guangdong	City:	
Institution hospital:	South University of Science and Technology of China	Address:	1088 Xueyuan Road, Nanshan, Shenzhen, Guangdong, China		
Country:	China	Province:	Guangdong	City:	
Institution hospital:	Shenzhen HarMoniCare Women & Children's Hospital	Address:	12018 Shenlan Road, Nanshan, Shenzhen, China		

Source(s) of funding:	Shenzhen Science and Technology Innovation Free Exploration Project
Target disease:	HIV
Target disease code:	
Study type:	Relative factors research
Study phase:	Other
Objectives of Study:	HIV-induced AIDS is a major medical problem that threatens all human beings in today's world, affecting the safety and health of all human beings. To date, there is no effective drug or clinical technique to completely cure AIDS. Fortunately, governments and scientists around the world have invested a lot of energy in HIV prevention and post-infection interventions. However, we are far from achieving the WHO's 2020 HIV prevention goals and have a long way to go to eliminate HIV. The only HIV-infected person who has been recognized as completely cured in the world is the Berlin patient". At that time, the patient developed leukemia and was diagnosed as HIV-positive before the bone marrow stem cell transplant. The German doctor used a bone marrow matching to creatively treats leukemia in this patient with a rare CCR5 genetic mutation existing in Western European population resistant to HIV-1. To date, "Berlin patient" has not detected with HIV in the body, creating a new medical model for HIV elimination. The current clinical trial is based on preclinical research of cell lines, animal models and human waste embryos. It recruits HIV-positive patients with infertility and informs the volunteers of the risks and benefits through sufficient informed consenting. The informed consent form is signed through one-on-one discussion. The study design was submitted to the ethics committee of the hospital for discussion and approval. Through the CCR5 gene editing of the human embryo in a comprehensive test system, we set to obtain healthy children to avoid HIV providing new insights for the future elimination of major genetic diseases in early human embryos.
Description for medicine or protocol of treatment in detail:	
Study design:	Case series
Inclusion criteria	1. Married couple living in the People's Republic of China with HIV seropositivity (female negative, male positive); 2. Men and women 22–38 years old; 3. Males are clinically stable, failing to detect viral load of <75 copies/mL; screening for CD4 counts > 250; at least in the past 12 months with a history of continuous antiretroviral therapy; 4. Clinically confirmed to meet the medical guidelines for IVF therapy; 5. Fully informed consent of the couple to understand the purpose, risks and benefits of the trial; 6. Both subjects are willing to commit to using preventive contraception or maintaining abstinence for at least two months before egg collection and within one month after birth.
Exclusion criteria:	1. The viral load of the father before sperm collection is > 75 copies / mL; 2. Mother or father has genetic variation within the target sequence of the CRISPR/Cas9 gene editing; 3. Mother or father has genetic variation, creating a novel, high-probability off-target site for CCR5-targeted gene editing; 4. During the study, natural pregnancy or fertilization failed after two oocyte stimulation cycles; 5. Previously multiple in vitro fertilization (IVF) attempts failed; 6. Contraindications to use drugs during pregnancy; 7. With endocrine-related diseases, sexual hormones are at abnormal levels; 8. Currently using chemoradiotherapy drugs to treat tumor-related diseases; 9. Participated in or recently participated in another clinical trial using a research diagnostic test, drug or device; 10. Subjects with other diseases, including alcohol abuse or mental illness, that may influence the current protocol based on the researcher or clinician's judgment.
Study execute time:	From2017-03-07To 2019-03-07

Interventions:

Group:	Case series	Sample size:	20
Intervention:	CCR5 gene editing	Intervention code:	

Countries of recruitment and research settings:

Country:	China	Province:	Guangdong	City:	
Institution hospital:	Shenzhen HOME Women's and Children's Hospital	Level of the institution:			

Outcomes:

Outcome:	Pregnancy and guarantee one or more live births	Type:	Primary indicator
Measure time point of outcome:		Measure method:	
Outcome:	Father, mother and progeny genome-wide deep sequencing analysis	Type:	Primary indicator
Measure time point of outcome:		Measure method:	

Collecting sample(s) from participants:

Sample Name:	BLOOD	Tissue:	
Fate of sample:	Destruction after use	Note:	
Sample Name:	EMBRYOS	Tissue:	
Fate of sample:	Others	Note:	

Recruiting status:	Recruiting	Participant age:	Min age 22 years Max age 38 years
		Gender:	Both

Randomization Procedure (please state who generates the random number sequence and by what method):	AIDS public welfare organizations randomly distributes questionnaires to find qualified volunteers, recruitment interviews, medical examinations at hospitals, and signing informed consent.
Blinding:	N/A
Calculated Results ater the Study Completed(upload file):	download
The time of sharing IPD:	Within six months after the trial complete
The way of sharing IPD"(include metadata and protocol, If use web-based public database, please provide the url):	Provide URL and data after six months of trial
Data collection and Management (A standard data collection and management system include a CRF and an electronic data capture:	Clinical trial data will be collected using the case report form (CRF). The data will be managed by an electronic data capture (EDC) system. Results will be reported 6 months after the study completes.
Data Managemen Committee:	有/Yes

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