The Association Between SNRK and Vascular Endothelial Aging

Version: 1.0

Date: April 30th, 2026

Ethics Committee

Tianjin Medical University General hospital

Protocol Abstract

Title	The Association Between SNRK and Vascular Endothelial Aging
Ethics Committee (Grant Number)	The ethics committee of Tianjin Medical University General Hospital (IRB2026-YX-172-01)
Project Executor	Minghui Zou (Ph.D.)
Sponsor	Tianjin Medical University General Hospital
Participant	Xuefu Street Community Health Service Center of Tianjin Nankai District, Santan Hospital of Tianjin Nankai District，Tianjin Hongqiao District Hospital of Traditional Chinese Medicine
Principal Investigator	Xintong Ge - Tianjin Medical University General Hospital
Research Coordinator	Wei Guo - Tianjin Nankai District Xuefu Street Community Health Service Center Jinyi Yang - Tianjin Nankai District Santan Hospital Tan Zhang - Tianjin Hongqiao District Traditional Chinese Medicine Hospital
Fundings	National Natural Science Foundation of China General Program
Execute Time	05/01/2026-04/30/2029
Recruiting Time	05/01/2026-04/30/2029
Objective	To investigate the correlation between *SNRKAS* and carotid vascular structure and endothelial function by measuring the levels of the SNRK-upstream lncRNA (*SNRKAS*) in subjects' peripheral blood in conjunction with carotid ultrasound examinations, thereby providing a scientific basis for elucidating new mechanisms underlying the onset and progression of vascular aging and identifying novel therapeutic targets.
Study Type	Experimental studies, Prospective cohort studies
Time Perspective	Prospective
Enrollment	180 participants
Biospecimen	Description: Serum; Retention: Samples without DNA
Condition	Vascular aging
Inclusion Criteria	1) Aged 18–80 years, with the capacity to make decisions independently or

	represented by an authorized legal guardian; 2) Able to provide complete personal information, medical history, and lifestyle history (e.g., smoking and alcohol consumption history); 3) No history of severe cardiovascular disease, and deemed eligible for inclusion by a physician.
Exclusion Criteria	1) Women who are pregnant or may become pregnant; 2) Patients with a history of neurological disorders, tumors, severe cardiovascular or pulmonary disease, liver failure, kidney failure, or blood disorders; 3) Patients who have undergone carotid stenting, carotid endarterectomy, or other similar procedures, or who have unilateral carotid artery occlusion due to any cause; 4) Patients who have participated in other clinical trial in the past 4 weeks; 5) Individuals deemed unsuitable for this clinical trial by the investigators.
Withdrawal Criteria	1) Failure to complete the required bilateral carotid ultrasound and blood tests within the study-specified timeframe; 2) Blood samples exhibiting severe hemolysis, lipemia, or improper storage, rendering subsequent parameter testing impossible; 3) Voluntary withdrawal from the study by the patient or their family; 4) Withdrawal of the patient from the study as determined by the physician or investigator.
Outcome Measures	1) Serum levels of SNRKAS detected by RT-PCR 2) Degree of bilateral carotid atherosclerosis detected by Doppler ultrasound 3) Blood lipids levels detected by automated biochemical analyzer
Reference standard	Boon RA, Hofmann P, Michalik KM, et al. Long Noncoding RNA Meg3 Controls Endothelial Cell Aging and Function: Implications for Regenerative Angiogenesis. J Am Coll Cardiol. 2016; 68: 2589-2591.
Statistical Analysis	All statistical analyses were performed using SPSS Statistics Version 27.0 (IBM, Armonk, NY, USA). A two-tailed p value of less than 0.05 was considered to be statistically significant.

1. Research Background and Objectives

Cardiovascular diseases pose a serious threat to public health, and their prevalence is on the rise year by year. Vascular aging is an independent risk factor for cardiovascular diseases, and endothelial cell senescence is an early event in vascular aging. Its occurrence can lead to endothelium-dependent vasodilation dysfunction, reduced vascular permeability, and the release of the senescence-associated secretory phenotype (SASP). These vascular pathological changes further damage the vascular media, leading to vascular remodeling and reduced compliance, accelerating the progression of atherosclerosis, and ultimately resulting in cardiovascular diseases such as coronary heart disease and hypertension. Recent research of the investigators has revealed that SNRK, a new member of the AMPK family of cellular energy sensors, plays a key regulatory role in vascular development. Based on this finding, the investigators propose the scientific hypothesis that SNRK responds to both physiological and pathological aging stimuli through differential mechanisms and regulates the process of endothelial cell senescence. In this study, the investigators will explore the correlation between *SNRKAS* and carotid vascular structure and endothelial function by measuring the levels of the SNRK upstream lncRNA (*SNRKAS*) in participants' peripheral blood, in conjunction with carotid ultrasound examinations. The findings will provide a solid scientific basis for elucidating new mechanisms underlying the onset and progression of vascular aging and for identifying novel therapeutic targets.

2. Study design

2.1 Overall design

This study is an experimental, observational, prospective cohort study.

2.2 Estimated number of subjects

Estimated by statistical analysis, a total of 180 subjects were included from individuals who come for physical examinations or medical visits to the leading and collaborating administrations of this project, and meet the inclusion criteria between April 2026 and March 2029. Enrollment will target three age groups, each consisting of 60 participants: <40 years, 40–60 years, and >60 years.

3. Inclusion, Exclusion and Withdrawal Criteria

3.1 Inclusion Criteria

1) Aged 18–80 years, with the capacity to make decisions independently or represented by an authorized legal guardian;

2) Able to provide complete personal information, medical history, and lifestyle history (e.g., smoking and alcohol consumption history);

3) No history of severe cardiovascular disease, and deemed eligible for inclusion by a physician.

3.2 Exclusion Criteria

1) Women who are pregnant or may become pregnant;

2) Patients with a history of neurological disorders, tumors, severe cardiovascular or pulmonary disease, liver failure, kidney failure, or blood disorders;

3) Patients who have undergone carotid stenting, carotid endarterectomy, or other similar procedures, or who have unilateral carotid artery occlusion due to any cause;

4) Patients who have participated in another clinical trial within the past 4 weeks;

5) Individuals deemed unsuitable for this clinical trial by the investigators.

3.3 Withdrawal criteria

1) Failure to complete the required bilateral carotid ultrasound and blood tests within the study-specified timeframe;

2) Blood samples exhibiting severe hemolysis, lipemia, or improper storage, rendering subsequent parameter testing impossible;

3) Voluntary withdrawal from the study by the patient or their family;

4) Withdrawal of the patient from the study as determined by the physician or investigator.

4. Study procedure, Testing Methods, and Testing Criteria

1) Researchers followed the inclusion and exclusion criteria; after confirming that participants had completed the informed consent form, they recorded participants' basic information, personal history, and medical history;

2) 10 mL of venous blood was drawn from each participant to measure blood lipids and serum levels of *SNRKAS* (using RT-qPCR), and to perform transcriptomic analysis;

3) Carotid ultrasound was used to measure degree of bilateral carotid artery atherosclerosis by carotid Doppler ultrasound.

5. Oucome measures

Primary outcome measure:

1) Serum levels of SNRKAS detected by RT-PCR (fold change) at enrollment;

2) Degree of bilateral carotid artery stenosis – intima-media thickness (mm) and lumen diameter (mm) of bilateral common carotid artery and internal carotid artery detected by Doppler ultrasound at enrollment;

3) Pulse wave velocity – peak systolic velocity (cm/s) of bilateral common carotid artery and internal carotid artery detected by Doppler ultrasound at enrollment.

Secondary outcome measures:

Blood lipids levels – Total Cholesterol (mmol/L), Triglycerides (mmol/L), High-Density Lipoprotein (mmol/L), Low-Density Lipoprotein (mmol/L) detected by automated biochemical analyzer (LABOSPECT 008, Hitachi) at enrollment.

6. Withdrawal of the subject

The subject has the right to withdraw from this trial at any time for any reason. The researcher should have a thorough understanding and a record of the reasons for withdrawal. Doctors and researchers also have the right to stop the subject from continuing to participate in the trial at any time during the research. Besides, subjects with early withdrawal should not be replaced by others.

As too many subjects withdrawing from the trial will lead to unreliable results, unnecessary withdrawal should be avoided. The falling rate of the trial should be controlled within 10%.

7. Statistical analysis

1) A one-way ANOVA followed by an LSD post-hoc test was used to compare differences in serum *SNRKAS* levels among individuals aged < 40, 40–60, and > 60.

2) A one-way ANOVA followed by an LSD post-hoc test was used to compare differences in circumferential strain and pulse wave velocity in the bilateral carotid arteries among individuals aged < 40, 40–60, and > 60.

3) Pearson's correlation coefficient was applied to analyze the correlation between *SNRKAS* levels and age, personal history, medical history, blood lipids level and the degree of arterial stiffness.

8. Trial Management

8.1 Ethics

To obtain the approval documents of the clinical trial, researchers should submit the trial protocol and a copy of the research documents including the informed consent to the ethics committee. The approval documents from the ethics committee should be accompanied by the name list of ethics committee members and their respective responsibilities. These documents will be delivered to the researchers in written form before the start of the study.

Any safety-related issues must be promptly reported to the ethics committee, which includes revision on the trial protocol and modification on the subject information page. The end or early termination of the trial should also be reported.

8.2 Informed consent and data protection agreement

It is the responsibility of the researchers to explain the objectives, study procedures, benefits and potential risks of the trial for each subject. The researchers should receive the informed consent signed by the subject before starting the trial, and keep it properly. The subject should also permit researchers and the clinical trial management agency to check his or her original data. Thus, the reliability of the research findings could be ensured.

The personal information of each subject, including name, gender, age, home address and telephone number, should be collected in detail. And the researcher/doctor should give the subject his or her contact information, so that the subject can contact with him or her when needed. This is also helpful for the research and medical care.

8.3 Subjects privacy

The researchers should protect the privacy of the subject. All research documents can only be identified using the subject's number instead of name or physical examination number. In addition, the grouped table that records the correspondence between the subject's name and number can only be kept by the researcher, and could not be submitted to any institution or individual.

8.4 Modification of the trial protocol

The trial protocol is approved by the ethics committee before starting the trial. During the research, any proposed modification on the trial protocol should be reported to the principal investigator, and then be submitted to the ethics committee for review. The clinical research can only be resumed after the re-approval of the ethics committee.

8.5 Original records certification

Researchers should ensure that the subject's privacy is protected when collecting and organizing data. In addition, the data manager is authorized to review the original records in order to confirm the accuracy of the original data.

8.6 Documents on file

According to relevant laws and regulations, researchers should keep the original records properly for at least 5 years from the end of the study.

8.7 Quality control

The clinical trial management agency has the authority to review the study progress, in order to ensure that the trial is carried out as predetermined and that the research data be veritably recorded.