

# Investigating the role of salt inducible kinases in atherosclerosis

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| <b>Submission date</b><br>10/06/2016   | <b>Recruitment status</b><br>No longer recruiting | <input checked="" type="checkbox"/> Prospectively registered<br><input type="checkbox"/> Protocol |
| <b>Registration date</b><br>28/06/2016 | <b>Overall study status</b><br>Completed          | <input type="checkbox"/> Statistical analysis plan<br><input checked="" type="checkbox"/> Results |
| <b>Last Edited</b><br>09/11/2020       | <b>Condition category</b><br>Circulatory System   | <input type="checkbox"/> Individual participant data  |

## Plain English summary of protocol

### Background and study aims

Cardiovascular disease (CVD) is a medical term used to describe a disease of the heart or blood vessels. This includes heart attacks (myocardial infarction, or MI) and stroke. In the early stages, however, it causes changes in the function of the blood vessels, particularly the arteries (vessels that transport blood being pumped from the heart to other areas of the body). Some of these changes in function is due to inflammation (swelling) and, in theory, reducing this inflammation could reduce the risk of an MI or stroke. Animal studies have shown that certain substances (called SIKs) promote inflammation in the arteries. This study is investigating whether this is the same for humans by doing tests in both healthy volunteers and people that have cardiovascular disease (for example, have had a heart attack or have narrowing of the leg arteries). SIK levels will also be compared with the results from different measures of artery function. If SIK levels are found to be high in cases of poor artery function then this might be a potential new treatment target to prevent cardiovascular disease.

### Who can participate?

Three different groups of people are participating in this study. People with peripheral vascular disease and about to have an amputation (group 1), people who have had a heart attack (group 2) and healthy volunteers (group 3). All participants are adults aged between 18-70.

### What does the study involve?

Participants in group 1 are asked to give blood for analysis and their amputated tissue is also analysed. Participants in group 2 are also asked to give blood samples and undergo tests to see how stiff their arteries are (arterial stiffness measurements) and how well blood vessels relax after being dilated (widened with increased blood flow). Participants in group 3 are also asked to give blood samples, flow-mediated dilatation (blood vessels widened with increased blood flow) and pulse-wave analysis (arterial stiffness analysis). All participants are followed up for signs of inflammation, their blood vessel function and SIK levels.

### What are the possible benefits and risks of participating?

The researchers do not expect there to be any direct risks or benefits to the patient in taking

part in the study. Routine clinical care will not be affected regardless of participation in the study. For volunteers, there is the small discomfort of having blood samples taken, however steps will be made to make this as easy as possible.

Where is the study run from?  
Ninewells Hospital, Dundee (UK)

When is the study starting and how long is it expected to run for?  
February 2016 to November 2017

Who is funding the study?  
Tenovus (UK)

Who is the main contact?  
Dr Faisal Khan  
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## Contact information

**Type(s)**  
Scientific

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## Additional identifiers

**Protocol serial number**  
2015CV11

## Study information

**Scientific Title**  
Investigating the role of salt inducible kinases in atherosclerosis: a observational cross-sectional study

**Study objectives**

The key hypothesis is that the SIK-CRTC3 signalling axis will play an important role in development of atherosclerosis. The researchers hypothesise that mechanisms to activate the cAMP response element binding protein (CREB) should protect against cardiovascular disease (CVD), and that inhibition of salt inducible kinase 2 (SIK2) will have beneficial effects on the cardiovascular (CV) system and thus offer a new target for therapy.

### **Ethics approval required**

Old ethics approval format

### **Ethics approval(s)**

East of Scotland Research Ethics Committee 2.

### **Study design**

Observational cross-sectional study

### **Primary study design**

Observational

### **Study type(s)**

Diagnostic

### **Health condition(s) or problem(s) studied**

STEMI, peripheral arterial disease

### **Interventions**

Three groups will be evaluated in this study:

Group 1. 10 patients with peripheral vascular disease (PVD) undergoing elective amputation. These patients will undergo blood sampling and amputated tissue analysis.

Group 2. 40 patients with acute myocardial infarction with ST elevation (STEMI) and requiring primary percutaneous coronary intervention (PPCI). These patients will undergo blood samples, flow mediated dilatation (FMD) and arterial stiffness measurements.

Group 3. 40 healthy subjects, matched to the STEMI group for age and gender. They will undergo blood samples, flow-mediated dilatation and pulse wave analysis.

### **Intervention Type**

Other

### **Primary outcome(s)**

Serum levels of inflammatory cytokines taken at the time of operation in PVD group, 48-72 hours after PCI in STEMI group and at the time of assessment in healthy volunteers.

### **Key secondary outcome(s)**

1. Tissue SIK levels in PVD patients at the time of surgery
2. Arterial stiffness and flow mediated dilatation in STEMI patients at 48-72 hours and in healthy volunteers at the time of assessment

### **Completion date**

03/11/2017

## Eligibility

### Key inclusion criteria

PVD:

1. Age between 18-70 years
2. Admitted for elective amputation for PVD
3. Able to give written informed consent

STEMI:

4. Age between 18-70 years
5. Admitted to CCU for STEMI and undergone PPCI
6. Able to give written informed consent

Healthy volunteers:

7. Age between 18-70 years
8. No current or previous significant medical illness
9. Able to give written informed consent

### Healthy volunteers allowed

No

### Age group

Adult

### Lower age limit

18 years

### Upper age limit

70 years

### Sex

All

### Total final enrolment

70

### Key exclusion criteria

Healthy volunteers:

1. Positive medical history of:
  - 1.1. Vascular diseases such as peripheral arterial disease, stroke, IHD... etc
  - 1.2. Haematological conditions such as hypercoagulability, deep venous thrombosis... etc
  - 1.3. Hypertension
2. Alcohol excess
3. Unable to give written informed consent

STEMI/PVD:

Unable to give written informed consent

### Date of first enrolment

01/08/2016

**Date of final enrolment**

16/11/2017

## **Locations**

**Countries of recruitment**

United Kingdom

Scotland

**Study participating centre**

**Ninewells Hospital**

Dundee

United Kingdom

DD1 9SY

## **Sponsor information**

**Organisation**

NHS Tayside/University of Dundee

**ROR**

<https://ror.org/000ywep40>

## **Funder(s)**

**Funder type**

Charity

**Funder Name**

Tenovus

**Alternative Name(s)**

Tenovus Cancer Care

**Funding Body Type**

Private sector organisation

**Funding Body Subtype**

Trusts, charities, foundations (both public and private)

**Location**

United Kingdom

## Results and Publications

**Individual participant data (IPD) sharing plan****IPD sharing plan summary**

Available on request

**Study outputs**

| Output type                   | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|-------------------------------|---------|--------------|------------|----------------|-----------------|
| <a href="#">Basic results</a> |         | 03/05/2019   | 17/05/2019 | No             | No              |