BROAD INSTITUTE

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June 14, 2010

To: Dina N. Paltoo, PhD, MPH
Chair, NHLBI Data Access Committee
NHLBI, NIH, DHHS

From: Sekar Kathiresan
Principle Investigator
Broad Institute
7 Cambridge Center
Cambridge, MA 02142

CERTIFICATION FOR GWAS DATA SUBMISSION: Broad Institute/MiGEn/ ATVB/Duga

The submission of data/samples to the NIH GWAS pursuant to this proposal is being made with appropriate institutional approvals. In the institution's reasonable belief, within the limits of the institution's knowledge of the future potential uses and users of the data:

- The proposed use of samples including data submission to the data repository is consistent with applicable federal and Massachusetts laws and regulations and applicable institutional policies;
- The research uses of the data and the uses that are specifically excluded by the informed consent documents are described;
  - Data/Tissue Sharing Restrictions (described in consent form):
    Cardiovascular Diseases only

- The proposal provides that the identities of research participants will not be disclosed to the data repository; and

- The Broad Institute's IRB (MIT COUHES) has reviewed the relevant aspects of the proposal and verified that:

  - The proposed submission of data to the general NIH data repository for subsequent sharing for research purposes as described in the NIH Policy http://www.genome.gov/Pages/Research/SequenceMapsBAC/MedicalSequencing/MEDSEQPOLICIES-03.12.2008.pdf is not inconsistent with the informed consent of study participants from whom the data were obtained;

  - The investigator's plan for de-identifying datasets is consistent with the standards outlined in the NIH Policy;

  - Based on the characteristics of the subject population and the data involved in the primary study, and within the limits of its knowledge of the future potential uses and users of the data, it has considered the risks to individuals, their families, and groups or populations associated with the proposed submission of the data to the NIH data

repository. The IRB understands that assessment of risks associated with specific future secondary uses will be performed by NIH's Data Access Committees; and,

- To the extent applicable, the genotype and phenotype data proposed to be submitted were collected in a manner consistent with 45 CC.F.R. Part 46.

Investigator:

Name: Sekar Kathiresan Title: *Principal Investigator*

Signature:  Date: June 14, 2010

Institutional Business Official:

Name: Stacey Donnelly Title: Director, Sponsored Research

Signature:  Date: 6-14-10

Enclosures/sf

MIT Committee On the Use of Humans as Experimental Subjects

MASSACHUSETTS INSTITUTE OF TECHNOLOGY
77 Massachusetts Avenue
Cambridge, Massachusetts 02139
Building E32-335
(617) 253-6787

To:	Sekar Kathiresan Ne83-512
From:	Leigh Firn, Chair COUHES
Date:	02/17/2006
Committee Action:	**Exemption Granted**
Committee Action Date:	02/17/2006
COUHES Protocol #:	0602001606
Study Title:	Genomewide Association Study for Myocardial Infaction

The above-referenced protocol is considered exempt after review by the Committee on the Use of Humans as Experimental Subjects pursuant to Federal regulations, 45 CFR Part 46.101(b)(4) .

This part of the federal regulations requires that the information be recorded by investigators in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects. It is necessary that the information obtained not be such that if disclosed outside the research, it could reasonably place the subjects at risk of criminal or civil liability, or be damaging to the subjects' financial standing, employability, or reputation.

If there are any changes to the protocol that significantly or substantially impact the rights of human subjects you must notify the Committee before those changes are initiated.

You should retain a copy of this letter for your records.

cc: Tom Duff

COUHES
Committee on the Use of
Humans as Experimental Subjects

MASSASCHUSETTS INSTITUTE OF TECHNOLOGY
77 Massachusetts Avenue
Cambridge, Massachusetts 02139
Building E25 – 143B
(617)253-6787

To: Sekar Kathiresan
Broad Institute
NE30

From: Leigh Firn, Chair
COUHES

Date: 04/01/2010

Committee Action: Amendment to Approved Protocol

COUHES Protocol #: 0602001606

Study Title: Genomewide Association Study for Myocardial Infarction

The amendment to the above-referenced protocol has been APPROVED following expedited review by the Committee on the Use of Humans as Experimental Subjects (COUHES).

If the research involves collaboration with another institution then the research cannot commence until COUHES receives written notification of approval from the collaborating institution's IRB.

It is the Principal Investigator's responsibility to obtain review and continued approval before the expiration date. Please allow sufficient time for continued approval. You may not continue any research activity beyond the expiration date without COUHES approval. Failure to receive approval for continuation before the expiration date will result in the automatic suspension of the approval of this protocol. Information collected following suspension is unapproved research and cannot be reported or published as research data. If you do not wish continued approval, please notify the Committee of the study termination.

Adverse Events: Any serious or unexpected adverse event must be reported to COUHES within 48 hours. All other adverse events should be reported in writing within 10 working days.

Amendments: Any changes to the protocol that impact human subjects, including changes in experimental design, equipment, personnel or funding, must be approved by COUHES before they can be initiated.

Prospective new study personnel must, where applicable, complete training in human subjects research and in the HIPAA Privacy Rule before participating in the study.

COUHES should be notified when your study is completed. You must maintain a research file for at least 3 years after completion of the study. This file should include all correspondence with COUHES, original signed consent forms, and study data.

cc: Tom Duff

BROAD INSTITUTE

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March 11, 2010

Dr. Leigh Firn
Chairman, MIT Committee on the
Use of Humans as Experimental Subjects
MIT Medical Department
77 Massachusetts Avenue Room E25-143B
Cambridge, MA 02139

PI: Kathiresan

RE: Genomewide Association Study for Myocardial Infarction

COUHES #: 0602001606

Dear Dr. Firn:

We are submitting an amendment for the above referenced study to add one additional collaborator. De-identified data generated from this study will be submitted in to dbGAP, a restricted access database administered by the NIH.

Enclosed in the packet you will find:

(1) Amendment for this study

(2) Ethics Committee approval from Ospedale Niguarda Ca' Granda approved on 10/28/98 for Protocol 613/92 with Associated Consent Form for the genentics study.

(3) Ethics Committee approval from Ospedale Niguarda Ca' Granda approved in 12/11/06 noting participation in the MIGen Consortium group.

Should you need any additional administrative documentation or have any questions please do not hesitate to contact Sekar Kathiresan, MD, Ph.D., Broad Institute, at sekar@broad.mit.edu or Susan Flynn, Biological Samples Compliance Manager, at sflynn@broad.mit.edu. We appreciate your kind attention to this matter.

Best regards,

Susan M. Flynn

Susan M. Flynn
Biological Samples Compliance Manager

Enclosures

	Massachusetts Institute of Technology Committee on the Use of Humans as Experimental Subjects	Existing COUHES #	0602001606
		Date	03/11/10

APPLICATION FOR CHANGES TO AN APPROVED PROTOCOL

Any change to a protocol that impacts human subjects must be approved by COUHES. If the change is minor and involves no more than minimal risks to subjects, an expedited review may be performed. All other changes are subject to a full Committee review.

Please answer every question. Positive answers should be amplified with details. You must mark N/A where the question does not pertain to your application. Any incomplete application will be rejected and returned for completion.

1. Title of Study	
Genomewide Association Study for Myocardial Infarction	
2. Investigator	
Name: Sekar Kathiresan	Building and Room #: The Broad Institute 5021B 7CC Cambridge MA
Title: Associate Member	Email: sekar@broadinstitute.org
Department: Program of Medical and Population Genetics	Phone: 617-584-6343

3. Proposed Change. *Please provide a detailed description of the proposed changes, and indicate how these changes will affect the potential risks and benefits to the subjects. Define all abbreviations and use simple words. Unless justification is provided, this part of the application must not exceed 2 pages.*

A. Dates of Research: 02/01/06- 01/31/11

B. Type and Number of Subjects Involved: New sample cohort: The Broad Institute will received anonymized samples from Milan, Italy to expand the current 3000 samples to 6000 samples.

The sample set, Italian Atherosclerosis, Thrombosis, and Vascular Biology Working Group (ATVB), is a hospital-based collection of 1500 cases and 1500 matched controls collected at Ospedale Niguarda Ca' Granda.

C. Procedures for obtaining informed consent:

All interactions with human subjects takes palce at the collaborating institutions: Ospedale Niguarda Ca' Granda in Milan, Italy, which has received approval from institute's ethical committee.

Please see attached IRB approvals

Please attach copies of all revised material (consent form, study protocol *PI & Dept. Head signature required,* recruitment, etc). Also, include a copy of all revised material with changes HIGHLIGHTED.

Signature of Investigator Sek K [signature] **Date** 3/11/10

Printed Name: Sekar Kathiresan

Signature of Dept. Head Stacey Donnelly **Date** 3-23-10

Printed Name: Stacey Donnelly

Please submit a signed hard copy of this application including all revised material to the COUHES office at E25-143b.