HARVARD MEDICAL SCHOOL
OFFICE FOR RESEARCH SUBJECT PROTECTION

HMS/HSDM COMMITTEE ON HUMAN STUDIES
25 SHATTUCK STREET, SUITE 412
BOSTON, MA 02115
TEL: (617) 432-3071
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31 August 2005

George M. Church, Ph.D.
Harvard Medical School
Genetics NRB Room 238
77 Avenue Louis Pasteur
Boston, MA 02115

Re: ORSP Protocol # M11665-101
Personal Genome Project

Dear Dr. Church:

The HMS/HSDM Committee on Human Studies met on August 31, 2005, and reviewed your protocol. The Committee voted to **grant approval** to the protocol. There are a few items that the Committee discussed that are outlined blow.

Protocol:

1. The current protocol is approved for only 1 participant, you, and has granted approval for 6 months. In 6 months the Committee asks that a continuing review be completed with a progress report of how the study has progressed along with any problems or issues that have occurred. At that time, the Committee will be able to review and possibly approve the inclusion of two additional participants.
2. The Committee feels that for the 6 months of the current approval, it is logical for the IRB to also function as the Data Safety Monitoring Committee. In that regard, the Committee asks that the monthly questionnaires, currently only being filled out by you, be forwarded to the IRB office once a month for review by the Committee Chair. This will give the Chair the opportunity to see how any risks are progressing and be able to determine if any changes may need to be made.
3. The Committee has agreed that no first degree relatives will need to be consented. The monthly questions about the family should suffice as an indicator of any family concerns.
4. The Committee also believes that as you are the PI and the sole participant at present, that consent should be witnessed by a member of the IRB Committee. When you are prepared to begin, please let me know and I will make the arrangements with the Committee member.
5. The Committee also asked that when you have posted your information on the web site, that you let us know, so that the members can have first hand experience of the protocol.

The Committee thanks you for your time and greatly appreciates your patience and the help you have provided.

If you have any questions or concerns, please do not hesitate to contact me.

Sincerely,

Lucas Breen, MS
IRB Coordinator
Office of Research Subject Protection
Harvard Medical School

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REPORT ON ACTION

Initial Application – Full Committee

Federalwide Assurance No.: FWA00007071

George Church, PhD
Principal Investigator

M11665-101
Human Studies Docket Number

Personal Genome Project
Title of Proposal

Molecular and Genomic Imaging Center; 1 P50 HG003170
Grant Title & Funding Agency

This is to certify that the PROPOSAL identified above has been reviewed by the HMS/HSDM Committee on Human Studies, appointed to review proposed research and related activities involving human subjects, which has considered specifically:

1. The adequacy of protection of the rights and welfare of the subjects involved.
2. The risks and potential benefits to the subject or importance of the knowledge to be gained.
3. The adequacy and appropriateness of the methods used to secure informed consent.

The judgment of the Committee is that:

✓ The PROPOSAL is approved.

_____ The PROPOSAL is approved CONTINGENT upon revisions/clarifications detailed in the attached memorandum.

_____ The PROPOSAL is deferred for the reasons stated in the attached memorandum.

8/30/05
Date of Action

Signature: Julie E Buring
Julie Buring ScD, Committee Chair

Proposal Expiration Date: 3/1/06

Note: Approvals are granted for a period of **one year only** and must be renewed annually. *Failure to obtain proposal renewal by the expiration date will result in immediate termination of your study with resultant notification of your funding source.* **Any modifications** made to this study must be reviewed and approved by the Committee in advance of use. In addition, **adverse events** of any kind must be reported immediately in writing to the Committee, as they occur. *Failure to report adverse events or changes to the protocol will also result in immediate termination of your study approval with resultant notification of your funding source.*

Responsibilities of the Investigator:

1. The investigator shall obtain the prior approval of the Committee before implementing *any* protocol changes, *unless* a change is necessary to eliminate apparent immediate hazards to the research subjects. If, because of the aforementioned, prior approval was not able to be obtained, the Committee must be informed, in writing, and with specificity, of the deviation from the approved protocol at the first available opportunity and, in no event, later than 5 days after the deviation. **Failure to obtain prior approval of a change in the protocol will jeopardize your ability to use the data collected during the lapsed period and may result in further disciplinary action.**

2. The investigator is solely responsible for seeking and obtaining Re-Approval before the expiration date listed on the previous page if s/he wishes to continue his research beyond the stated approval period. Failure to do so will result in a lapse in approval. **If your approval lapses you may not gather any additional data in connection with your research and your sponsor may need to be notified.**

3. Unless you have specifically asked for, and been granted, a waiver from the requirements of informed consent and/or the documentation of same, an exact duplicate of the **HMS/HSDM Committee stamped consent form, attached hereto, shall be the only form used to enroll subjects.** At no time may a subject be enrolled with an expired consent form or one that has been revised, without prior approval of the Committee. In addition, **if an amendment to the consent form has been approved, the newly amended consent form is the *only* form that may be used, going forward, to enroll new subjects.**

4. **Serious Adverse Events or Unexpected Effects must be reported to the HMS/HSDM as soon as possible and, <u>in no event, later than 72 hours after the incident</u>.** If the event/effect changes the risk/benefit analysis of the study or there is other additional information that ought to be provided in the consent process otherwise the investigator should submit appropriately amended consent forms for approval before enrolling any additional subjects.

In conducting this review, the Chair or the Chair's designee has given due consideration to ensuring the following:

- Risks to subjects are minimized: (i) by using procedures which are consistent with sound research design, and which do not unnecessarily expose subjects to risk, and (ii) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.
- Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result. In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive, even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.
- Selection of subjects is equitable. In making this assessment, the IRB should take into account the purposes of the research, and the setting in which the research will be conducted, and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons.
- Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by §46.116.
- Informed consent will be appropriately documented, in accordance with, and to the extent required by §46.117.
- When appropriate, the research plan makes adequate provision for monitoring the data collected, to ensure the safety of subjects.
- When appropriate, there are adequate provisions to protect the privacy of subjects, and to maintain the confidentiality of data.
- When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects. Additionally, descriptions of plans for including children, or the justification for excluding them, should be included in the submission, as well.

Consent Form

Protocol Title: **Personal Genome Project**
Principal Investigator: **George M. Church, Ph.D.**
Site-Responsible Investigator's /Institution: **Harvard Medical School**
Co-Investigators & Study Staff: **Chris Varma, Jay Shendure**
Description of Subject Population: **Volunteers knowledgeable of Genetics & Human Subjects Research.** **Women and minorities are encouraged to participate.**

PURPOSE

We would like to invite you to participate in a research study. You have been asked to participate because you are a healthy individual with sufficient training in human genetics and human subjects research to be able to give informed consent for a public and open-ended study. This study is being sponsored by the National Institutes of Health.

The main scientific goal of this study is to explore ways to connect human genotype and phenotype information, i.e. human genome sequence, medical records, and non-medical physical traits, so that such data can be used for hypothesis-generating exercises and computational efforts worldwide. Additional goals include the determination of risks of such studies, developing a fully consented dataset to help in therapies and diagnostics, developing computational tools for data/model sharing and user interfaces for scientists, clinicians and patients. The ethical and human goals include educating participants and the general public about the risks and potential alternative pathways that genetics can take. We also seek to develop a model system to allow a meeting place for experts on genetic counseling, insurance, employment, education, and research. We hope that our proposed specific datasets will help extend such discussions to planned case studies. We also hope to discover what consumers, clinicians, and researchers might want and not want and why.

PROCEDURES

- A buccal (cheek) or blood sample (50 ml or approximately 3 tablespoons) will be taken for genome sequencing by a member of the Personal Genome Project (PGP) staff. If cells from previous medical procedures are available, then these may be used for additional genome measures.
- Your full face image, name, date of birth, height, weight, and blood pressure will be taken by a member of the PGP study team, and this information posted on a public web page, along with your genome sequence.
- Any of your medical records available in electronic format including medical history, blood chemistry, infections diagnosed, drugs prescribed, and imaging data will also be copied to the web page. This will be done in consultation with your primary care physician and your medical care provider's medical informatics staff. Signing this form constitutes your authorization for PGP to access your "Protected health information" (PHI) under the Health Insurance Portability and Accountability Act (HIPAA). You may revoke this authorization at any time.

- Your initial participation will take about 60 minutes.
- Other than the questionnaires below, you are under no obligation to receive study notices or participate after providing the initial DNA sample and exchange of the above information. However, additional imaging and measures can be voluntarily submitted at later dates at your initiative or may be requested by the Personal Genome Project (PGP) (without obligation to comply) as frequently as three times per year.
- You will be encouraged to discuss this study and the potential risks (as outlined below) with your immediate family members.

QUESTIONNAIRES

The first Tuesday of each month we will send out an email request to each participant containing the following questions:

1. What negative and/or positive events have happened to you and/or your relatives?
2. What are the reactions or responses of relatives and acquaintances to the posting of your genetic and medical data?
3. Please report incidents of being contacted regarding their data being posted online.
4. In what ways has this study positively or negatively influenced your health care or interactions with your medical care providers?

It will be requested that answers to the questions or a "no change" reply be retuned to the Investigator within a week of receipt.

Additionally, at the end of your participation in the study (4 years from the start), you will be asked to write your thoughts about the consent form and the whether it adequately described the procedures and risks associated with study participation.

RISKS AND DISCOMFORTS

- There are no known or foreseeable risks or side effects associated with conventional buccal sampling procedures.
- The blood draw may involve a small amount of pain and may also cause temporary bruising.
- The risks of public disclosure of your genotype and phenotype information could affect employment, insurance, and social interactions for you and your immediate family. For example, data such as facial images can be used to identify you which could result in higher than normal levels of contacts from the press and other members of the public motivated by positive or negative feelings about the study. This could mean a significant loss of privacy and personal time.
- You should also be aware of the ways in which knowledge of your genotype and phenotype might be used. For example, anyone with sufficient knowledge could take your genome and/or posted medical information and use them to (1) infer paternity or other features of your genealogy, (2) claim statistical evidence that could affect your employment or insurance, (3) claim your relatedness to infamous villains, (4) make synthetic DNA and plant it at a crime scene, (5) reveal the possibility of a disease or unknown propensity for a disease.

- The genetic and medical record information posted on the study website, while directly associated only with you, may also have relevance to your family members. The Investigators believe that the risk to you is small, since you are recruited as a healthy individual and the risk to your relatives smaller still. Anything that is later inferred solely from your DNA sequence will be speculative with respect to you, and even less predictive with respect to your family, since inheritance of nearly all alleles is 50:50 random.
- Additional risks will be posted on the study web page as they become apparent. http://arep.med.harvard.edu/PGP/
- A Data Safety Monitoring Committee (DSMC) will be formed to monitor risks to study participants and study progress. The open web version of your medical and genetic data will be maintained for 10 years, unless removal is requested before that (see below).

BENEFITS

There are no known benefits to you from your participation in this study. However, the study may have a greater benefit for the community as a whole.

COSTS

There are no costs to you for participating in this study.

ALTERNATIVES

- The alternative is not to participate in this research study.
- If you choose not to participate, your medical treatment at your hospital and other medical care providers will be unaffected.

CONFIDENTIALITY

- Your genotype and phenotype will not be sent to your health care provider, therefore this information will not become part of your medical record.
- Your reply to the monthly email questionnaires will be confidential. However, the DSMC or study sponsor may request this information in order to judge the risks to you and any other study participants.
- The results of this study may be published in a medical book, journal, website or webpage, or used for teaching purposes. Your name and other identifiers (such as your photograph and medical information provided during the course of the study) may be used in such publications or teaching materials with your specific permission, as indicated by signing this document.

REFUSAL OR WITHDRAWAL OF PARTICIPATION

- Participation in this study is voluntary. You do not have to participate in this study.
- You may withdraw your participation and/or your data from this study at any time, however you are advised that once this information is posted on the Internet, it is impossible to confirm that it is ever fully removed. To aid removal, standard methods will be added to the web pages to prevent web indexing (e.g. Google). All users of the

data will submit an online agreement requiring any duplicates be register with the PGP and protected with the same rapid removal option as the original data pages.

- The Investigator may decide to end your participation in this study at any time after he/she has explained the reasons for doing so.

RESEARCH-RELATED CONTACT INFORMATION:

- If you have any questions or concerns about the study, or if you suffer a research related injury, you may contact the investigator: George Church, PhD, at (617) 432-7562 or church@rascal.med.harvard.edu .
- If you wish to discuss your rights as a participant in a research study, or if you feel under any pressure to enroll in this study you may contact: Carolyn Connelly, PhD, the Director of the Office for Research Subject Protection at Harvard Medical School (617) 432-0651 or Carolyn_connelly@hms.harvard.edu.

SIGNATURE

I confirm that the purpose of the research, the study procedures, possible risks and discomforts, and potential benefits that I may experience have been explained to me. Alternatives to my participation in the study also have been discussed. All my questions have been answered. I have read this consent form. My signature below indicates my willingness to participate in this study.

Study Participant Signature: _____ Date: _____

I have explained the purpose of the research, the study procedures, identifying those that are investigational, the possible risks and discomforts as well as potential benefits and have answered any questions regarding the study to the best of my ability.

Person Obtaining Consent: _____ Date: _____