

SUMMARY STATEMENT
(Privileged Communication)

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Application Number: 1 R21 HG005747-01

Principal Investigator

BLOSS, CINNAMON S PHD

Applicant Organization: SCRIPPS HEALTH

Review Group: ELS
Ethical, Legal, and Social Implications of Human Genetics Study Section

Meeting Date: 09/30/2009
Council: JAN 2010
Requested Start: 04/01/2010

RFA/PA: PA09-164
PCC: X5JM

Project Title: Response to Testing Among Individual Consumers of DTC Personal Genomics Services

SRG Action: Priority Score

Human Subjects: 30-Human subjects involved - Certified, no SRG concerns
Animal Subjects: 10-No live vertebrate animals involved for competing appl.
Gender: 1A-Both genders, scientifically acceptable
Minority: 1A-Minorities and non-minorities, scientifically acceptable
Children: 1A-Both Children and Adults, scientifically acceptable
Clinical Research - not NIH-defined Phase III Trial

Project Year	Direct Costs Requested
1	75,000
2	75,000
TOTAL	150,000

DC Recommended

ADMINISTRATIVE BUDGET NOTE: The budget shown is the requested budget and has not been adjusted to reflect any recommendations made by reviewers. If an award is planned, the costs will be calculated by Institute grants management staff based on the recommendations outlined below in the COMMITTEE BUDGET RECOMMENDATIONS section.

1R21HG005747-01 Bloss, Cinnamon

RESUME AND SUMMARY OF DISCUSSION: The principal investigator (PI) proposes to study individuals who have chosen to obtain direct to consumer (DTC) personal genomic services. The PI has access to the Scripps Genomic Health Initiative (SGHI) cohort, a collection of over 4000 individuals who have chosen to purchase the Navigenics Health Compass genomic risk assessment service. Individuals in the cohort are surveyed for basic demographic information, family medical history and health behaviors at pre-disclosure of genetic test results, and 3-months and 12-months follow-up. The PI wants to characterize several aspects of the individuals in the SGHI including: their attitudes about genetic testing, their perception of risk, their health behaviors, and the distress and anxiety they experience as a result of genetic testing. In addition, the PI will evaluate the variables that may moderate the response of individuals to genetic testing.

The application was received with exceptional enthusiasm by the members of the review panel. The significance of the project was judged to be very high. The reviewers noted DTC personal genomics services have raised a lot of concerns and the topic represents a very controversial subject. This project proposes to generate some much needed data that will inform the field and help to focus future research projects along productive lines of study. The reviewers noted several strengths about this application. The application is well written and presents a detailed and clearly articulated research plan. The SGHI resource represents a rich source of longitudinal data from thousands of individuals, which is large enough to permit the applicants to look for between-group differences in attitudes and concerns about genetic testing. The applicants found the plan to collaborate with a genetic services company to be an innovative approach.

The reviewers did note some weaknesses with the application. The expertise of the research team is very strong in genetics and genomics, but their expertise in behavior research and some key social science methodologies is less strong. The individuals that make up the SGHI cohort have all been recruited from Scripps Health employees, their family members, and Scripps Health patients. This caused the reviewers to question how generalizable the findings from this project might be. But these weaknesses did not dampen enthusiasm to any great degree. The timeliness of this project, the value of the SGHI cohort, and a well crafted, detailed application with a solid research plan compelled the reviewers to express strong support for this proposal.

DESCRIPTION (provided by applicant): Results from several genome-wide association (GWA) studies have recently emerged showcasing the discovery of specific genetic variations found to be associated with several common, complex diseases. Leveraging these findings and fueled by the rapidly decreasing costs of performing genome-wide single nucleotide polymorphism (SNP) scans, a small number of companies have begun offering tests that aim to calculate an individual's risk for these common diseases using this genome-wide technology, direct-to-consumer (DTC) over the internet. While the offering of these tests - both at this stage of scientific discovery and directly to the consumer - has been the subject of much intense controversy, it is nevertheless the case that many individual consumers are purchasing these products. Despite this, however, relatively little is known about the characteristics of consumers of DTC personal genomics services, including why they chose to pursue this type of testing, and perhaps most critically, how they are responding to their results. The Scripps Genomic Health Initiative (SGHI) represents an opportunity to begin to address these questions. The SGHI is a large longitudinal cohort study in which participants purchase the Navigenics Health Compass DTC genomic risk assessment product at a discounted rate and are administered baseline (i.e., pre-risk disclosure), as well as 3- and 12-month follow-up (i.e., post-risk disclosure) web-based demographic, family medical history, and behavioral health assessments. In addition, items pertaining to attitudes about genetic testing and the perceived impact of the results, including distress related to receiving information pertaining to one's genomic risk profile, are administered. The SGHI is, to a large degree, exploratory in that it is one of the first studies to evaluate response to testing among individual consumers of DTC personal genomics services. To date, over 4,000 individuals have enrolled in the SGHI, and although the ongoing recruitment of individuals into the study is currently funded, analysis of

the assessment data that is being collected is unfunded. Therefore, we are requesting two years of funding via the NIH Exploratory/Developmental Research Grant Program (R21) for analysis of these data. Our specific aims are as follows: First we will characterize consumers of DTC personal genomics services in terms of their demographics, baseline level of genetic risk for disease, behavioral health characteristics, and attitudes regarding genetic testing. Second, we will assess response to testing among consumers with respect to general anxiety and distress related to testing, perception of new disease risk, changes in health behaviors, and attitudes regarding the impact of results. Third, we will evaluate potential moderators of response to testing, including demographic characteristics, perception of risk, risk estimates reported in the Health Compass, and utilization of genetic counseling services.

PUBLIC HEALTH RELEVANCE: The proposed project would leverage data from the Scripps Genomic Health Initiative (SGHI), a large longitudinal cohort study of over 4,000 consumers of GWAS-based DTC personal genomics services (i.e., specifically the Navigenics Health Compass product). We aim to characterize consumers of DTC personal genomics services, as well as assess behavioral and psychological response to DTC genetic testing, including potential moderators of response such as level of genetic risk and utilization of genetic counseling services. At this time there is essentially nothing known about the impact of this technology on consumers despite its relatively wide availability and the fact that many individual consumers have already purchased these products. Thus, the proposed work will provide an initial examination of these important questions to which timely answers are critical given efforts currently underway to determine how best to regulate the sale and use of these tests.

CRITIQUE 1:

Significance: 1
Investigator(s): 5
Innovation: 2
Approach: 5
Environment: 4

Overall Impact:

Strengths

- This study addresses several important issues about a controversial service.

Weaknesses

- There are concerns about the extent to which the sample is generalizable and this limitation may lead to incorrect conclusions about use of personal genomic services.

1. Significance:

Strengths

- The proposed research addresses an important issue in genetic testing. By characterizing individuals who utilize a personal genomic services and evaluating responses to genetic risk information, the proposed research will provide empirical data on an emerging technology that is highly controversial.
- This information has the potential to address concerns about direct-to-consumer genomic services.

Weaknesses

- None noted.

2. Investigator(s):

Strengths

- The investigative team has considerable experience in genetic and genomic research.

Weaknesses

- There seems to be limited expertise in behavioral science methods even though evaluating the psychosocial and behavioral impact of personalized genomics is the focus of the proposed research.

3. Innovation:

Strengths

- Characterizing individuals who use personal genomic services is highly innovative and moves the field from hypothetical scenarios to an actual personalized testing service.

Weaknesses

- None noted.

4. Approach:

Strengths

- The applicants propose to measure many of the same constructs that were evaluated when genetic testing for single gene disorders first became available (e.g., BRCA1/2 mutation testing). This has the potential to draw comparisons between testing services that are provided in different contexts.

Weaknesses

- The study population is a significant limitation. As described in the application, subjects were recruited from the employee population of the applicant's institution. There is a strong concern that the sample will not be generalizable and may result in incorrect conclusions.
- While characterizing individuals who use personal genomic services is an important question, it seems like that most significant issue (e.g., who accepts and declines this service) will not be measured.
- It seems that individuals who decline genomic services will not be included in the study; thus, it is highly likely that attitudes and experiences will be biased towards those who have positive attitudes.

5. Environment:

Strengths

- The environment is strong and is uniquely qualified for the research in that it has collected data to support the proposed research questions and specific aims.

Weaknesses

- The team has limited expertise in behavioral science and it is not clear how the collaboration with Dr. Madlensky will be structured to ensure that success of the proposed research.

Protections for Human Subjects

Acceptable Risks and/or Adequate Protections

Inclusion of Women, Minorities and Children

G1A - Both Genders, Acceptable

M1A - Minority and Non-minority, Acceptable

C1A - Children and Adults, Acceptable

Budget and Period of Support

Recommend as Requested

Resource Sharing Plans

- Not addressed.

CRITIQUE 2:

Significance: 1

Investigator(s): 2

Innovation: 2

Approach: 2

Environment: 2

Overall Impact:

Strengths

- Timely and important investigation of ACTUAL DTC subjects
- Prospective, longitudinal study
- Use of a cohort already largely collected and maintained
- Social scientist impartial to the outcome of the analyses
- Complementary use of private industry funding
- Excellent study design attending to details such as potential group differences based on how much consumers paid for testing and manipulation checks for threats to validity

Weaknesses

- No mention of how the data might also be used in the future for marketing or other purposes (or that it wouldn't)

1. Significance:

Strengths

- Priority research topic, previously neglected

- More comprehensively designed study than other two existing studies reviewed in the background (the Multiplex Initiative failing to collect data on behavior change)

Weaknesses

- None noted

2. Investigator(s):

Strengths

- Impressive team of investigators, Lisa Madlensky specifically selected to implement the proposed study
- Obtained signed pledge from Navigenics and Affymetrix executives stating that they will not censor or impede publication of results, no matter the outcome

Weaknesses

- May not be possible to have a completely disinterested investigator or executives without influence

3. Innovation:

Strengths

- Design of collaborating with a private company and using a (largely) existing cohort, the Scripps Genomic Health Initiative
- More comprehensive study than others aimed at answering related questions on the impact of DTC testing-prospective and longitudinal studies are sufficiently absent to call the proposed study design innovative

Weaknesses

- None noted

4. Approach:

Strengths

- Proposed study is to fund research of a DTC cohort on participants expectations of testing, and 3-month and 12-month follow-up data on understanding of output and health behavior change reflecting actual testers' experiences
- Prospective and longitudinal design allows for testing whether perceptions of DTC results or a slew of independent variables (perceived susceptibility, seriousness, control, impact, and distress are associated with a change in health screening behaviors, alcohol use, diet, exercise and psychological functioning.
- Social scientist is a disinterested collaborator without direct ties to Navigenics
- Study design includes plans to assess potential group differences based on how much consumers paid for testing and manipulation checks for threats to validity
- Use of published, validated measures for comparisons to outcomes from studies of Mendelian genetic testing
- Variables from Diffusion theory are included, although there is not a single theoretical framework for the study

Weaknesses

- Results will reflect early users and may not be generalizable to the larger population of DTC users over time (particularly the employees who were first encouraged to enroll)

5. Environment:

Strengths

- Use of the Scripps Genomic Health Initiative facilitates a substantial study of early adopters of DTC

Weaknesses

- None noted.

Protections for Human Subjects:

Acceptable Risks and/or Adequate Protections

- IRB approval obtained

Inclusion of Women, Minorities and Children:

G1A - Both Genders, Acceptable

M1A - Minority and Non-minority, Acceptable

C3A - No Children Included, Acceptable

Budget and Period of Support:

Recommend as Requested

- Extremely modest budget for proposed work

Resource Sharing Plans

Acceptable

Additional Comments to Applicant:

- Beautifully written proposal with a coherent and comprehensively proposed study

CRITIQUE 3:

Significance: 1

Investigator(s): 1

Innovation: 1

Approach: 3

Environment: 1

Overall Impact:

Strengths

- Potential high impact in a clinically and public health important area.

- This is a strong proposal from a junior investigator that brings a strong transdisciplinary team from two institutions.
- The focus on psychosocial and behavioral outcomes among those who actually undergo GWAS-based DTC genomic testing is novel.
- Many of the measures employed have sound psychometric properties.
- Diffusion of Innovations Theory is an appropriate theoretical framework to test some of the key variables considered
- The large sample size will allow for interesting exploratory subgroup comparisons

Weaknesses

- External generalizability may be somewhat limited because of the sampling method and sociodemographic composition of the study population.

1. Significance:

Strengths

- An understanding of why consumers are purchasing GWAS-based DTC personal genomic services and how they are responding to their test results is critical for effective translation of such tests
- Incorporation of cognitions, emotions and behavior with regard to level of risk associated with test results will be informative.
- The inclusion of the 12-month assessment is a strength and knowledge about provider communication of test results will provide important information about how genomic information may personalize health care
- Behavioral responses to actual GWAS-based DTC tests are largely unknown despite the fact that many people are using these testing services.
- Potential benefits and problems regarding DTC tests need to be characterized. This study takes advantage of an existing data source and is a logical (and efficient) first step to understanding receptivity and responses to testing.

Weaknesses

- The study population is generally well educated and female
- In addition to Diffusion of Innovations Theory, a Stress and Coping Framework may inform the analysis and interpretation of the study's findings.

2. Investigator(s):

Strengths

- The PI is a well trained psychologist who has assembled an excellent team
- Research team has complementary expertise
- PI and co-investigators have expertise in genomics, behavioral science, health services, medicine and clinical genetics

Weaknesses

- The team would benefit from one or two senior-level behavioral scientists with experience in this line of behavioral research.

3. Innovation:

Strengths

- Study population has paid for (discounted) and undergone GWAS testing
- Focus on factors influencing the decision to undergo testing and behavioral responses among individuals who have undergone testing in a close to real world setting

Weaknesses

- None noted.

4. Approach:

Strengths

- Characteristics of those who decline testing will be compared to those tested using available data
- Study population includes actual consumers of Navigenetics Health Compass product
- Incorporation of methods to minimize threats to internal validity in the setting of a pre- post-test design (no control group)
- Use of CHIS items to compare study population to state-wide population-based data
- Many of the measures have strong psychometric properties and have been used in similar studies of single-gene disorders. Comparative data will move the field forward.
- Proposed exploratory analyses consider test results according to disease risk

Weaknesses

- Statistical power will be limited for some of the subgroups studied but data will inform effect size for future work.
- Limited consideration of specific disease contexts within levels of risk associated with genomic test result. For example, although risk estimates associated with restless leg syndrome and multiple sclerosis are similar, disease-specific concerns are likely to impact behavioral outcomes.
- Measures used to maximize response rates are not explicated.

5. Environment:

Strengths

- Excellent. Scripps Translational Science Institute is a leader in translational science.
- The Scripps Genomic Health Initiative represents an unprecedented opportunity to investigate decision-making factors and responses to genomic testing.

Weaknesses

- None noted.

Protections for Human Subjects:

Acceptable Risks and/or Adequate Protections

Inclusion of Women, Minorities and Children

G1A - Both Genders, Acceptable

M1A - Minority and Non-minority, Acceptable - Minorities are under-represented but the study population is limited to an existing dataset

C1A - Children and Adults, Acceptable

Budget and Period of Support:

Recommend as Requested

THE FOLLOWING RESUME SECTIONS WERE PREPARED BY THE SCIENTIFIC REVIEW OFFICER TO SUMMARIZE THE OUTCOME OF DISCUSSIONS OF THE REVIEW COMMITTEE ON THE FOLLOWING ISSUES:

PROTECTION OF HUMAN SUBJECTS (Resume): ACCEPTABLE. The reviewers expressed no concerns about possible harms to the participants.

INCLUSION OF WOMEN PLAN (Resume): ACCEPTABLE. The applicants propose to recruit individuals from an existing cohort, the Scripps Genomic Health Initiative. Women comprise about 58% of this cohort.

INCLUSION OF MINORITIES PLAN (Resume): ACCEPTABLE. Approximately 16% of the subjects in the Scripps Genomic Health Initiative cohort are minorities.

INCLUSION OF CHILDREN PLAN (Resume): ACCEPTABLE. The applicants propose to recruit participants from an existing cohort that is comprised of individuals 18 years of age or older. As such, children between the ages of 20 and 18 years of age may be involved in this study.

COMMITTEE BUDGET RECOMMENDATIONS: The budget was recommended as requested.

ROP

NOTICE: In 2008 NIH modified its policy regarding the receipt of resubmission (formerly termed amended) applications. Detailed information can be found by accessing the following URL address: <http://grants.nih.gov/grants/policy/amendedapps.htm>