

# **Pennsylvania Department of Health Final Performance Summary Report Formula Grants**

## **Overview of the Health Research Project Performance Review Process and Criteria**

An applicant that receives a health research grant under Tobacco Settlement Act / Act 77 of 2001, Chapter 9, is subject to a performance review by the Department of Health upon completion of the research project. The performance review is based on requirements specified by Act 77 and criteria developed by the Department in consultation with the Health Research Advisory Committee.

As part of the performance review process, each research project contained in a grant is reviewed by at least three experts who are physicians, scientists or researchers. Reviewers are from the same or similar discipline as the research grant/project under review and are not from Pennsylvania. Reviewers use the applicant's proposed research plan (strategic plan), the annual progress report and final progress reports to conduct the review. A grant that receives an unfavorable performance review by the Department may be subject to a reduction in funding or become ineligible for health research funding in the future. The overall grant evaluation rating is based on the ratings for the individual research projects contained in the grant.

This performance review report contains the outcome of the review for the grant as a whole (outstanding, favorable, or unfavorable), strengths and weaknesses of each research project, as well as recommendations for future improvement.

The following criteria were applied to information submitted by research grant recipients:

- **Criterion 1 - How well did the project meet its stated objectives? If objectives were not completely met, was reasonable progress made?**
  - Did the project meet the stated objectives?
  - Were the research design and methods adequate in light of the project objectives?
  - Consider these questions about data and empirical results: Were the data developed sufficiently to answer the research questions posed? Were the data developed in line with the original research protocol?
  - If changes were made to the research protocol, was an explanation given, and, if so, is it reasonable?
  - Consider (only for clinical research projects) the extent of laboratory and clinical activities initiated and completed and the number of subjects relative to the target goal.
  - Were sufficient data and information provided to indicate or support the fact that the project met its objectives or made acceptable progress?
  - Were the data and information provided applicable to the project objectives listed in the strategic research plan?

- **Criterion 2 - What is the likely beneficial impact of this project? If the likely beneficial impact is small, is it judged reasonable in light of the dollars budgeted?**
  - What is the significance of this project for improving health?
  - Consider the value of the research completed towards eventual improvement in health outcomes.
  - Consider any changes in risk factors, services provided, incidence of disease, death from disease, stage of disease at time of diagnosis, or other relevant measures of impact and effectiveness of the research being conducted.
  - Consider any major discoveries, new drugs and new approaches for prevention, diagnosis and treatment, which are attributable to the completed research project.
  - What are the future plans for this research project?
  
- **Criterion 3 - Did the project leverage additional funds or were any additional grant applications submitted as a result of this project?**
  - If leveraging of funds were expected, did these materialize?
  - Are the researchers planning to apply for additional funding in the future to continue or expand the research?
  
- **Criterion 4 - Did the project result in any peer-reviewed publications, licenses, patents, or commercial development opportunities? Were any of these submitted/filed?**
  - If any of the above listed were expected, did these materialize?
  - Are the researchers planning to submit articles to peer-reviewed publications, file for any licenses, or patents or begin any commercial development opportunities in the future?
  - Consider the number/quality of each.
  
- **Criterion 5 - Did the project enhance the quality and capacity for research at the grantee's institution?**
  - Were there improvements made to infrastructure?
  - Were any new investigators added or were any researchers brought into the institution to help carry out this research?
  - Were funds used to pay for research performed by pre- or post-doctoral students?
  
- **Criterion 6 - Did the project lead to collaboration with research partners outside the institution, or new involvement with the community?**
  - Are the researchers planning to begin any collaborations as a result of the research?
  - For clinical research only: consider the number of hospitals and health care professionals involved and the extent of penetration of the studies throughout the region or the Commonwealth.

## **Overall Evaluation Rating**

An overall evaluation rating is assigned to each research project. The rating reflects the overall progress the project attained in meeting the stated goals and objectives. The rating is based on a scale of 1–3, with 1 being the highest. An average rating is obtained from all the reviews (minimum of 3) of each project and is the basis for the determination of the final overall rating for each project as follows:

1.00 – 1.33 = *Outstanding*

1.34 – 2.66 = *Favorable*

2.67 – 3.00 = *Unfavorable*

The grant level rating is an average rating from all projects as above. The numerical rating appears in parentheses for the grant and each project in the ***Overall Grant Performance Review Rating*** section of the report.

***Overall Grant Performance Review Rating***

**Grant Rating:** Outstanding (1.33)

**Project Rating:**

<b>Project</b>	<b>Monell Chemical Senses Center</b>	<b>Average Score</b>
0864001	Effect of Genotype on Smoking, Taste and Obesity in Mothers and Children	Outstanding (1.33)

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**Project Number:** 0864001  
**Project Title:** Effect of Genotype on Smoking, Taste and Obesity in  
Mothers and Children  
**Investigator:** Reed, Danielle R.

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## ***Section A. Project Evaluation Criteria***

***Criterion 1 - How well did the project meet its stated objectives? If objectives were not completely met, was reasonable progress made?***

### ***STRENGTHS AND WEAKNESSES***

#### Reviewer 1:

The role that nature and nurture play in determining human behavior has been a topic of debate among scientists, medical practitioners and philosophers for at least 200 years. The present study, to determine the interaction of genotype on human health-related behaviors with a focus on taste, smoking and preference for high-fat, high sugar foods, was designed to increase understanding of the important question of the roles that genetics and experience play in the directing human behavior. More specifically, this study had the aim of determining how alleles in a human bitter receptor gene, the opioid receptor gene, and the gene for the cannabinoid receptor affect sweet and fat taste perception and preferences as well as smoking behavior and body weight in women and their children. The results show that although women who smoked were, on the average, more obese as compared to non-smokers, they did not show any differences in allele frequencies for the genes that were tested. Given the design, methods, hypothesis, number of women and children tested, and the sophistication of the data analysis, this project met its stated objectives.

Although not to be taken as a weakness, was a family history of smoking behavior collected from the mothers enrolled in the study? That is, was data collected on the environments in which the mothers were raised? Did their mothers and fathers smoke in the home? Were, as children, the mothers exposed to second hand smoke? For the children enrolled in the study, were there any differences in the results for the mothers who smoked while they were pregnant as compared to those who smoke but did not smoke while pregnant? Was data collected on the type of cigarette smoked (e.g., menthol versus non-menthol)? Is the sample size sufficient to divide the smokers into those who smoked menthol cigarettes as compared to those who smoked non-menthol products? The hypothesis here might be that menthol would affect taste receptors in a different way than non-menthol products.

#### Reviewer 2:

This project did a superb job of meeting its objectives. The project itself was well thought out, bringing to bear appropriate expertise in several disciplines - genetics, taste psychophysics, and nutrition - in order to examine how genetic variation affects interactions among smoking, taste of

food, and body weight, all of which are important to health. The focal issues concern specific genetic predispositions (conveyed by alleles of the TAS2R38 gene) to respond strongly or weakly to certain bitter substances, and, significantly, correlations were also investigated between the dependent variables and the presence of alleles of other potentially pertinent genes. Given the empirical evidence at hand, it was plausible to ask, as the PI did, whether genetically-based sensitivity to bitters may affect smoking (given that there is a bitter component to tobacco smoke), sensitivity to sweet and fat tastes (as prior evidence suggests), and whether and how these variables may then be associated with food cravings, obesity, etc., in mothers and their children.

Given the research background, the study proposed a series of carefully conceived and well-designed experiments to test specific hypotheses, to wit, that bitter, sweet, and fat tastes would show patterns of heritability, that children genetically sensitive to bitter will have relatively high thresholds for sweet and will prefer foods with relatively high concentrations of sugar and fat, and that mothers genetically sensitive to bitter will be less likely to smoke and will have relatively high preferences and cravings for foods high in sugar and fat. The PI also suggested that the presence of the bitter-taste related TAS2R38 gene may be associated with overweight or obesity in the mothers and children.

The project met the stated objectives by carefully and thoroughly conducting all of the proposed experiments, exceeding the original experimental plan by testing even more subjects than initially proposed (the original proposal was to test 50 mother-child pairs; in the end, the investigators tested half again as many mothers, 76 in all, and nearly twice as many children, 96). The data themselves were thoroughly analyzed, mined in a variety of ways. Overall, the project was admirably thought out from every perspective: theoretical, empirical, and analytical. Especially impressive is the extensive set of converging empirical tests used. For example, smoking behavior was assessed not only by asking the mothers to report on whether they currently smoke (or smoked in the past), but also confirmed these reports by measuring levels of carbon monoxide in their breath, latent CO in the lungs being an objective marker of smoking.

Several of the demographic findings concur with well-known evidence: that the smokers completed fewer years of school than non-smokers and had lower incomes, and that the smokers were heavier, most being obese. Importantly, the children of smokers were much less likely than children on non-smokers to be of normal body weight. Mothers who smoked tended to be obese and so did their children. Mothers who smoked had more body fat and burned more calories than those who never smoked; so did their children. And mothers who smoked reported higher levels of liking for and intake of high-fat foods and inability to control intake of sweets. Direct behavioral measurements showed that mothers who smoked preferred high concentrations of sucrose in water, as well as sucrose and fat in pudding. On the other hand, children showed similar responses in both contexts. In general, children preferred higher levels of sucrose than did their mothers. Mothers preferred higher fat in pudding, and this was especially true of mothers who smoked. By implication, preferences for fat and sweet tastes shift in opposite ways in development with sweet preference decreasing and fat preference increasing. It is not clear whether smoking has a causal effect on this, or other correlated basis.

Given the thorough and carefully conducted experiments, the results provide a set of important and reliable measures of the interrelations among the variables of interest. There has been a great deal of research in recent years on the genetics of bitter taste, with the identification of an allele of TAS2R38 that governs sensitivity to thiouracil-type compounds. Much of the genetic work has been done in conjunction with psychophysical testing that suggests stratification of bitter responsiveness at both threshold levels (distinguishing tasters who detect low concentrations from non-tasters who do not) and at suprathreshold levels (within the category of tasters, distinguishing homozygotic 'super-tasters,' who are exceptionally responsive, from heterozygotic 'regular tasters'). Further evidence suggests differences among these groups defined functionally (behaviorally) with regard to sweet taste and fat taste.

In light of these earlier findings, the present study, which looked at genetic markers directly, is especially important both for its positive and negative results - for example, for the lack of a clear relation between bitter alleles and either smoking or obesity. It is of course possible that relations do exist but did not appear in this study; however, the quality of the study and the size of the subject population imply that if correlations do exist, they are likely to be extremely small. It is noteworthy that other genes, such as the TAS1R family, the so-called fat-obesity gene, FTO, and the craving-addiction genes, DRD1 and OPRM1, were also examined and found not to be related to smoking.

Reviewer 3:

The aim of the study was focused on examining the interaction of specific taste receptor genotypes and genotypes related to obesity and reward: on sweet taste, the perception of fat, and its interaction with smoking and body weight.

Strengths: The rigorous approach to gathering data on subjects related to smoking behavior, body phenotype, preferences for sweet and fat, and the psychophysical evaluations, etc. were a significant strength of the study. Indeed, the investigators conducting these aspects of the study are internationally known for their expertise in collecting these type of data.

Weaknesses: 1) The overall question being asked lacked focused and was overreaching, especially given the size of the data set. There is the potential for so many interactions that it is difficult to see how the design of the study (especially in terms of a limited data set) could adequately illuminate on the global question posed or even focused sub-questions.

2) Related to the above, the results of this study, which this reviewer views as preliminary, do not support any of the "a priori" hypotheses. Establishing gene/phenotype relationships (even in more focused studies) requires very large sample sizes given the various environmental contributors to subject variability. Are the negative results an indication of what is "true" or a function of an inadequately focused set of questions? No information was provided in the current study of the minor allele frequencies of the genes under study. It is unclear, given the data stratification, whether there is enough statistical power to really evaluate the multitude of questions.

3) One interesting finding of the study was that current smokers and never-smokers differ in their liking of sweet and fat preference (without an impact on weight). It would have been very useful for the investigators to consider, even briefly, the physiologic and/or molecular effect of smoking on the tongue.

***Criterion 2 - What is the likely beneficial impact of this project? If the likely beneficial impact is small, is it judged reasonable in light of the dollars budgeted?***

### ***STRENGTHS AND WEAKNESSES***

#### Reviewer 1:

Since there are two major factors that are responsible for reducing longevity and productivity in humans, any study that leads to a more complete understanding of what affects obesity and smoking behaviors in humans has obvious beneficial effects for society. As individual differences in taste sensitivity are better understood, it should be possible to suggest how individuals could, if they wish, choose more healthy behaviors.

#### Reviewer 2:

The present study did not aim to test diagnoses or treatments per se, but aimed instead at a better understanding of the interrelations among genetic factors, smoking, and obesity in women and their children. Long-range goals would include more effective interventions to reduce both smoking and obesity, both being major health hazards with major behavioral components.

Toward this end, as already indicated, the present study bears significant implications for health-both in its positive and its negative findings. Several of the positive findings are notable - for instance, the strong connection between the body weight of mothers and their children to the mothers' smoking status, smokers being heavier, typically obese, and having children of greater body weight than those of non-smokers. The implication that preferences for sweet tastes decline with development, whereas preferences for fat increase, also bears important implications for individual and public programs to help reduce obesity.

What is less clear is the role of taste-pertinent genes to smoking and to the smoking-taste-obesity nexus. The present results suggest these genetic influences may be less important than other (experiential, environmental) influences, although genetic influences on food preferences, per se, are certainly plausible.

In any case, the complex interrelations among genetics, smoking, taste preferences, and body weight are still poorly understood. The present project made significant advances in understanding which relations are likely to be most important for future investigation. As the PI notes, one future direction could involve developmental studies in humans and appropriate animal models.

Reviewer 3:

The focus of the research was predicated on the proposition that a better understanding of how individual differences in specific taste receptors contribute to specific negative health-related behaviors such as smoking and the development of obesity. The extensive descriptive data of the population under study, notwithstanding the negative findings of the study, would suggest minimal to no significance for improving health.

***Criterion 3 - Did the project leverage additional funds or were any additional grant applications submitted as a result of this project?***

***STRENGTHS AND WEAKNESSES***

Reviewer 1:

There was no leveraging of additional funds. The study, as of the reporting date, did not result in any submitted grant applications. The Final Progress Report indicates the data collected will provide the groundwork for a grant to be submitted to the National Institutes of Health.

Reviewer 2:

No additional funds were leveraged. The investigators do plan, however, to seek further funding through NIH.

Reviewer 3:

The project did not leverage additional funds. The investigators are planning to pursue the observation that current smokers and never-smokers differ in their liking of sweet and fat preference.

***Criterion 4 - Did the project result in any peer-reviewed publications, licenses, patents, or commercial development opportunities? Were any of these submitted / filed?***

***STRENGTHS AND WEAKNESSES***

Reviewer 1:

The project did not result in any peer-reviewed publications, licenses, or patents. In the Final Progress Report, however, the investigators indicated plans to prepare a manuscript for publication in a journal like the American Journal of Clinical Nutrition.

Reviewer 2:

There were no publications, licenses, or patents.

Reviewer 3:

There have been no publications, etc. submitted to this point, although the investigators indicate one is planned for submission to the American Journal of Clinical Nutrition or similar journal.

***Criterion 5 - Did the project enhance the quality and capacity for research at the grantee's institution?***

***STRENGTHS AND WEAKNESSES***

Reviewer 1:

The development of a laboratory-based test for fat preferences suitable for both adults and children is expected to aid in an understanding of the physiological basis of fat preference, especially as related to gene expression.

Reviewer 2:

The new lab-based test for fat preference will enhance future research at the institution.

No new investigators or outside researchers were brought into this project, nor were funds used to pay pre-doctoral or post-doctoral students. But five undergraduate students did participate.

Reviewer 3:

There were no changes to infrastructure, etc. The only impact noted by the progress report was the development of a laboratory-based test for fat preference in children and adults.

***Criterion 6 - Did the project lead to collaboration with research partners outside of the institution or new involvement with the community?***

***STRENGTHS AND WEAKNESSES***

Reviewer 1:

The project did not lead to collaborations with research partners outside the institution, but it did result in the recruitment of subjects from Women, Infant, and Children (WIC) programs, homeless shelters, and other programs in the area that serve women and children.

Reviewer 2:

The only community involvement that was identified came through the recruitment of subjects (mothers and children) through WIC programs, homeless shelters, and so forth.

## ***Section B. Recommendations***

### ***SPECIFIC WEAKNESSES AND RECOMMENDATIONS***

#### Reviewer 3:

1. The behaviors the investigators are studying are very complex. We have seen a surge in obesity over a relatively short time-span. This is a function of a myriad of contributing factors. The investigators have attempted to reduce the question to, perhaps, taste genetics (and preferences) and/or smoking behavior. Likewise, they have attempted to implicate taste genetics in smoking behavior. Further, they wish to connect all of these to each other. It is difficult to see how these questions can be evaluated with the sample size.
2. There is a lack of physiologic consideration of smoking on taste function. Some consideration should be given to how smoking affects taste. For example, what happens to bitter, sweet, umami, sour, etc. sensitivity in smoke?