

# Monell Chemical Senses Center

## Annual Progress Report: 2008 Formula Grant

### Reporting Period

July 1, 2009 – December 31, 2009

### Formula Grant Overview

The Monell Chemical Senses Center received \$217,894 in formula funds for the grant award period January 1, 2009 through December 31, 2009. Accomplishments for the reporting period are described below.

### Research Project 1: Project Title and Purpose

*Effect of Genotype on Smoking, Taste and Obesity in Mothers and Children* - The purpose of this project is to explore the interaction between behavior and genotype as it impacts human health, focusing on smoking and its relationship with taste, food preferences and obesity in mothers and their children. Previous work from our laboratory as well as others have indicated that alleles of a particular gene (a bitter receptor, *TAS2R38*) is associated with these behaviors (smoking, taste preferences and food choice). We will initiate a new study to determine how alleles of this gene and other candidate genes are related to smoking, bitter taste sensitivity and fat and sugar preference in mothers and their children. The information gleaned from this research may enable a better understanding of how individual differences in taste sensitivity contributes to health-promoting behaviors in the context of development.

### Duration of Project

1/1/2009 - 12/31/2009

### Project Overview

This project will determine the effects of genotype on the perception of fat and sweet taste and its interaction with smoking and body weight. Sophisticated psychophysical methods will be used to measure important aspects of sensory perception, such as sensitivity and preference, in tandem with recent techniques to measure genotypes, such as single nucleotide polymorphisms. This research will be conducted on genetically related subjects, i.e., mothers and children.

To these aims, a group of 50 racially and ethnically diverse, healthy women and their children aged 5 to 10 years will be tested on two occasions. They will be phenotyped for obesity (height, weight, percent body fat) as well as preferences for fats and sugar using psychophysical testings (e.g., two-alternative, forced-choice tracking procedure). Bitter sensitivity will also be assessed as a control procedure, to validate the integrity of data collection. Mood states, smoking history, and food habits and cravings will be assessed by standardized questionnaires. Mother-child pairs

will contribute cheek swabs from which DNA will be isolated, purified and quantitated. The genotypes of mothers and children will be assayed for alleles of the *TAS2R38* gene, a bitter receptor associated with smoking and dietary fat and sweet preference. Other candidate genes will also be assessed for their suggested role in taste-related behaviors (*TAS2R16*, *TAS1R3* and *FTO*). We hypothesize that the taste measures will be heritable (bitter, sweet and fat perception and preferences) but that some component will be due to shared environment as well as shared genes. We further hypothesize that children with bitter-sensitive alleles of the *TAS2R38* gene will prefer higher concentrations of fat and sugar and have higher thresholds for sweet taste compared with children with the insensitive alleles. *TAS2R38* genotypes may also be related to body weight or obesity in mothers and their children. For the mothers, we hypothesize that those with bitter sensitive alleles will be less likely to smoke and have higher fat and sweet preferences and cravings for these foods. Consequently, their children will have more exposure to these foods. This work will demonstrate that genotype affects health behaviors such as smoking, taste and food preferences and this information could be helpful in the future to devise tailored strategies for behavioral change.

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### **Other Participating Researchers**

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### **Expected Research Outcomes and Benefits**

One of the valuable points to emerge from biomedical research is that people's behaviors directly affect their health. Nowhere is this clearer than in the realm of smoking or diet. Smoking not only contributes to lung cancer and heart disease but also exacerbates the negative symptoms of other illness like diabetes. Likewise, obesity is a leading public health problem, which is often a direct result of overeating, especially of foods high in fat and sugar, e.g., doughnuts, ice cream, and pastries. For both overeating and smoking, there is a strong behavioral component, e.g., people choose to eat certain foods or choose to smoke.

While many people endanger their lives by smoking and by eating an unhealthy diet (e.g., too much refined sugar and fatty foods), not everyone does so. An important question is why people differ in these behaviors. There are a range of potential influences from genotype to culture to be considered and in this study we focus on two aspects, genetic variation and the mother-child environment. We know from previous studies that a person's genetic constitution can markedly affect their behavior, and we also know that the experience children receive from their mother, for instance, the smell of cigarette smoking if she smokes, or the foods she chooses to feed, can have an impact on the health and behavior of the child. Therefore in this project, we will

examine the effect of genetic variation on the liking and perception of sweet and the preference for dietary fat in mothers and children as well as how the variation interacts with whether the mother is a smoker or not. Using this family structure to collect data gives us several advantages: we can assess the heritability of these traits (like fat preference), as well as the effect of development, e.g., similarities and differences between the mother and the child. This research design also allows us to understand how the maternal likings for foods and smoking habits of the mother, which may be genetically mediated, impacts the child. Another benefit to this model is that children may be more sensitive to genetic effects because they have a shorter lifetime of experience to cloud the relationship. Thus genetic effects are more marked. We expect that the information gleaned from this research will enable us to understand how genetic variation interacts with development to impact important health behaviors.

### **Summary of Research Completed**

*Description of subject population.* We projected that fifty mother-child pairs would be tested on two separate days during the project period (January 1<sup>st</sup> 2009 to Dec 31<sup>st</sup> 2009). This goal for subject recruitment and testing was met and exceeded. The final total of subjects tested was 76 mothers and 97 children.

*Smoking behavior of mothers by self-report.* Just over half of the women were never-smokers, about 33% of the women were current smokers and a little over 10% of women were former smokers. Because of the small numbers of former smokers, their lack of uniformity in their smoking patterns and the possibility they might not provide sufficient statistical power for data analysis, they were not considered further.

To evaluate nicotine self-administration behavior in smokers, subjects were given the Fagerstrom test of Nicotine dependence and the Michigan Nicotine Reinforcement questionnaire. For women who reported they were current smokers, there was a wide range of nicotine dependence, with some women scoring 14 on the Fagerstrom scale (indicating extreme dependence) whereas a few women reported relatively low measures of nicotine dependence, with the average rating being 7.3. The average rating corresponds to a high level of dependence, which is consistent with the inclusion criterion, that to be considered smokers, women had to smoke at least five cigarettes a day and had to have smoked for at least a year. Thus women who are not very nicotine dependent, like casual smokers who have an occasional cigarette in social situations, were excluded from this study.

*Direct measures of carbon monoxide in breath.* At the beginning of each test day, the mother and child were asked to breathe into Vitalograph (Lenexa, KS) to obtain a measure of carbon monoxide levels. In all cases, the self-report of smoking behavior was consistent with the amount of breath carbon monoxide.

*Subject characteristics by maternal smoking status: age, education, income and obesity.* Next we focused on whether there were differences in the characteristics of mothers based on whether they were current or never-smokers. Mothers were stratified by smoking status and compared for age, education, income and obesity. Current smokers completed fewer years of school compared with women who were never-smokers, with current smokers having fewer years of

formal education and earning less money per household than never-smokers. Overall, current smokers were heavier than never-smokers, and almost all were obese by CDC standards. Children were compared for the same characteristics, stratified by maternal smoking. The largest difference between children based on maternal smoking was for body weight: 38% of children of current smokers were at a healthy body weight as defined by the CDC, whereas 67% of children from non-smoking mothers were within this healthy weight category.

*Additional obesity phenotypes.* We used three additional measures of obesity: waist circumference, waist-to-hip ratio and % body fat. All measures were in agreement with the main findings as assessed by BMI, women who smoke and their children were heavier and fatter than women who reported never smoking in their lifetime.

*Sweet and fat preferences by self-report.* Mothers answered questions about their own preference for sweet and fat and those of their children. Mothers who smoke reported higher liking and intake of high-fat foods and an inability to control their intake of sweets compared with never-smokers. Children did not differ in the liking for fat or sweet food by maternal smoking.

*Direct measures of sweet and fat preferences.* The most preferred level of (1) sucrose dissolved in plain water or (2) sucrose or (3) fat mixed in vanilla pudding was assessed by a forced-choice tracking technique developed at the Monell Center. We tested whether there were generational differences in sweet preference (mothers versus children). When children and mothers were grouped by whether the mother currently smoked, we found that women who smoked had child-like preferences for sucrose dissolved in water. We also learned that mothers liked puddings with a higher fat content than did children, and mothers who smoked liked a higher-fat pudding than never-smoking women or children. Fat and sweet preferences apparently change in opposite directions during development: sweet preference decreases and fat preference increases. The direction of causality is unclear: (a) smoking may prevent the drop in sweet preference and encourage a rise in fat preference or (b) women who smoke may have inborn sweet and fat preferences that are impervious to developmental effects.

*Bitter taste and other genes by smoking status.* Cigarettes can have a bitter taste and it is possible that people who are more sensitive to these bitter tastes are less likely to smoke. This hypothesis has recently gained support because bitter receptors, similar to those that sense bitter chemicals on the tongue, are also found in the airways.

Thus we genotyped the DNA of subjects to determine their alleles for the *TAS2R38* gene. The *TAS2R38* gene is a bitter receptor gene involved in taste and there are two major forms (alleles/haplotypes). If people have one form (AVI/AVI), they are insensitive to a particular bitter chemical whereas if they have the other form, they are sensitive and find this chemical to be very bitter.

Women were grouped by their smoking status to determine whether smokers were more likely to be insensitive to some bitter compounds (i.e., have the AVI/AVI form of the taste receptor; there are two copies of each gene and thus two haplotypes for each person). The results indicate no

difference in the frequency of the nontaster haplotypes between never-smokers and current smokers.

We also tested other gene-related hypothesis with no positive results. There were no differences in allele frequencies between smoking groups for genes relevant to other taste behavior (sweet perception; *TAS2R38* and *TAS1R3*), obesity (*FTO*), or addiction (*DRD2* and *OPRM1*). We also proposed to test the genotype of the cannabonid receptor in this project but technical problems (poor primer probe matches to the genomic DNA) prevented us from obtaining these results.