



## Understanding the Bio-behavioral Basis of Smoking Behavior

Tobacco use and its related diseases cause more than 450,000 deaths each year, including 170,000 from cancer alone. In order to address the smoking problem, innovative approaches to tobacco control must be taken.

Toward this end, the National Cancer Institute, the National Institute on Drug Abuse, and the Robert Wood Johnson Foundation are supporting a new initiative – Transdisciplinary Tobacco Use Research Centers – or TTURCs.

These TTURCs have set out to change the way research is conducted on tobacco use by using a “transdisciplinary” approach. The TTURCs combine scholars in such fields as medicine, law, communications, psychology, public policy, ethics, history, pharmacology, and neuroscience to solve problems in a collective manner.

Under the direction of Caryn Lerman, Ph.D., a collaborative effort between the University of Pennsylvania and Georgetown University was selected as one of the seven centers.

**This center is exploring the role of genetic factors in smoking initiation, smoking cessation, and harm from tobacco products.**

### Projects include:

- Georgetown Adolescence Tobacco Research study (GATOR study);
- Pharmacogenetic Trials of Smoking Cessation (Zyban/NRT);
- Determinants of Tobacco Smoke Exposure and Harm (Smoking Topography);
- Ethical Issues in Smoking and Genetics.

Dr. Lerman, Principal Investigator of the UPENN/Georgetown TTURC commented, “By increasing our understanding of the role of genetic factors in tobacco use and dependence, we hope to discover better ways to prevent smoking and to help people quit.”

### **GENES & SMOKING CESSATION**

**At the University of Pennsylvania and SUNY Buffalo, Caryn Lerman, Ph.D., Len Epstein, Ph.D. and colleagues are studying the role of genetic factors in smokers’ responses to different pharmacological treatments for smoking cessation.**

*“By identifying individual differences in response to particular types of smoking treatment, we may be better able to target different approaches to those smokers most likely to benefit,” Dr. Lerman stated.*

Thus far, over 400 smokers have participated in the bupropion (Zyban) clinical trial and over 140 are enrolled in the nicotine replacement therapy trial. A pooled analysis of data from the bupropion trial and the Brown University trial (Ray Niaura, Ph.D, P.I.) is underway. This analysis will determine whether smokers with particular variants of dopamine-related genes are more or less likely to benefit from treatment.

## Taking a Bite Out of Teen Smoking— the GATOR Project

Each day 4,800 of America’s teens try their first cigarette. Nearly 2,000 of them will become regular smokers — that is almost two million a year!

The **Georgetown Adolescence Tobacco Research, or GATOR project** intends to determine why some teens just experiment with smoking, while others seem to transition quickly to become regular smokers.

The GATOR project follows over 1,100 teens from five public high schools in Northern Virginia — through grades 9 to 12— to gain a better understanding of who adopts a regular smoking habit. Teens are asked to complete annual surveys and provide a cheek swab. GATOR will examine the role of social factors (peer smoking and tobacco advertising), psy-

chological factors (mood and personality) and biological factors (genetic influences).

“If we can gain a better understanding of the bio-behavioral predictors of adolescent smoking, then we can hopefully prevent adolescents from beginning to smoke, by targeting those most at-risk,” stated Janet Audrain, Ph.D., director of the GATOR project. “For instance, we have discovered that some teens are more affected by tobacco advertising than others.”

She also noted that social, psychological factors and biological influences have to be considered together to fully explain smoking behavior.

The next survey of these participants will be conducted, spring 2001.



## Moving Research into Clinical Practice

**FEB.22-** Thirty prestigious individuals, representing 13 different professions recently visited Georgetown's campus to participate in a conference entitled, "Emerging Ethical Issues in Smoking and Genetics." Traveling from across the nation, these scholars met to identify and discuss key ethical issues that need to be addressed in order for the full benefits of TTURC research to be realized.

The 'Ethical Issues' project is headed by Alexandra Shields, Ph.D., at Georgetown's Institute for Health Care Research and Policy (IHCRP), and is sponsored by the Robert Wood Johnson Foundation. The project represents a collaboration between Dr. Shields and Caryn Lerman, Ph.D., TTURC - P.I. Dr. Lerman's research on the role of genetic factors in nicotine dependence and response to treatment is being used as a case study through which to examine broader issues in tobacco research and new genetics. The 'Ethical Issues' mission is to anticipate and address the challenges surrounding the translation of new research into clinical practice and public policy.

"The field of genetics is exploding with major shifts toward complex pharmacogenomic approaches. The case of smoking and genetics engages many of the issues that we are likely to be confronted with in the coming years," stated Dr. Shields. "This is the perfect case study in



*Dr. Alexandra Shields (P.I.) and Dr. Judy Feder (Dean of Policy Studies at Georgetown) outline points for the agenda.*

the broader scope of bio-behavioral genetics aimed at improving health."

Using a transdisciplinary approach, the conference utilized the insights and methods of multiple disciplines including: law, psychology, anthropology, communications, public policy, ethics, pharmacology, human genetics, and medicine.

**"Our charge is to work together to discover key ethical issues brought about by this research..." Dr. Shields remarked. "Where do we need to extend empirical data, define terms, criteria and conditions, or further public debate and dialogue?"**

Thoughtful discussion was held on several issues central to the future adoption of this research. Topics such as the pleiotropic nature of the test (i.e. when a genetic test provides information about seemingly unrelated conditions), increased prevalence of the 'at-risk' genotype in identifiable sub-populations, and implications for informed consent were debated among the group.

As noted by Patricia King, J.D., Professor of Law at Georgetown, "A research agenda item for ethics is the appropriate use of race and ethnicity in the study of human variation-- because this is what I would call the 'dilemma of difference'." "We need to know when to take the difference into account... when to use it and why."

On the topic of privacy, Gary Claxton, formerly Deputy Assistant Secretary for Health Policy, at the U.S. Department of Health and Human Services asked, "How much are people informed about what this really might say about them in the future? How much else might be known about this particular genetic marker?" These issues have important implications for health insurance. As he noted, "Once this [genetic] information has left and gone into the broader healthcare system, the information's gone. You can't get it back."

Karen Pollitz, M.P.P., with Georgetown's IHCRP added, "As the genetic markers become clearer, that may actually improve the prospects for smoking cessation treatment, whereas now it is a named exclusion on a lot of policies."

A national research consortium will be developed including many participants of this conference. This group will be conducting original research on these issues over the next few years.

The University of  
Pennsylvania/  
Georgetown University  
**TTURC**

### TTURC Project Leaders:

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### TTURC Investigators:

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