

Institute for Behavioral Genetics  
University of Colorado at Boulder

# **Annual Report**

**July 1, 2004–June 30, 2005**

John K. Hewitt, Director

Toni N. Smolen, Assistant Director

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# MISSION

## Mission

During IBG's recent program review, the Internal Review Committee reported that IBG is "... among the strongest of the research institutes on campus. The Institute has an outstanding faculty and research staff that has established unique and highly successful interdisciplinary research programs." The research record of "... the resident faculty members ... is outstanding in terms of international recognition, publications, and extramural funding." The Extramural Review Committee concurred, referring to IBG as "... the leading center for human and animal behavioral genetic studies in the U.S. and, arguably, in the world." In its summary findings, the Program Review Panel stated that the "... Institute for Behavioral Genetics is an independent academic enterprise that is peerless in its field and a superb asset to the University of Colorado and to the Boulder Campus." (Program Review Final Report, May 2002)

The mission of IBG, an organized research unit of the University of Colorado at Boulder, is to conduct and facilitate research on the genetic bases of individual differences in behavior and to conduct research training in this interdisciplinary area. Throughout its history, IBG has been characterized by the breadth of its interdisciplinary research and training programs. Although the methodology of behavioral genetics is generally applicable to the study of individual differences for any character, current research at IBG is focused on behaviors of obvious societal relevance.

The human research, in addition to studies of drug-related behaviors, includes large-scale family, twin, and adoption studies of cognitive abilities and personality, and of disorders such as learning disabilities and psychopathology. The detection, localization, and identification of individual quantitative trait loci, using both linkage and association methods, is a high priority.

Laboratory animals are used to study drug-related behaviors, particularly those associated with the use of alcohol and nicotine. For these studies, a large number of different strains and genetically selected stocks of mice are maintained in the IBG specific-pathogen-free mouse laboratory. These include inbred and recombinant strains of mice that provide efficient tools for screening behaviors for genetic influence and mapping quantitative trait loci. Selection studies in which mice are bred for certain characteristics provide definitive proof of genetic influence and also yield animal models that are valuable for subsequent research in functional genomics.

# DIRECTOR

## From the Director

The academic year 2004–05 was another successful one for the institute and also the last year of my first four-year period as director. I am happy to say that this has been the most rewarding experience of my career and has been marked by a number of significant accomplishments as a result of efforts of the institute’s faculty fellows, individually and collectively, and the institute’s staff, researchers, and students. This is truly a great group.

We have continued our strong record of publication and research productivity. During the past year, IBG faculty published 70 journal articles, 13 book chapters, and 58 abstracts.

The total IBG budget during 2004–05 (including general fund support, grants, and gifts) was \$12,973,489. Most significantly, of that amount, \$11,442,867 represented research expenditures, a 17.8 percent increase over the previous year.

Reflecting on my first four years, one of my first tasks as the new director was to work on our program review. Gratifyingly, in its summary findings the Program Review Panel stated that the “. . . Institute for Behavioral Genetics is an independent academic enterprise that is peerless in its field and a superb asset to the University of Colorado and to the Boulder Campus” (*Program Review Final Report*, May 2002). This judgment necessarily reflects the strength of the research and educational leadership provided by our faculty, and so faculty appointments and recruitment are among our most important activities. In 2002 we appointed six new faculty fellows: Ken Krauter (MCD biology), Tom Crowley (University of Colorado at Denver and Health Sciences Center psychiatry), Soo Rhee (psychology), Kent Hutchison (psychology), Jim Sikela (pharmacology), and Richard Radcliffe (pharmaceutical sciences). Two new graduate school faculty (and faculty fellows) were hired in 2003–04: Jerry Stitzel (molecular genetics and pharmacogenetics) and Marissa Ehringer (molecular genetics and bioinformatics). They both have academic appointments in the Department of Integrative Physiology, as does Professor Tom Johnson. We also congratulate one of our Senior Research Associates, Chris Link, on his appointment as a research associate professor in integrative physiology this year. Each of these new appointments has contributed to the further strengthening of our interdisciplinary expertise, and to the leadership provided by the faculty.

The new wing of the main IBG building is all but completed, and will be occupied in January 2006. This provides us with 5,700 square feet of new testing and laboratory space, faculty offices, and a large “interaction space” that will hopefully facilitate interdisciplinary collaborations within the institute. We especially owe thanks to Drs. Andy and Toni Smolen and Mr. Sean Shelby of IBG for their contributions to this endeavor. Of course, many individuals in the university’s Department of Facilities Management and other departments have worked diligently to see this building completed to a high standard, and we are very grateful to them for their work.

In 2003 we created a new IBG ad hoc committee on research faculty appointments and titles to make recommendations on the reorganization of our research career structure so that we can recognize different degrees of seniority and accomplishment. Since then, we have implemented the use of the senior research associate title and have promoted 10 of our research associates to this title. We have also now implemented a similar program for our professional research assistants, involving the use of the titles of PRA I, PRA II, and Senior PRA.

Our graduate and postdoctoral training mission has been strengthened by the renewal of our training grants, which are supported by the National Institute on Mental Health and the National Institute of Child Health and Human Development, plus the award of a new grant for Research Training in the Genetics of Substance Abuse, which is supported by the National Institute on Drug Abuse. Together these awards now allow the institute to fully support 13 graduate students and five postdoctoral trainees in behavior genetics. Additionally, the director of IBG serves as co-PI on an NIAAA postdoctoral training grant based at UCDHSC. This grant funds seven postdoctoral fellows, including one who worked at IBG during 2003–04.

IBG also hosts annual one-week training workshops, supported by the National Institute of Mental Health, that are internationally recognized as the premier short courses in human statistical genetics for the study of behavior and complex traits. They attract up to 100 “students” (often senior-level researchers and academics) each year.

The following IBG students and faculty won awards in 2004–05: Heather Gelhorn won both the Dozier Award, for the best graduate student in psychology, and the Thompson Award, for the best presentation by an associate member at the Behavior Genetics Society annual meeting. Norm Henderson, Maria Turri, John DeFries, and Jonathan Flint won the 2005 Fulker Award for the best paper published in *Behavior Genetics* in 2004 for their paper “QTL Analysis of Multiple Behavioral Measures of Anxiety in Mice” (*Behavior Genetics*, 2004, 34: 267–93). This work was conducted at the institute and had in fact been initiated by the late David Fulker, a professor and faculty fellow of the institute, for whom the award is named.

Once again I want to thank all of the faculty, staff, and students of the institute for their superb professional and scientific performance and for the collegiality that remains a distinguishing and necessary characteristic of the institute. A special thanks goes to Assistant Director Dr. Toni Smolen, and to Ms. Debbie Aguiar and Mr. Sean Shelby for their work in preparing this report.

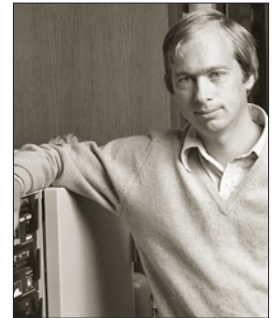
John K. Hewitt  
Director

# FELLOWS

## Faculty Fellows

### **Michael D. Breed**

Professor, Department of Ecology and Evolutionary Biology, University of Colorado at Boulder; PhD, University of Kansas, Lawrence, 1977. Professor Breed's research emphasis is the genetics of social recognition systems in animals. His current interests include behavioral and genetic studies of the recognition cues used by honeybees to discriminate nestmates from non-nestmates. He is presently engaged in investigating the role of cuticular compounds in recognition, and the patterns of inheritance of chemical cuticular signatures.



### **Gregory Carey**

Associate Professor, Department of Psychology, University of Colorado at Boulder; PhD, University of Minnesota, 1978. Dr. Carey's research interests are in the areas of genetics and human psychopathology. Within these areas, his work concentrates on the anxiety disorders and on the development of externalizing behavior (antisocial tendencies, drug abuse, and alcohol abuse) during adolescence. A second major interest is the use of quantitative models to represent mechanisms of assortative mating, development, cultural transmission, and sibling interactions.



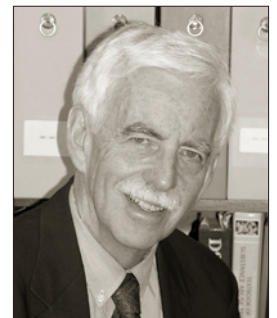
### **Allan C. Collins**

Professor of Psychology and Pharmacology, Department of Psychology, University of Colorado at Boulder; PhD, University of Wisconsin, 1969; NIAAA Research Scientist Award, 1978–83; NIDA Level V Research Scientist Award, 1993–2003. Professor Collins is a biochemical pharmacologist whose primary research specialization is neurochemistry. His current research interests include neurochemical correlates of nicotine use, tolerance development, and withdrawal; neurochemical bases of alcohol tolerance; biochemical bases of behavior; and utilization of genetics as a tool to determine the mechanism of action of drugs.



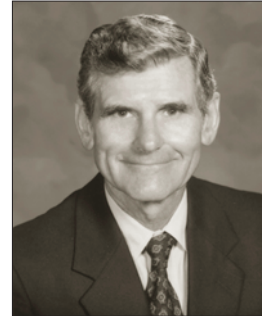
### **Thomas Crowley**

Professor, Department of Psychiatry; Director, Division of Substance Dependence, School of Medicine, University of Colorado at Denver and Health Sciences Center; MD, University of Minnesota, 1962. Thomas Crowley currently heads a number of studies that focus on genetic and environmental influences on the development of behavior problems and substance abuse issues among adolescents. Additional interests include the feasibility of executive cognitive functioning tasks in adolescents with serious substance and conduct problems compared to community controls, as well as the feasibility of conducting fMRI research in troubled adolescents and a control group of general population adolescents.



**John C. DeFries**

Professor, Department of Psychology, University of Colorado at Boulder; PhD, University of Illinois, 1961; President of the Behavior Genetics Association, 1982–83; Distinguished Research Lectureship, Council on Research and Creative Work, University of Colorado at Boulder, 2001–02. Professor DeFries’ primary field of specialization is quantitative behavioral genetics. His current research interests include twin and adoption studies of human cognitive abilities; the genetics of learning disabilities; and the use of DNA markers to map quantitative trait loci (QTLs) that influence behavioral characters.



**Richard A. Deitrich**

Professor, Department of Pharmacology, University of Colorado at Denver and Health Sciences Center; PhD, University of Colorado, 1959; NIGMS Research Career Development Award, 1965–75; NIAAA Research Scientist Award, 1986–2001; President of the Research Society on Alcoholism, 1981–83; Co-Scientific Director of the University of Colorado Alcohol Research Center, 1977–02; NIAAA Merit Award, 1996–2004. Professor Deitrich is a pharmacologist whose current research concerns the molecular basis of the actions of alcohol. His research uses genetically selected lines of mice and rats to discover mechanisms of central nervous system depression, tolerance, and dependence. These data are used to identify specific genes responsible for these actions in animals, and eventually to identify similar genes in humans at risk for development of alcoholism.



**Marissa A. Ehringer**

Assistant Professor, Department of Integrative Physiology, University of Colorado at Boulder; PhD, University of Colorado at Denver and Health Sciences Center, 2001. Dr. Ehringer is a molecular geneticist who utilizes the genomics and bioinformatics resources to study behavior genetics. Her current research involves the study of candidate genes that may underlie genetic mechanisms that contribute to alcohol, tobacco, and substance use.



**John K. Hewitt**

Director of IBG and Professor of Psychology, University of Colorado at Boulder; Professor of Psychiatry (Attendant Rank), School of Medicine, University of Colorado at Denver and Health Sciences Center; PhD, University of London, 1978; President of the Behavior Genetics Association, 2000–01; Editor-in-Chief, *Behavior Genetics*. Professor Hewitt uses cross-sectional and longitudinal studies of twins and families to study behavioral development, and genetic and environmental influences on behavior, personality, and health. His recent research has focused on the development of behavior problems in childhood and adolescence; vulnerability to drug use, abuse, and dependence; genetics and health; and linkage and association studies of behavioral traits.





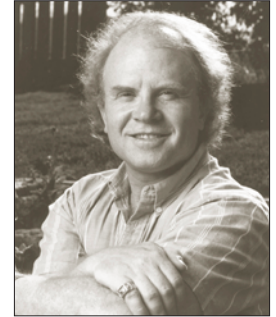
### **Kent Hutchison**

Associate Professor, Department of Psychology, University of Colorado at Boulder; PhD, Oklahoma State University, 1995. Dr. Hutchison is a clinical psychologist whose research examines mechanisms that underlie substance abuse and dependence (e.g., craving and drug reinforcement), individual difference variables that may moderate these mechanisms, and behavioral and pharmacological treatments that may moderate these mechanisms with the intention of reducing substance use. His studies employ research techniques that include: Ecological Momentary Assessment using palm pilot computers to collect daily data from participants in the field; novel medications that are useful for teasing apart the pharmacology of substance abuse as well as treating substance abuse; and novel phenotypic and physiological markers. His lab also has an active interest in how stress may moderate the pharmacological and behavioral effects of alcohol and drugs.



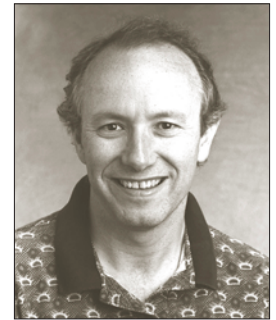
### **Thomas E. Johnson**

Professor of Behavioral Genetics, Department of Integrative Physiology, University of Colorado at Boulder; PhD, University of Washington, 1975; NIH Research Scientist Award, 1994–2004. In 2002 Dr. Johnson received the Kleemeier Award (the premier award in aging research) for his discovery of the first gerontogene, *age-1*, which doubles the life span and opened up a new area of scientific research. He is also cloning quantitative trait loci conferring sensitivity to alcohol in mice. His lab uses multiple techniques—behavioral, biochemical, molecular, pharmacological, quantitative, and genetic—to analyze both aging and the action of genes leading to addiction. He recently discovered a biomarker for aging that explains a three-fold difference in longevity among isogenic worms grown in a common environment. For more information, visit his web site at <http://ibgwww.colorado.edu/tj-lab>.



### **Kenneth Krauter**

Professor, Department of Molecular, Cellular, and Developmental Biology, University of Colorado at Boulder; PhD, Albert Einstein College of Medicine, 1980. Dr. Krauter is a molecular biologist whose research focuses on two aspects of human genome research. The first is in the area of comparative genome analysis using “high-throughput” mapping and DNA sequence analysis to examine similarities between human and mouse genes including the skeletal myosin heavy chains. By developing high resolution maps and complete DNA sequence of the analogous genes in the two species, it is possible to identify potentially important elements responsible for regulation and function of the genes. The second area of interest is the use of genetic analysis to identify genes involved in complex traits such as adolescent antisocial behavior. This latter study is done in collaboration with the Center for the Genetics of Antisocial Drug Dependence at the University of Colorado at Denver and Health Sciences Center and the Institute for Behavioral Genetics at the University of Colorado at Boulder.



### **Carol B. Lynch**

Professor, Department of Ecology and Evolutionary Biology, University of Colorado at Boulder; PhD, University of Iowa, 1971. Professor Lynch’s research interests are the genetic basis of evolutionary adaptation and brain mechanisms underlying adaptive behaviors. Her current research uses a model system, which has been the study of cold adaptation in mice, with emphasis on nest building. This involves the use of replicated genetic lines of mice that have been selectively bred for over sixty generations for differences in nest building. These lines also differ in genetically correlated traits, such as body weight and litter size, as well as circadian rhythms and brain (hypothalamus) neurochemistry and neuroanatomy. These lines facilitate studies of both constraints on adaptive evolution and the path from genes to behavior.





**Richard K. Olson**

Professor, Department of Psychology, University of Colorado at Boulder; PhD, University of Oregon, 1970. Professor Olson is a developmental psychologist whose primary research is on the varieties, etiology, and remediation of learning disorders. His research has examined the component processes in reading and related language skills that are associated with both normal and subnormal development. Heritability of these component processes is being evaluated through twin analyses. Additional projects are focused on the use of computer speech feedback in the remediation of reading disabilities.

**Bruce F. Pennington**

John Evans Professor, Department of Psychology, and Director of the Developmental Cognitive Neuroscience Program, University of Denver; PhD, Duke University, 1977. Professor Pennington is a developmental neuropsychologist whose research focuses on understanding disorders of cognitive development. The disorders he studies include developmental dyslexia, attention deficit hyperactivity disorder, and several mental retardation syndromes: early treated phenylketonuria, fragile X syndrome, Down's syndrome, and infantile autism. The long-term goal of this work is to understand how different genetic influences alter brain development to produce the distinct profiles of cognitive strengths and weaknesses found in each of these disorders.

**Dennis R. Petersen**

Professor of Pharmacology and Pharmacogenetics, School of Pharmacy, University of Colorado at Denver and Health Sciences Center; PhD, University of Wyoming, 1974; NIAAA Research Scientist Development Award, 1987-92. Professor Petersen's research concerns biochemical pharmacology and toxicology of alcohols and aldehydes. This research focuses on enzyme systems in liver, kidney, and brain that are involved in the biotransformation of endogenous and exogenous aldehydes. Of particular interest is the interaction of acute or chronic alcohol consumption with these enzymatic pathways. His recent research efforts have emphasized the use of genetics in studying the molecular and biochemical mechanisms underlying the hepatotoxic potential of various drugs and chemicals.

**Richard A. Radcliffe**

Assistant Professor of Pharmacology, School of Pharmacy, Department of Pharmaceutical Sciences, University of Colorado at Denver and Health Sciences Center; PhD, University of Colorado at Denver and Health Sciences Center, 1996. Dr. Radcliffe's research focuses on the genetic and molecular basis of drug and alcohol addiction. Current projects include gene expression microarray analyses of CNS systems involved in behavioral responses to methamphetamine and alcohol, QTL mapping of alcohol-related traits, genetic characterization of acute alcohol tolerance in zebrafish, and studies of the role of protein kinase C in central nervous system apoptosis.



**Soo Rhee**

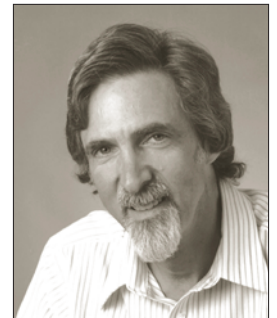
Assistant Professor of Psychology, Department of Psychology, University of Colorado at Boulder; PhD, Emory University, 1999. Dr. Rhee's primary research interests are the etiology and development of childhood disruptive disorders, the etiology and development of substance use disorders, the causes of comorbidity between psychiatric disorders and substance use disorders, and the development of methods discriminating correct models for causes of comorbidity.

**James Sikela**

Professor, Department of Pharmacology and Human Medical Genetics Program, University of Colorado at Denver and Health Sciences Center; PhD, Case Western Reserve University, 1983. Dr. Sikela is a genome scientist and has been a key pioneer in the development of EST technology and large-scale human gene mapping. His laboratory was part of the international gene-mapping consortium that determined the chromosomal location for the majority of human genes. He contributed to the discovery of the PSN2 gene that causes Alzheimer's disease. Currently his research involves applying genomics approaches to the discovery of genes involved in neurogenetic diseases such as alcoholism and mental retardation. His laboratory is also involved in the identification of genes important to human and primate evolution, including those that are specific to the human lineage and related to the structure and function of the human brain.

**Andrew Smolen**

Senior Research Associate, Institute for Behavioral Genetics, University of Colorado at Boulder; PhD, University of Colorado, 1979. Dr. Smolen is a pharmacologist whose primary interests are in the areas of neurochemistry and pharmacogenetics. His current research activities include the assessment of the contribution of specific candidate genes to complex behaviors such as substance abuse and Attention Deficit Hyperactivity Disorder.

**Toni N. Smolen**

Assistant Director, Institute for Behavioral Genetics, University of Colorado at Boulder; PhD, University of Colorado, 1981. Dr. Smolen's research interests are in the areas of pharmacogenetics and neuropharmacology. Her current projects use genetically inbred and selected lines of mice in studies of biochemical and neurochemical mechanisms that underlie the development of drug tolerance and dependence, the role of the adenosine neuromodulatory system in the mediation of the effects of acute and chronic alcohol administration, and drug metabolism in young and aging mice.



**Michael Stallings**

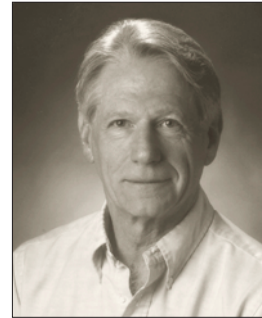
Assistant Professor, Institute for Behavioral Genetics and Department of Psychology, University of Colorado at Boulder; PhD, University of Southern California, 1993. Dr. Stallings' research interests include quantitative genetics, substance abuse, and personality. His current research utilizes biometrical modeling and quantitative trait loci (QTL) methodology to understand genetic and environmental influences on the development of substance use disorders and comorbid psychopathology.

**Jerry A. Stitzel**

Assistant Professor, Department of Integrative Physiology, University of Colorado at Boulder; PhD, Johns Hopkins University, 1992. Dr. Stitzel is a molecular biologist whose primary interest is the use of genetic strategies to identify the underlying biological bases for the behavioral and physiological actions of drugs of abuse with special emphasis on nicotine. Current projects include the molecular, biochemical, and cellular characterization of naturally occurring variants of neuronal nicotinic receptors and quantitative trait loci mapping of a nicotine preference phenotype.

**Boris Tabakoff**

Professor and Chair, Department of Pharmacology, University of Colorado at Denver and Health Sciences Center; PhD, University of Colorado, 1970; President of the Research Society on Alcoholism, 1983–85; President of the International Society for Biomedical Research on Alcoholism, 1986–90; RSA Award for Scientific Excellence in Alcohol Research and Jellinek Award for alcoholism research, 1988; Florence Rena Sabin Award, 2002, University of Colorado at Denver and Health Sciences Center. Member, National Advisory Council for the National Institute on Alcohol Abuse and Alcoholism. Professor Tabakoff's research concerns physiological, pharmacological, and biochemical correlates of alcohol and opiate/cannabinoid abuse. Current studies focus on behavioral genetic factors mediating tolerance development; the involvement of brain glutamate receptors in addiction; and the interaction of addictive drugs with adenylyl cyclase signaling in brain. Studies are pursued with both human and non-human subjects using genetic, molecular genetic, and microarray technology.

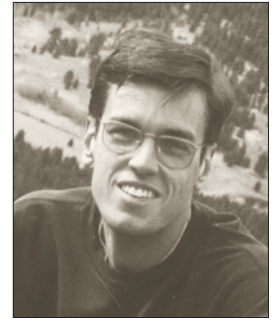
**Jeanne M. Wehner**

Professor of Psychology, University of Colorado at Boulder; PhD, University of Minnesota Medical School, 1976; NIAAA Research Scientist Development Award, 1991–96; 1997–2002. Professor Wehner is a biochemist whose primary research interests are pharmacogenetics and neurobiology. Current projects include biochemical and genetic studies of learning and memory, the role of nicotinic receptors in modulation of learning, and the role of protein kinase C in alcohol's actions.

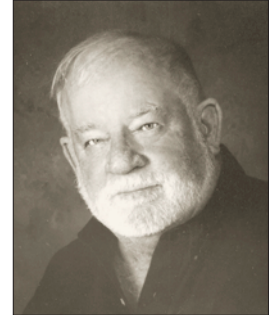


**Erik G. Willcutt**

Assistant Professor of Clinical Psychology, University of Colorado at Boulder; PhD, University of Denver, 1998. Professor Willcutt's current research focuses on the causes and consequences of Attention Deficit Hyperactivity Disorder, learning disabilities, and their comorbidity. He uses genetic linkage and association techniques in studies of families and twins to identify genes which increase susceptibility to these difficulties.

**James R. Wilson**

Professor Emeritus, Department of Psychology, University of Colorado at Boulder; PhD, University of California, Berkeley, 1968. Professor Wilson's primary field of specialization is behavioral biology. His research interests have included the endocrinological and genetic bases of maternal behavior, sexual behavior, activity differences, and learning differences in mice; and genetic studies of cognitive functions in humans. Work in the mid-'90s involved genetic selection in mice for alcohol dependence, behavioral genetic studies of alcohol dosing and cigarette withdrawal in humans, and studies of neuroelectric treatment for cigarette addiction and alleviation of migraine headaches.



# POSTDOCS & ASSOCIATES

## Postdoctoral Fellows, Senior Research Associates, and Research Associates

**Beth Bennett**, PhD, University of Colorado, 1986. Molecular identification of genes underlying initial sensitivity to alcohol and alcohol preference; development and characterization of the largest existing panel of murine RI strains.

**Rebecca Betjemann**, PhD, University of Denver, 2005. Cognitive processes involved in learning disabilities; language components including semantics and comprehension in children with reading disability and ADHD.

**Barbara Bowers**, PhD, University of Colorado, 1990. Evaluation of the role of protein kinase C and its regulation of the serotonergic system in ethanol consumption and behavioral impulsivity. Characterization of genes and proteins involved in ethanol sensitivity and ethanol tolerance in the presence or absence of protein kinase C gamma activity. Investigation of the role of neuronal nicotinic acetylcholine receptors in modulating ethanol's behavioral effects.

**Christopher M. Butt**, PhD, University of Kentucky, 2000. Studies of ethanol and nicotine interactions using neurochemistry, behavior, and a merging of classical genetics with null-mutation technology.

**Tanya Button**, Ph.D., Kings College London, 2005. Examination of the relationship between conduct problems and substance use problems, and the interplay of genetic and environmental risks for both conduct problems and substance problems.

**Nomita Chhabildas**, PhD, University of Denver, 2003. Neuropsychological and psychiatric correlates of Attention-Deficit/Hyperactivity Disorder, as well as broader comorbidity issues in childhood psychopathology and learning disabilities.

**Robin Corley**, PhD, University of Colorado, 1987. Longitudinal analysis of specific cognitive abilities and problem behaviors.

**Jim Cypser**, PhD, University of Colorado, 2002. Discovery and characterization of biomarkers of aging, e.g., physiological or molecular characteristics that predict individual subsequent life span (in the nematode *C. elegans*). Also the demographic patterns of mortality displayed by long-lived mutants, and the relationship between stress resistance and the rate of aging.



- Christopher Downing**, PhD, State University of New York at Albany, 2001. Classical and molecular genetic methods, such as QTL analysis, congenic and transgenic mice, and gene expression techniques to identify and evaluate genes mediating drug-related phenotypes.
- Maria L. Florez-McClure**, PhD, University of Colorado at Denver and Health Sciences Center, 2004. Investigating the role of autophagy in neurodegenerative diseases, especially Alzheimer's disease, using *C. elegans* as a model organism.
- Naomi Friedman**, PhD, University of Colorado, 2002. Working memory and executive functions, including individual differences and behavioral genetic analyses of executive functions such as inhibition.
- Sharon Grady**, PhD, University of Michigan, 1973. Function of nicotine in the central nervous system of mice, specifically, nicotine-stimulated release of neurotransmitters from synaptosomes.
- Wail Hassan**, PhD, The University of Southern Mississippi, 2004. Gene expression profiling of *Caenorhabditis elegans* worms expressing amyloid beta peptide (the main constituent of the senile plaques of Alzheimer's disease).
- Samuel Henderson**, PhD, University of Chicago, 1992. Study of DAF-16 in regulating longevity and stress resistance in the nematode *C. elegans*.
- Nate Kahn**, PhD, University of Denver, 1999. Molecular genetics of stress resistance and aging, using transgenic *C. elegans* for analysis of loci and molecular mechanisms involved in stress responses and longevity.
- Jeffrey Lessem**, PhD, University of Colorado, 1999. Research into the methodology for detecting quantitative trait loci; particularly in relation to substance use disorders and conduct disorders.
- Christopher Link**, PhD, University of Massachusetts, 1981. Molecular genetics; modeling of neurodegenerative diseases using transgenic *C. elegans*.
- Michael Marks**, PhD, University of Michigan, 1974. Genetic influences on molecular, biochemical, physiological, and behavioral factors mediating the responses to nicotine in mice.
- Sharon Mexal**, PhD, University of Colorado at Denver and Health Sciences Center, 2005. Genetic and environmental factors underlying the development of conduct disorder, ADHD, and substance use problems; links between executive cognitive function and developmental psychopathology.
- Junji Mitsushita**, MD, PhD, Shinshu University School of Medicine, 2004. General mechanism of longevity by using *C. elegans* as a model animal, particularly the role of oxidative stress and longevity in genetic and/or epigenetic regulation.
- Shane Rea**, PhD, University of Queensland, 2000. Demographics of aging in the nematode *C. elegans*. Identification of long-lived individuals in genetically homogeneous populations. Elucidation of the molecular basis of life extension in the mitochondrial Mit mutants of *C. elegans*.
- Brad Rikke**, PhD, University of Texas, 1992. Genetic mapping and identification of genes underlying the ability of dietary restrictions to retard aging in mice.
- Outi Salminen**, PhD, University of Helsinki, 2000. The central effects of nicotine, using combined biochemical, behavioral, and gene null mutation approach.
- Stephanie Schmitz**, PhD, University of Colorado, 1996. Genetic and environmental influences on the development of temperament, personality, and problem behavior; behavior genetics of psychopathology and health behaviors, their correlates, antecedents, and possible outcomes.
- Gary Stetler**, PhD, University of Utah, 1980. The application and development of high-throughput methods for the identification of genes involved in human behavior and learning.
- David Timberlake**, PhD, University of California, San Diego, 2003. Investigations of heritability of tobacco use and associations between nicotine dependence and candidate genes.
- Rolando Tiu, Jr.**, PhD, Case Western Reserve University, 2003. Exploration of the relationships between general and specific cognitive abilities and achievement.
- Natascia Ventura**, MD, PhD, University of Rome Tor Vergata, 1999/2001. The paradoxical role of frataxin, a nuclear encoded mitochondrial protein, in the prolongation of life-span in *C. elegans* and apoptosis (programmed cell death) such as that seen in the human inherited recessive condition Friedreich's Ataxia.
- Sally Wadsworth**, PhD, University of Colorado, 1994. Genetic and environmental influences on development of learning disabilities and academic achievement.
- Paul Whiteaker**, PhD, University of Bath, UK, 1996. Molecular basis of nicotine's central effects, using a combined biochemical, immunochemical, receptor binding, and gene null mutation approach.
- Deqing Wu**, PhD, Peking University, 1995. Statistical and genetic analysis of aging in *C. elegans*.
- Susan Young**, PhD, University of Colorado, 1998. Genetic and environmental factors underlying the development of conduct disorder, ADHD, and substance use problems; links between executive cognitive function and developmental psychopathology.
- Joanna Zeiger**, PhD, Johns Hopkins University Bloomberg School of Public Health, 2001. Genetic and environmental factors, particularly gene-environment interaction, that increase risk to common diseases.

# SUPPORT

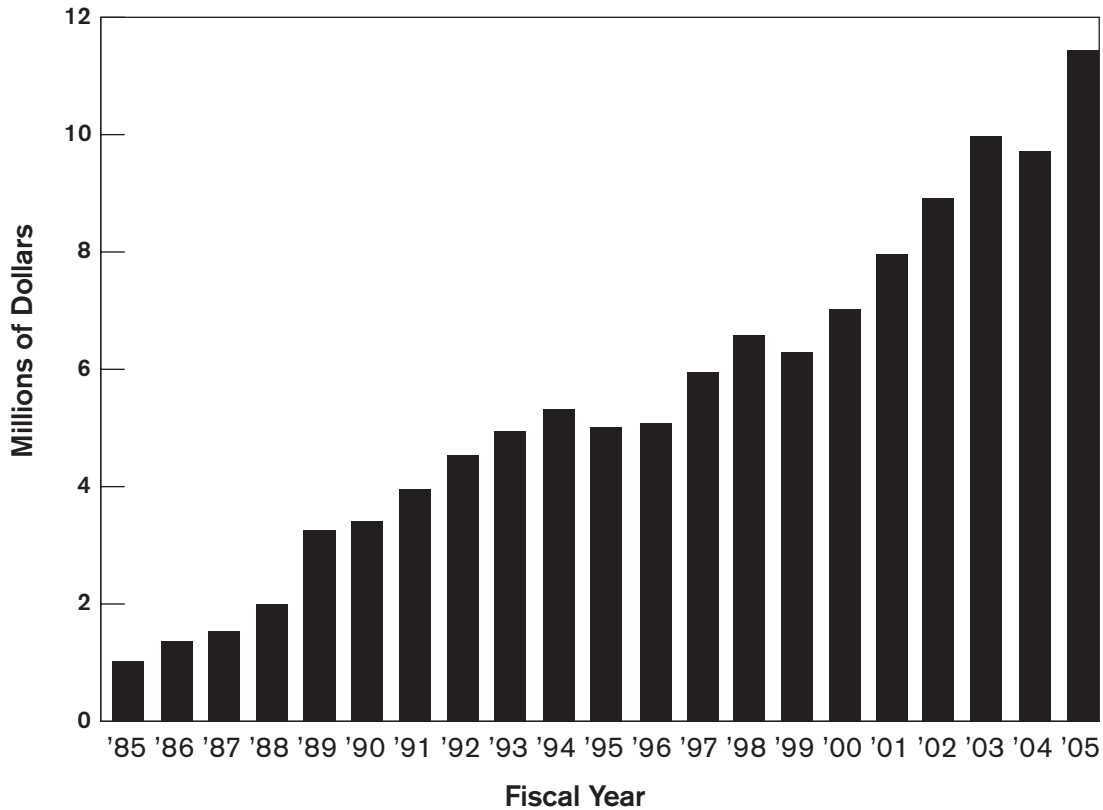
## Research, Training, and Education Support: 2004–05 Fiscal Year

Source of Funding	Number of Awards	Fiscal Year Dollars	Total Grant Dollars
<b>Federal Agencies</b>			
National Institute on Aging	6	1,533,524	6,853,498
National Institute on Alcohol Abuse and Alcoholism	10	2,061,313	12,416,627
National Institute of Child Health and Human Development	5	2,479,483	12,117,065
National Institute on Drug Abuse	10	2,429,272	10,785,013
National Institute of Mental Health	6	1,046,070	5,636,668
National Eye Institute	1	314,335	1,620,719
National Institute on Deafness and Other Communication Disorders	1	272,563	1,396,834
National Institute of Neurological Disorders and Stroke	1	25,000	100,000
<b>Associations, Foundations, and Programs</b>			
Alzheimer's Association	1	7,127	250,000
American Cancer Society	1	227,593	347,807
Colorado Tobacco Research Program	4	318,903	624,725
Council on Research and Creative Work	1	6,998	6,998
The Ellison Medical Foundation	1	50,000	200,000
<b>Training Grants</b>			
National Institute of Child Health and Human Development	1	222,342	2,126,692
National Institute on Drug Abuse	1	246,567	1,240,481
National Institute of Mental Health	1	191,669	961,729
<b>Education Grant Program</b>			
National Institute of Mental Health	1	146,582	755,555
<b>TOTAL</b>	<b>52</b>	<b>\$11,579,341</b>	<b>\$57,440,411</b>



# EXPENDITURES

Expenditures



“The most accurate way to make year-to-year comparisons of data on research and other sponsored project activity is to look at actual expenditures.”

Sponsored Research  
University of Colorado at Boulder  
Fiscal Year 2003–04, pg. 29

# RESEARCH

## Research Activities For Fiscal Year 2004–05

[Dollar figures in parentheses: first figure = total amount for project period; second figure = amount for fiscal year.]

### Aging

NIA (AG-008761)-“Oldest Old Mortality–Demographic Models and Analysis” (\$8,574,896; \$1,730,414), 5/15/04–4/30/09: The research proposed in this P01 (J. Vaupel, PI) is driven by the concepts and methods of demography. All six projects focus on research on exceptional longevity. Longevity has proven to be remarkably plastic: Environmental and genetic alterations can produce large increases in longevity. Our overarching goal is to explore the nature of and limits to this plasticity.

“IBG Subcomponent” (\$667,549; \$205,254): The major goal of this subproject is to examine mortality kinetics as a function of age in large populations of normal and mutant nematodes.

Principal Investigator: Thomas E. Johnson

Alzheimer’s Association (TLL-01-2752)-“Investigation of Proteins That Directly Interact With Intracellular Abeta Peptide” (\$250,000; \$7,127), 8/1/01–7/31/04: The major goals of this project are to use co-immunoprecipitation and mass spectrometry to identify intracellular proteins that interact with the human A $\beta$  peptide in a transgenic *C. elegans* model.

Principal Investigator: Christopher D. Link  
Co-Investigator: Thomas E. Johnson

The Ellison Medical Foundation (AG-NS-0169-02)-“QTLs Specifying the Retardation of Reproductive Senescence by Dietary Restriction” (\$200,000; \$50,000), 8/1/02–7/31/06: To map quantitative trait loci underlying the extension of female fertility by DR using the LSXSS and LXS recombinant inbred strains.

Principal Investigator: Brad A. Rikke

NIA (AG-012423)-“Transgenic *C. elegans* as Amyloid Disease Model” (\$1,388,497; \$332,494), 5/1/03–3/31/07: The goal of this project is to understand the cellular and molecular basis of  $\beta$ -amyloid peptide (A $\beta$ ) toxicity using genetic and molecular genetic analysis of transgenic *C. elegans* animals expressing the human A $\beta$  peptide.

Principal Investigator: Christopher D. Link

NIA (AG-021037)-“Comparative Modeling of Neurodegenerative Diseases” (\$1,150,374; \$288,090), 6/1/03–5/31/07: The goal of this project is to use transgenic *C. elegans* models to investigate whether age-associated neurodegenerative diseases (other than Alzheimer’s Disease) have a common underlying toxic mechanism.

Principal Investigator: Christopher D. Link

NIA (AG-016219)-“Molecular Genetics of Aging in *C. elegans*” (\$1,831,517; \$380,872), 9/15/04–7/31/09: The main goal of this project is to extend the understanding of mechanisms underlying the increased life expectancy of long-lived (Age) mutants in the nematode *Caenorhabditis ele-*

*gans*, these mutants having revealed the relationship between increased longevity and increased ability to respond to stress.

Principal Investigator: Thomas E. Johnson

NIA (AG-024354)-“Genes Specifying Aging and Longevity in the Mouse” (\$1,615,261; \$276,814), 9/30/04–6/30/09: Under this grant we will determine lifespan on the 77 LXS mouse strains and relate their longevity to physiologic studies of dietary restriction.

Principal Investigator: Thomas E. Johnson  
Co-Investigators: Yuji Ikeno, James Nelson, Brad Rikke

### Alcohol

NIAAA (AA-011984)-“High Efficiency Mapping of Alcohol Sensitivity Genes” (\$1,185,095; \$14,728), 3/1/00–2/28/05: These studies will complete the construction of a large number of recombinant inbred strains from the inbred Long Sleep (ILS) and the inbred Short Sleep (ISS) strains of mice and will map, genetically, eight traits involved in the actions of alcohol.

Principal Investigator: Thomas E. Johnson

NIAAA (AA-008940)-“Mapping of Genes Predisposing to Alcohol Sensitivity” (\$2,803,556; \$488,305), 5/1/03–4/30/08: The major goals of this project are to continue fine-scale mapping of quantitative trait loci that specify sensitivity to the anesthetic effects of alcohol and to use gene sequence data available for both mice and humans to identify candidate genes in these QTL regions. We also will test the hypotheses that these candidates differ between ILS and ISS and map to the defined Lore interval.

Principal Investigator: Thomas E. Johnson  
Co-Investigators: Beth Bennett, James Sikela

NIAAA (AA-013901)-“5HT2 and 5HT1A Receptors in PKC-gamma Null Mutant Mice” (\$445,500; \$148,500), 7/1/03–6/30/06: The goal of this project is to elucidate the specific role of PKC $\gamma$  in complex behaviors associated with alcohol dependence.

Principal Investigator: Barbara J. Bowers

NIAAA (AA-014250)-“Genetic Association and Stratification: Alcoholism” (\$631,479; \$216,580), 9/30/03–8/31/06: The main goal of this project is to test for association between three phenotypes related to alcohol dependence and abuse and seven candidate genes while controlling for the effects of population stratification in a nationwide probability sample.

Principal Investigator: Andrew Smolen  
Co-Investigators: Marissa A. Ehringer, John K. Hewitt, Jeffrey M. Lessem

NIAAA (AA-014666)-“Mouse Models of Alcohol Induced Behavior” (\$1,674,563; \$334,125), 4/1/04–3/31/09: This project will provide support for the maintenance and production of mouse stocks that are valuable for alcohol related research.

Principal Investigator: Allan C. Collins  
Co-Investigator: Jeanne M. Wehner

NIAAA (AA-014425)-“Genetic Analysis of Ethanol-Mediated Stress Reduction” (\$2,127,480; \$407,738), 6/1/04–5/31/09: The major goal of this proposal (L. Lu, PI) is to extend transcriptome QTL mapping and trait association in RI strains to the hippocampus of the LXS mice under alcohol and stress exposure to test the role of shared genetic mediation of responses to both treatments.

“IBG Subcomponent” (\$427,817; \$69,850): The genetic specification of anxiety and aggression will be examined using the LXS RI mouse panel.

Principal Investigator: Beth Bennett

## The Colorado Adoption Project and Longitudinal Studies

NIMH (MH-063207)-“Behavior Genetic Analyses of Executive Functions” (\$1,133,060; \$219,196), 6/1/01–5/31/06: The goal of this project is to conduct the first behavioral genetic study of individual differences in executive functions in a genetically informative twin sample already characterized for general and specific cognitive abilities.

Principal Investigator: John K. Hewitt  
Co-Investigators: John C. DeFries, Akira Miyake, Susan E. Young

NICHD (HD-031921)-“National Study of Adolescent Health—Survey 2000” (\$21,397,072; \$783,829), 2/1/99–10/31/04: The primary purpose of this grant (K. Harris, PI) is to increase understanding of how contextual factors in the lives of adolescents influence their health and risk behaviors.

“IBG Subcontract: Behavioral Genetic Analysis of Adolescent Health Risk” (\$237,824; \$64,091), 7/1/02–10/31/04: This study focuses on the pairs sample of MZ twins, DZ twins, full-siblings, half-siblings, and unrelated children reared together, for the purposes of conducting behavior genetic analyses of health risks and outcomes.

Principal Investigator: John K. Hewitt  
Co-Investigator: Andrew Smolen

NICHD (HD-010333)-“Determinants of Behavioral Development in Children” (\$1,192,034; \$320,710), 6/1/03–5/31/07: The broad purpose of this component of the Colorado Adoption Project is to investigate the genetic and environmental etiologies of individual differences in psychological development during late adolescence in the context of a longitudinal prospective “full” adoption, sibling, and twin study spanning 16 years. The continuation to project Years 27 through 30 will complete testing of 405 pairs of twins aged 13 through 16, previously tested at 1,

2, 3, 4, 7, 9, 10, 11, and 12 years of age, using many of the same measures as the CAP adoptive and nonadoptive participants.

Principal Investigator: Sally J. Wadsworth  
Co-Investigators: Robin Corley, John C. DeFries, John K. Hewitt, Robert Plomin

NICHD (HD-036773)-“Nature and Nurture in Social Demography: An Adoption Study” (\$1,653,437; \$321,540), 8/6/03–5/31/08: This project addresses familial influences on educational attainment, family determinants of union- and family-formation choices of young adults, and how the quality of early family relationships shapes adult child-parent relationships.

Principal Investigator: Michael C. Stallings  
Co-Investigators: Robin P. Corley, John C. DeFries, Scott Hofer, Frank Lawrence, Andrea Piccinin, Robert Plomin, Michael Shanahan, Sally J. Wadsworth

## Substance Abuse Vulnerability

NIDA (DA-012845)-“Genetics of Adolescent Antisocial Drug Dependence” (\$8,148,882; \$825,030), 9/1/00–8/31/05: The purpose of this multisite project (T. Crowley, PI) is to conduct a whole-genome search for chromosomal loci influencing early-onset antisocial drug dependence.

“IBG Subcomponent” (\$471,861; \$117,890): The primary roles of this subcomponent are data collection and monitoring of data collection efforts for the Colorado site, integration and management of the multi-site data from Colorado, and data analysis and the reporting of scientific results.

Principal Investigator: Michael C. Stallings  
Co-Investigators: Stacey Cherny, Robin P. Corley, John K. Hewitt

NIAAA (AA-011949)-“NYS Family Study: Problem Alcohol Use and Problem Behavior” (\$6,889,482; \$732,862), 9/30/00–8/31/05: The research (S. Menard, PI) will estimate the heritability of cue-elicited craving; will determine whether the polymorphism influences cue-elicited craving using a within-family design that controls for population effects; will examine how the polymorphism interacts with the environment over a two year period marked by a transition from initial tobacco use to dependence; and test whether an association between the polymorphism and the transition to dependence is mediated by the effect of the polymorphism on the development of cue-elicited craving.

“IBG Subcomponent” (\$1,388,450; \$265,734): This project is a major intergenerational and life course study of problem alcohol use and related problem behaviors, including the victimization and perpetration of violent and other criminal offenses, illicit substance use, high risk sexual behavior, and mental health problems.

Principal Investigator: John Hewitt  
Co-Investigators: Robin Corley, John DeFries, Andrew Smolen, Michael Stallings, Susan Young

NIDA (DA-011015)-“Antisocial Drug Dependence: Genetics” (\$8,823,379; \$1,742,020), 8/15/03–4/30/08: This grant supports the Center on Antisocial Drug Dependence (T.J. Crowley, PI). This center was established to study genetic influences on, and treatment of, antisocial drug dependence. The center is a joint program of the Addiction Research and Treatment Service of the University of Colorado at Denver and Health Sciences Center, the Institute for Behavioral Genetics, and the Department of Molecular, Cellular, and Developmental Biology. It includes six research components and Administrative, Assessment, and Molecular Genetics Cores:

“Component 1: Adolescent Drug/Alcohol Dependence: Genetics and Treatment” (\$61,912; \$12,723): The major goal of this component is a whole-genome search for chromosomal loci containing genes influencing early-onset dependence on drugs and antisocial behavior.

Principal Investigator: Thomas J. Crowley  
Co-Principal Investigator: Michael C. Stallings  
Co-Investigator: John K. Hewitt

“Component 2: Familial Aggregation of Antisocial Substance Dependence” (\$1,314,485; \$265,460): The goal of this component is a five-year follow-up assessment of 285 families of subjects formerly in treatment for substance use disorder (SUD) and conduct disorder (CD) as adolescents and 200 community control families. The study will provide important information regarding family influences underlying SUD and CD, the generality versus specificity of familial influences on these behaviors, and the identification of family factors that differentiate persistent versus adolescent-limited problem behavior.

Principal Investigator: Michael C. Stallings  
Co-Investigators: Robin P. Corley, Soo Rhee

“Component 3: A Longitudinal Adoption Study of Adolescent Substance Experimentation” (\$772,661; \$151,926): The major goal of this component is to assess genetic and environmental influences on experimentation with tobacco, alcohol, marijuana, and other drugs using a longitudinal adoption design. This study builds on more than 20 years of data collected as part of the Colorado Adoption Project (CAP), and focuses on the transmission of substance use and antecedent behaviors such as conduct disorder symptoms, other behavioral problems, and academic achievement difficulties.

Principal Investigator: Robin P. Corley  
Co-Investigators: Gregory Carey, Michael C. Stallings, Susan E. Young

“Component 4: Heritable Early Indicators of Risk for Drug Dependence” (\$1,118,759; \$226,480): The major goal of this component is to use an augmented twin study to understand how genes and environmental influences contribute to vulnerability to drug abuse and antisocial behavior as they develop during adolescence. A second wave of assessments will be conducted with 1,300 pairs of twins and their siblings five years after the initial interview.

Principal Investigator: John K. Hewitt  
Co-Investigators: Soo Rhee, Susan E. Young

“Component 5: Genotyping of Specific Candidate Genes” (\$18,925; \$18,925): The goal of this component is to provide data on specific candidate genes that will be used to test for associations between those genes and the propensity for drug abuse in adolescents.

Principal Investigator: Andrew Smolen

“Administrative/Educational Core A” (\$261,419; \$53,871): The major goal of the administrative and educational core is to facilitate interactions among an interdisciplinary group of clinicians, behavioral geneticists, and molecular biologists at the University of Colorado at Denver and Health Sciences Center and University of Colorado at Boulder campuses.

Principal Investigator: Thomas J. Crowley  
Co-Principal Investigator: John K. Hewitt

“Assessment Core B” (\$250,694; \$50,307): The major goal of this assessment core is to ensure that the genetic phenotypic information from each of these components is collected, organized, and stored in a way that facilitates direct comparisons across components and combined analyses among components.

Principal Investigator: Robin P. Corley  
Co-Principal Investigator: Susan Mikulich  
Co-Investigator: Michael C. Stallings

“Pilot Project A: Targeting SNPs in the DNR1 Gene for Marijuana Association Study” (\$29,400; \$24,500), 5/1/04–4/30/06: This pilot project is aimed at examining variations in the cannabinoid receptor gene in adolescents who have experimented with the drug. Our preliminary findings suggest some variations may be associated with progression to marijuana dependence symptoms, suggesting that these variations may be important in developing addiction.

Principal Investigator: Marissa A. Ehringer

“Pilot Project D: An Association Study of Serotonin Receptor (5HTR1B) Polymorphisms in Subjects with Conduct and Substance Use Disorders” (\$29,400; \$24,500), 5/1/04–4/30/06: Recent research at IBG (Sakai, et al.) has shown a significant association with a functional polymorphism in the serotonin transporter gene with conduct disorder/aggressive behavior. We will extend the investigation of the serotonin regulatory pathway in this population by investigating polymorphisms in the serotonin receptor gene, which has also been associated with aggression in both animal models and human studies.

Principal Investigator: Gary Stetler

NIDA (DA-014642)-“Progression of Craving and Addiction: Genetic Factors” (\$1,466,216; \$294,000), 9/30/01–6/30/06: Our preliminary research (K. Hutchison, PI) has suggested that the DRD4 VNTR polymorphism influences cue-elicited craving for tobacco and alcohol and that this effect is specifically related to dopamine neurotransmission. This research will estimate the heritability of cue-elicited craving to determine whether the polymorphism influences cue-elicited craving using a within-family design that controls for population effects.

“IBG Subcomponent” (\$438,412; \$69,425): This project investigates the heritability of cue-elicited craving for tobacco and whether the DRD4 VNTR polymorphism influences craving during nicotine consumption.

Principal Investigator: Andrew Smolen  
Co-Investigators: John Hewitt, Michael Stallings

NIDA (DA-015522)-“A Family Study of Substance Use and Conduct Disorder” (\$2,643,042; \$538,128), 9/10/03–6/30/08: This family study of adjudicated adolescent boys and girls with Substance Use and Conduct

Disorder (C.J. Hopfer, PI) has two primary goals. The first is to test competing models of the comorbidity between Substance Use and Conduct Disorder and the second is to examine the familial transmission of these disorders.

“IBG Subcomponent” (\$110,988; \$22,340): This study examines the familial transmission of risk for substance dependence and antisocial behavior and investigates whether common risk factors may account for the co-aggregation of these problem behaviors in families.

Principal Investigator: Michael C. Stallings  
Co-Investigators: Robin P. Corley, Soo Rhee

Council on Research and Creative Work (CRCW), Grant-in-Aid-“Searching for Genes Involved in Alcohol and Tobacco Addiction” (\$6,998), 7/1/04–6/30/05: The focus of this University of Colorado Grant in Aid is to examine two candidate genes that may be involved in smoking and nicotine dependence in a different sample from those being investigated in other projects. This grant provides supply money to facilitate data collection that is intended to support projects as investigators work toward obtaining funding through extramural resources.

Principal Investigator: Marissa A. Ehringer

## Learning Disabilities

NICHD (HD-038526)-“A Longitudinal Twin Study of Early Reading Development” (\$2,372,158; \$384,560), 3/1/99–2/28/06: This research will assess the etiology of individual differences in prereading and early reading development, and their covariation with individual differences in attention/hyperactivity.

Principal Investigator: Richard K. Olson  
Co-Investigators: Brian Byrne, John C. DeFries, Bruce F. Pennington, Sally Wadsworth, Erik G. Willcutt

NIMH (MH-062120)-“DSM-IV ADHD in an Ethnically Diverse Community Sample” (\$1,581,867; \$263,375), 8/1/00–7/31/05: The goal of this project is to assess ethnic group differences in the manifestation of DSM-IV ADHD. A large community sample of children will be ascertained in the Denver metropolitan area to test the internal and external validity of DSM-IV ADHD in an ethnically diverse population that includes a large proportion of African American and Hispanic children.

Principal Investigator: Erik G. Willcutt  
Co-Investigators: John C. DeFries, Andrew Smolen

NICHD (HD-027802)-“Differential Diagnosis in Learning Disabilities” (\$6,661,612; \$1,388,582), 3/20/01–11/30/06: The long-range objectives of this Learning Disabilities Research Center (J.C. DeFries, PI) are the identification, characterization, validation, and amelioration of etiologically distinct subtypes or dimensions of learning disabilities. The center includes five research projects and an administrative core unit:

“Twin Studies” (\$909,542; \$190,282): The objectives of this research project are to collect psychometric test data from twin pairs. The data will be used to assess the genetic and environmental etiologies of reading deficits, ADHD, and their comorbidity, as well as their covariation with measures of other psychopathologies, reading and perceptual processes, mathematics performance, and executive functions.

Principal Investigator: John C. DeFries  
Co-Investigators: Sally J. Wadsworth, Erik G. Willcutt

“Reading and Language Processes” (\$1,481,997; \$309,119): The objectives of this research project are to assess component processes and knowledge in reading and related language skills in twins and siblings selected for deficits in reading and/or ADHD, and in normal-range control twins.

Principal Investigator: Richard K. Olson  
Co-Investigators: Donald Compton, Janice M. Keenan

“Validity of Subtypes of ADHD” (\$1,204,642; \$256,561): The overall goal of this research is to test the internal and external validity of subtypes of ADHD using converging methods.

Principal Investigator: Bruce F. Pennington  
Co-Investigator: Erik G. Willcutt

“Genomic Analyses” (\$944,537; \$195,125): The goal of this project is to compare the contributions of loci influencing reading disability to the contributions of candidate genes that have been identified as contributing to ADHD in order to determine the genetic basis of comorbidity for these traits.

Principal Investigator: Shelley D. Smith

“Early Reading, Language and Attention Development” (\$698,636; \$139,826): This research will assess genetic and environmental influences on the early development of reading and attention, in order to identify the specific psychological processes that mediate these influences.

Principal Investigator: Richard K. Olson  
Co-Investigator: Bryan Byrne

“Administrative Core Unit” (\$1,414,088; \$292,548): This unit is responsible for coordinating the four research projects as well as maintaining communication among them, ascertaining and scheduling subjects, obtaining questionnaire data, managing a master file of combined data sets, and administering the center budget and other fiscal matters.

Principal Investigator: John C. DeFries  
Co-Investigator: Richard K. Olson

NIMH (MH-063941)-“Validity of DSM-IV ADHD Subtypes in a Community Sample” (\$1,679,145; \$339,457), 9/1/01–8/31/06: A study of 750 children with ADHD and 150 children without ADHD designed to test the validity and etiology of ADHD subtypes.

Principal Investigator: Erik Willcutt  
Co-Investigators: Caryn L. Carlson, John C. DeFries, Andrew Smolen

NIDCD (DC-05190)-“Longitudinal Twin Study of Reading Disability” (\$1,396,834; \$272,563), 2/15/02–1/31/07: This project will initiate the first longitudinal twin study of reading disability and its relation with ADHD and other psychopathology.

Principal Investigator: Sally J. Wadsworth  
Co-Investigators: John C. DeFries, Richard K. Olson, Erik G. Willcutt



## Linguistics

Butcher Foundation-“Linguistic and Genetic Relationships in Northern Cameroon (Central Africa)” (\$98,598; \$82,165), 5/1/04–10/30/05: The purpose of this interdisciplinary study is to examine the correlation between linguistic sub-grouping and genetic makeup of selected populations in the extreme north province of Cameroon.

Principal Investigator: Zygmunt Frajzyngier  
Co-Investigator: John K. Hewitt

## Nicotine

NIAAA (AA-011156)-“Ethanol, Nicotine, and Brain Nicotinic Receptors” (\$1,106,231; \$47,234), 9/1/00–8/31/04: The goal of this project is to study alcohol and nicotine interactions, focusing on ethanol effects on brain nicotinic receptors.

Principal Investigator: Allan C. Collins

NIAAA (AA-013018)-“Role of Nicotinic Receptors in Effects of Alcohol” (\$2,243,361; \$459,238), 5/1/02–3/31/07: The goal of the study is to determine whether any nicotinic receptors mediate the action of alcohol using null mutants and conditional null mutants.

Principal Investigator: Jeanne M. Wehner  
Co-Investigator: Allan C. Collins

NIDA (DA-012242)-“Alpha-Conotoxin MII: A Selective Nicotinic Receptor Probe” (\$1,310,300; \$260,160), 7/1/02–6/30/07: The goal of this project is to investigate the nicotinic receptors that interact with  $\alpha$ -conotoxins.

Principal Investigator: Michael J. Marks  
Co-Investigator: Paul Whiteaker

Colorado Tobacco Research Program (2I-034)-“Candidate Genes for Tobacco Use and Nicotine Dependence” (\$110,250; \$24,716), 7/1/02–12/31/04: The focus of this CTRP grant is to investigate single nucleotide polymorphisms within two candidate genes that may be involved in smoking and nicotine dependence. The two candidates, the alpha4 subunit of neuronal nicotinic acetylcholine receptor and the protein kinase C gamma genes, have been strongly implicated in pharmacological and behavioral responses to nicotine in mouse models.

Principal Investigator: Marissa A. Ehringer

NIDA (DA-015663)-“Studies with Nicotinic Null Mutant Mice” (\$1,474,167; \$297,000), 5/1/03–6/30/07: This is a Program Project which provides support for the production and maintenance of multiple nicotine receptor knock-out mouse strains.

Principal Investigator: Allan C. Collins  
Co-Investigators: Michael J. Marks, Jeanne M. Wehner

NINDS (NS-042196)-“Cognitive Dysfunction after TBI: Role of alpha7 nAChRs” (\$1,092,310; \$264,480), 4/1/02–3/31/06: The focus of this study (J. Pauly, PI) is the role of nicotinic receptors in responses of the brain to head injury.

“IBG Subcomponent” (\$100,000; \$25,000): This study evaluates the effects of chronic nicotine administration on cognitive deficits induced by chronic brain injury.

Principal Investigator: Michael Marks

Colorado Tobacco Research Program (3I-030)-“Immunochemical Protocols for Nicotinic Receptors” (\$295,572; \$148,047), 7/1/03–9/30/04: The aim of this project is to develop antibody-based protocols for isolating nicotinic receptors on the basis of their subunit composition.

Principal Investigator: Paul Whiteaker

Colorado Tobacco Research Program (3F-034)-“Presynaptic Nicotinic Receptor Subtypes in Dopamine Neurons” (\$92,228; \$46,140), 7/1/03–6/30/05: The goal of this project is to determine which is (are) the subunit composition(s) of nicotinic acetylcholine receptor(s) mediating the dopamine release in brain dopaminergic terminal areas in naive and nicotine-treated animals. This will eventually add up to understanding of nicotine addiction.

Principal Investigator: Outi Salminen

American Cancer Society (RSG-01-139-01-CNE)-“Genetic Analysis of Nicotine Preference in Mice” (\$347,807; \$227,593), 1/1/04–6/30/06: The goal of this project is to perform QTL (quantitative trait locus) analysis and subsequently fine map genes that influence nicotine oral self-selection in mice.

Principal Investigator: Jerry Stitzel

Colorado Tobacco Research Program (4S-003)-“Candidate Genes for Tobacco Use and Nicotine Dependence” (\$126,675; \$100,000), 7/1/04–6/30/05: The focus of this CTRP grant is to investigate single nucleotide polymorphisms in six neuronal nicotinic receptor subunit genes that may be involved in smoking and nicotine dependence. These candidates have been implicated in pharmacological studies and in mouse model systems, and will be examined in an adolescent human sample.

Principal Investigator: Marissa A. Ehringer

NIDA (DA-003194)-“Genetics of Nicotine Tolerance: Role of Receptors” (\$1,776,221; \$324,373), 7/15/04–4/30/09: The major goal of this research is to use genetic strategies to study the development of tolerance to and physical dependence on nicotine.

Principal Investigator: Allan C. Collins  
Co-Investigators: Sharon Grady, Michael Marks

NIDA (DA-014369)-“Identification of Functional nAChR Variants in Mice” (\$437,318; \$218,820), 7/16/04–1/31/06: In this proposal we will screen a large set of inbred mouse strains for amino acid-altering polymorphisms in several nAChR subunit genes. All identified variants will be assessed for pharmacological and functional properties using electrophysiological techniques.

Principal Investigator: Jerry A. Stitzel

NIDA (DA-019655)-“Immunochemical Protocols for Nicotinic Receptors” (\$409,594; \$195,446), 4/1/05–3/31/07: This project aims to develop antibody-based protocols for isolating nicotinic receptors on the basis of their subunit composition, and quantitating subunit protein expression using Western blotting.

Principal Investigator: Paul Whiteaker



## Schizophrenia

NIMH (MH-066115)-“Abnormal Eye Movement in Schizophrenia: Genome-wide Scan” (\$1,672,187; \$334,569), 1/9/04–12/31/08: The aims of the proposal (R. Ross, PI) are to perform a genome-wide scan looking for a linkage to a schizophrenia-associated endophenotype, an elevated frequency of leading saccades during a smooth pursuit eye movement (SPEM) task. SPEM abnormalities have been associated with schizophrenia for almost 100 years, and have been suggested as a potential marker of genetic risk for over 20 years.

“IBG Subcomponent” (\$121,978; \$23,271): The purpose of this subcontract is to assist Dr. Randal Ross in conducting extended pedigree and sibling-pair linkage analyses to detect quantitative trait loci that increase risk for schizophrenia.

Principal Investigator: John K. Hewitt  
Co-Investigator: Erik G. Willcutt

NIMH (MH-068582)-“Molecular Neurobiology of Schizophrenia” (\$9,735,511; \$2,002,432), 9/27/04–6/30/09: This proposal (R. Freedman, PI) examines the neurobiological effects of genetic polymorphisms in genes associated with schizophrenia.

“IBG Subcomponent” (\$569,993; \$89,224): The aim of this subcontract is to provide genetically modified mice to other components of the CONTE Center for schizophrenia research.

Principal Investigator: Allan C. Collins  
Co-Investigator: Jerry Stitzel

## Statistical Models

NEI (EY-012562)-“Variance Components Models for Mapping QTLs” (\$1,620,719; \$314,335), 9/1/02–8/31/07: The goal of this project is to further extend the methodology of variance components analysis to accommodate more general data structures and models that are of practical importance to the design and analysis of modern genetic studies, and to integrate these into a comprehensive software package.

Principal Investigator: John K. Hewitt  
Co-Investigators: Goncalo Abecasis, Lon Cardon, Stacey Cherny, Shaun Purcell, Fruhling Rijdsdijk, Pak Sham

## Research Career Awards and Fellowships

NIAAA (K02-AA-000195)-“Identifying Genes Predisposing to Alcoholism” (\$510,575; \$17,019), 9/1/99–8/31/04: This award allows the principal investigator to pursue his research on the genetic basis of alcohol action.

Awarded to: Thomas E. Johnson

NIDA (K01-DA-013956)-“Causes of Comorbidity: Substance Use Disorder, ADHD & CD” (\$498,497; \$95,126), 9/1/01–8/31/06: This award allows the PI to examine the causes of comorbidity among substance use disorders (SUD), attention-deficit/hyperactivity disorder (ADHD), and conduct disorder (CD).

Awarded to: Soo Rhee

NIMH (K01-MH-001865)-“Executive Function: Links to Drug Use and Psychopathology” (\$550,625; \$111,547), 12/17/01–11/30/06: The major goal is to investigate the possible genetic link between executive cognitive function and substance use disorders and externalizing psychopathology.

Awarded to: Susan E. Young

## Research Training and Education Grant Program Awards

NIMH (MH-019918)-“Workshop on Methodology of Twin and Family Studies” (\$755,555; \$146,582), 7/1/03–6/30/08: The major goal of this project is to hold a series of international workshops on the methodology of twin studies at the Institute for Behavioral Genetics in Boulder, Colorado.

Principal Investigator: John K. Hewitt

NIDA (DA-017637)-“Research Training-Genetics of Substance Abuse” (\$1,240,481; \$231,931), 7/1/04–6/30/09: This training program, which supports four pre- and two postdoctoral trainees, is geared toward training pre- and postdoctoral fellows who will pursue research careers that focus on the study of genetic influences on substance abuse.

Principal Investigator: Allan C. Collins

NIMH (MH-016880)-“Research Training-Biological Sciences” (\$961,729; \$180,805), 7/1/04–6/30/09: This institutional training grant (supporting four pre- and one postdoctoral trainees) is for training in the field of behavior genetics. The goals of behavior genetics are to elucidate the genetic and environmental components that regulate individual differences for a multitude of complex normal and abnormal phenotypes.

Principal Investigator: Jeanne M. Wehner

NICHD (HD-007289)-“Research Training-Developmental Behavioral Genetics” (\$1,123,009; \$222,342), 5/2/05–4/30/10: This training grant (supporting five pre- and one postdoctoral trainees) is for training in the field of developmental behavioral genetics. Developmental behavioral genetics integrates the perspectives of quantitative genetics, molecular genetics, neurobiology and, increasingly, the resources of bioinformatics into the study of behavioral development.

Principal Investigator: John K. Hewitt

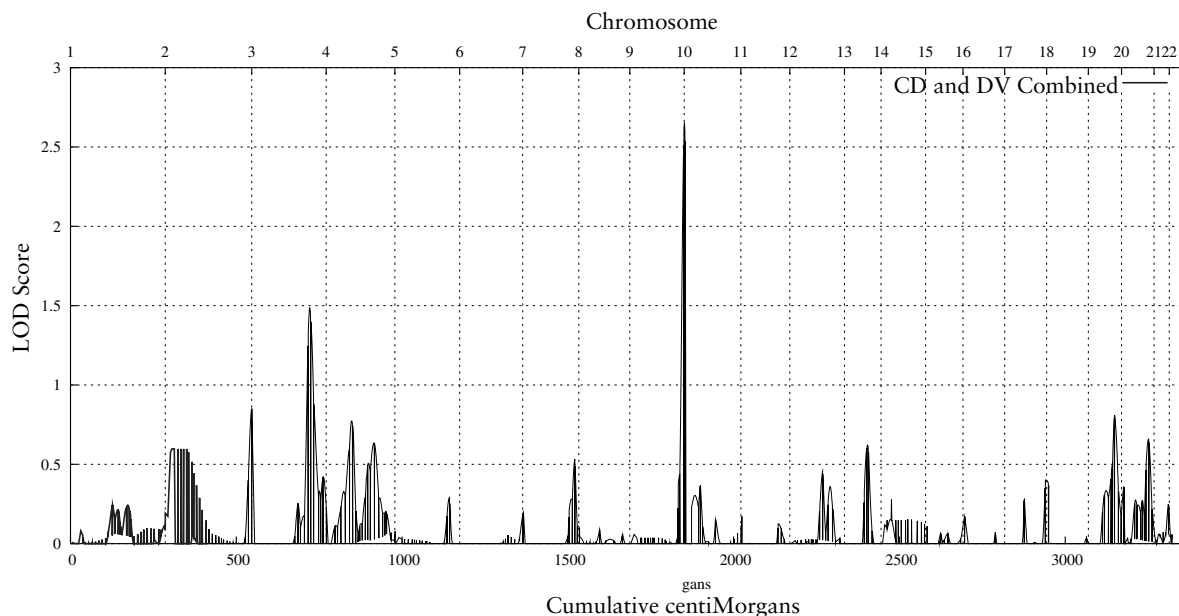
## The Center on Antisocial Drug Dependence

Individuals with early-onset substance use disorders (i.e., onset in childhood or early adolescence) often demonstrate significant antisocial behavioral problems as well, such as deceitfulness, aggression, hostility, low empathy, and poor impulse control. There is increasing evidence to suggest that this early-onset form of substance use disorder is characterized by a spectrum of risk behaviors related to the inability to inhibit inappropriate behavior in general—that includes impulsive personality traits and externalizing psychopathology such as attention-deficit hyperactivity disorder, conduct disorder, and antisocial personality disorder. All of these behaviors: a) show substantial heritable influences, b) externalizing behavioral problems typically precede significant substance involvement, and c) there is evidence to suggest that the comorbidity among these various risk factors may be explained, in part, by common genetic influences.

Our Center on Antisocial Drug Dependence (CADD; DA-011015), initially funded in 1997 by the National Institute on Drug Abuse (NIDA), was specifically designed to address this hypothesis. The Center involves a joint collaboration among researchers at the Institute for Behavioral Genetics and the Department of Molecular, Cellular, and Developmental Biology at the University of Colorado at Boulder; and clinical research scientists from the Division of Substance Dependence in the Department of Psychiatry at the University of Colorado at Denver and Health Sciences Center in Denver. Study participants include clinical families (i.e., families of adolescents in residential and outpatient treatment for severe substance use and other behavioral or conduct problems), as well as community twin, family, and adoption study samples (approximately 9,000 participants in all). A common assessment battery, which includes structured interviews, family history, and questionnaire assessments of substance use and antisocial behavior, psychopathology, cognitive abilities, personality, family environment, and other psychosocial

domains, is utilized across all components of the center. This unique design allows for joint and comparative analyses across three different behavioral genetic designs, and across selected and unselected clinical and community samples. In addition to the extensive phenotypic assessment, DNA samples have been obtained (non-invasively through buccal cell samples) on approximately 98 percent of the targeted samples.

An important goal of the CADD studies is the identification of mediating factors underlying the familial aggregation of problem substance use and antisocial behavior. Although it is fairly well established that these behaviors tend to aggregate in families, the mechanisms underlying such familial resemblance are still not well understood. Our studies have confirmed the strong familial aggregation of substance-related behaviors (Stallings et al., 1997; Miles et al., 1998; Hopfer et al., 2003) and demonstrated that general mechanisms such as marital assortment, vertical transmission of genetic and/or environmental risk from parents to children, and horizontal influences among siblings (e.g., sibling interaction/imitation, peer influences) are all important sources underlying the familiarity of substance misuse and antisocial behavior. Analyses of twin and non-twin siblings can partition the source of sibling resemblance into environmental and genetic sources, and recent analyses by Rhee et al. (2003) have confirmed that both environmental and heritable factors contribute substantially to problem substance use. More importantly, substance use disorders do not aggregate independently in families (Hopfer, Stallings & Hewitt, 2001; Rhee et al., in press). Instead, they tend to occur together, and recent work (Young et al., in review) indicates that common genetic influences contribute substantially to this comorbidity. In fact, in Rhee et al. (in press) we concluded that



among adolescents dependence symptoms for specific substances appear to be manifestations of the same underlying liability, or very highly correlated liabilities. Whether this is a developmental phenomenon that may not hold true for adults is an important question we are currently pursuing. CADD studies investigating the comorbidity of antisocial behavior and problem substance use (Stallings, et al., 1997; Young et al., 2000; Button et al., in review) have reached similar conclusions, suggesting that antisocial behavior and substance misuse also share common familial and genetic antecedents.

This body of work has led to our first attempt to identify specific genetic mechanisms underlying substance dependence vulnerability. We recently performed the first genome-wide scan for quantitative trait loci (QTL) influencing dependence vulnerability in adolescents (Stallings et al., 2003). Results indicated two promising chromosomal regions (3q24-25 and 9q34) likely to contain genes that influence substance dependence risk in adoles-

cence. We have recently extended this work (Stallings et al., 2005), searching for QTL that may influence both adolescent conduct disorder (CD) and dependence vulnerability (DV). The strongest evidence for linkage (LOD = 2.65) was found for a composite index reflecting antisocial substance dependence (DV + CD), suggesting evidence for a QTL influencing both DV and CD on chromosome 9q34 (see the figure above). Evidence for a QTL primarily influencing DV on chromosome 3q24-25 and CD on chromosome 17q12 was also found. These results provide the first evidence for a potential molecular genetic basis for the comorbidity between drug dependence vulnerability and antisocial behavior.

We have two exciting opportunities to replicate and extend this work. The first is our NIDA-funded multisite collaboration (DA-012845) with substance abuse researchers in San Diego (Sandra Brown), Pittsburgh (Duncan Clark), and Colorado. The goal of this multisite collaboration is to provide a replication sample of selected proband-sibling pairs exhibiting both substance

use problems and conduct disorder like our CADD probands. To date we have collected data on over 400 proband-sibling pairs (approximately 300 have been genotyped) and we plan to conduct our first replication analyses early this year. In addition to providing a replication sample, we are utilizing SNP-chip technology to genotype 10,000 genetic markers on each of these individuals—providing substantially greater power to detect linkage than in our previous analyses. In addition, we recently obtained renewed funding of the CADD in 2003 for an additional five-year period. A limitation of our initial CADD studies has been their cross-sectional nature—at least in adolescence. Although CADD participants in the Colorado Adoption Project (CAP) and part of the twin sample (those participating in the Colorado Longitudinal Twin Study) have had longitudinal assessments almost yearly since birth, at this point in time we have only a single phenotypic assessment in adolescence for most CADD participants. Antisocial behavior

and substance use disorders develop over time. To be fully understood, longitudinal assessment is imperative, particularly for individuals who have not completely passed through the age of greatest risk. An important feature of our CADD renewal is that we are now collecting longitudinal assessments up through age 25–28 on this valuable data resource. We know that some substance experimentation and conduct problems are normative in adolescence. Additional assessments in young adulthood will allow us to begin to distinguish subjects with adolescent-limited problem behavior from those at risk for lifecourse-persistent problems. Our working hypothesis is that these two patterns of behavior arise from different etiologies, with persistent patterns showing stronger familiarity and comorbidity, and evidencing a more heritable form.

Michael Stallings  
*Assistant Professor and Faculty Fellow*

## **Genetical Genomics in the Laboratory Mouse Applied to the Study of Human Alcoholism**

During an old friend's days as a medical student, he would come home for breaks and regale us with stories of "life on the wards." On more than one occasion, he told me he believed that patients in the hospital were generally there for one of four reasons: drinking, smoking, diabetes, or bad luck. I don't know much about diabetes or luck, but his impressions of smoking and especially alcohol drinking were right on. Consider the following:

- 30 to 40 percent of all people in the hospital are there as a direct or indirect result of alcohol abuse
- Hospital stays for heavy drinkers tend to be four times longer on average than non-drinkers
- Nearly 40 percent of car crash fatalities involve alcohol

This burden on our health care system, along with lost productivity, alcohol-related criminal activity, and other problems, extracts a staggering toll on the U.S. economy—over \$180 billion per year. But from my perspective, it is the personal cost of excessive drinking that is most tragic: the despair, poor health, broken families, conflicts, and surrender of personal control. This, I think, is what drives scientists like myself to study and try to understand the factors that contribute to alcohol abuse.

Pathological drinking behavior is known to run in families. This basic observation supports a role for heritable transmission, but does not directly address the question of genetic influences on alcoholism. After all, family members not only share genetic composition, they also share many features of their environment. In fact, alcohol researchers

have come to the basic conclusion that alcoholism is a *complex trait*, meaning that it is influenced by both genetic and environmental factors, and, perhaps more importantly, complex interactions between the two. It is easy to imagine environmental circumstances that could contribute to alcoholism risk: abusive parents, coercive peers, chronic failures with relationships or employment, etc. Identification of the genetic factors, however, has proved elusive. This is for a variety of reasons, but one of the most important is that there is not a single “alcoholism gene” that can explain the majority of genetic variance associated with drinking behavior. Many genetic as well as environmental factors, each of relatively small effect, contribute to the final outcome and isolating these small effects has been difficult.

Many alcohol researchers have turned to model organisms to study the genetics of alcohol actions. These scientists do not study alcoholism *per se*. Rather, alcoholism is broken down into its many principle features, each of which is postulated to contribute in some way to the overall pathology. In my research we use a model organism that has long been used with great benefit at IBG—the laboratory mouse. We study the genetic factors that contribute to variation in alcohol sensitivity and tolerance using simple behavioral tests in inbred mice. Currently, one of our most important models is the Inbred Long and Short Sleep mouse strains (ILS and ISS), selectively bred for differential sensitivity to alcohol by the founder of IBG, Dr. Gerry McClearn. These strains are extremely divergent in their response to a so-called “hypnotic” dose of alcohol and have been widely used to study alcohol actions.

We recently observed that a single administration of alcohol causes the ILS to become less sensitive to an alcohol challenge just one day later, but the ISS are completely unaffected. In other words, the ILS have developed what is known as *rapid tolerance* and the ISS have not. Furthermore, we have been able to determine that the rapid tolerance effect is the result of an increase in the rate or magnitude of “within-session,” or acute

tolerance in the ILS. Acute tolerance appears to be very high already in the ISS and perhaps cannot be changed, at least not by this short-term procedure. The rapid tolerance model provides us with a tool with which we can study acute tolerance and the longer lasting rapid tolerance. Moreover, the model has a clear genetic component and can be quickly assessed in a large number of animals, usually a fundamental condition of genetic experiments.

The importance of the ILS/ISS rapid tolerance model goes beyond simple alcohol pharmacology, an area worthy of investigation in itself. Exposure to alcohol or other drugs of abuse influences certain brain pathways involved in reward, motivation, and behavioral control. Some individuals seem to be more vulnerable to the disruptive effects of drugs on these pathways, so much so that their neuronal circuitry becomes modified to a state of “motivational toxicity,” perhaps permanently, in which normally rewarding behaviors are supplanted by an all-consuming obsession to



Renee Good and Dr. Mike Lee discuss results of an assay to genotype for a specific single nucleotide polymorphism.



obtain and use the drug. It is these individuals who may have a genetic predisposition for alcoholism risk. While we do not directly measure these things in the mice, we postulate that the molecular mechanisms of behavioral plasticity—for simple behaviors in mice and more complex behaviors in humans—overlap, at least to some extent. Thus, it is our goal to identify the genetic factors that mediate variation in the ability of mice to become tolerant to alcohol with the larger goal of shedding insight into the molecular basis of alcohol-induced neuronal plasticity that may be relevant to human alcoholism.

Our experimental approach is one that has become known as “Genetical Genomics,” an exciting innovation in the area of complex traits analysis. One way in which central nervous system cells regulate their activity is through gene expression; that is, mRNA is increased or decreased in response to internal and external influences to achieve the appropriate level of the relevant proteins. This variation in gene expression, like variation in behavior, is influenced by both environmental and genetic factors. Genetical genomics examines the genetic component of gene expression variation in much the same way that one would examine the genetic effects on a behavioral trait such as alcohol tolerance. Moreover, genomic tools, specifically gene expression microarrays, allow one to simultaneously interrogate the expression level of virtually all expressed genes in a tissue sample. This has two important implications. First, knowledge of the effects on a single gene might not be very informative because the gene may have generalized or pleiotropic effects. But in the context of many other affected genes, one can start to construct gene networks and pathways that are influenced by a perturbation such as alcohol administration. Second, it is possible to identify genes whose expression variance is mediated by *cis*-acting regulatory elements; that is, polymorphisms within some regulatory portion of a gene can affect its expression. Since genetic variance for any trait, behavior or otherwise, is mediated by DNA sequence polymorphisms, genes with these *cis*-regulatory effects are important candidates for controlling genetic variance in higher order traits such as alcohol tolerance.

We have been studying gene expression in certain brain structures of the ILS and ISS mice as a function of time following a rapid tolerance-inducing

alcohol treatment. In this kind of analysis, genes that show an alcohol treatment-by-strain interaction are postulated to be important in strain-dependent responses to alcohol, such as rapid tolerance. Indeed, among the more than one thousand genes that show interaction effects, we have identified co-regulated gene clusters that fall into some very interesting cellular pathways. Our next step will be to map chromosomal locations, or *quantitative trait loci* (QTL), where genes mediate genetic variation in alcohol tolerance and related traits using a mapping population known as the LXS recombinant inbred strains, a special segregating population derived from the ILS and ISS. We will also map brain gene expression effects in these animals both before and after alcohol administration and relate the expression effects back to the behavioral effects. This experiment will give us better understanding of the genetic regulation of the interaction genes and will more precisely define the role of these genes, specifically in acute and rapid alcohol tolerance.

We postulate that genes important in mediating the dynamic processes of acute and rapid alcohol tolerance are also important in the alcohol-induced molecular changes that take place in the brain on the path to chronic alcohol abuse. The experiments described herein will provide us with candidate genes and pathways we can use to test this general hypothesis. Ultimately, we hope that our research will offer insight into the molecular and genetic basis of individual differences in alcohol-related behaviors and will also suggest novel targets for the development of therapies to ease the suffering of alcoholism.

Richard A. Radcliffe, PhD  
*Assistant Professor and Faculty Fellow*



# ANIMAL

## Animal Production

A 4,000-square-foot specific-pathogen-free laboratory provides space for the development and production of unique selected lines and inbred strains of mice at IBG.

Ongoing work includes the development of congenic lines for several alcohol-related phenotypes, made by intergressing chromosomal regions containing QTLs for the traits from an ILS or ISS inbred background onto the opposite background (supported by NIAAA grants to Dr. Thomas E. Johnson).

These breeding studies are complemented by the availability of other selected lines, inbred strains, and an outbred population used in behavioral genetic research:

- A/Ibg, BALB/CBy Ibg, C57BL/6Ibg, DBA/2Ibg, C3H/2Ibg, & 129 Svev/Taconics inbred strains, C58/J
- Heterogeneous Stock (HS)
- Open-field Activity lines
- Long-Sleep (LS) and Short-Sleep (SS) selected lines
- ILS and ISS inbred strains
- LSXSS recombinant inbred strains
- Nesting behavior lines
- PKC null mutants
- ISS X ILS recombinant inbred strains

- High Acute Functional Tolerance (HAFT 1) &
- Low Acute Functional Tolerance (LAFT 1)
- Congenic ILS.Lore Short & ISS.Lore Long Bilineal Selection
- B6.D2 Congenic for voluntary ethanol consumption
- D2.H2 Nicotinic Congenics
- Nicotinic Knockouts

### Faculty Director:

Jerry Stitzel

### Lab Supervisor:

Jerry Salazar

### Staff:

Mark Conner

Anthony Giordano

Ryan Morrow

Cornell Strover

William van Morter

Jean C. Yu

### Professional Research Associates:

Vanessa Crittenden

Heather Henderson

Colin Larson

Christine Martin

Cathy Ruf



Specific-Pathogen-Free (SPF) laboratory staff and researchers (left to right): Mark Conner, Bill van Morter, Jean Yu, Jerry Salazar, Ryan Morrow, Tony Giordano, Colin Larson.

# FACILITIES

## Research Facilities

The institute's research facilities include

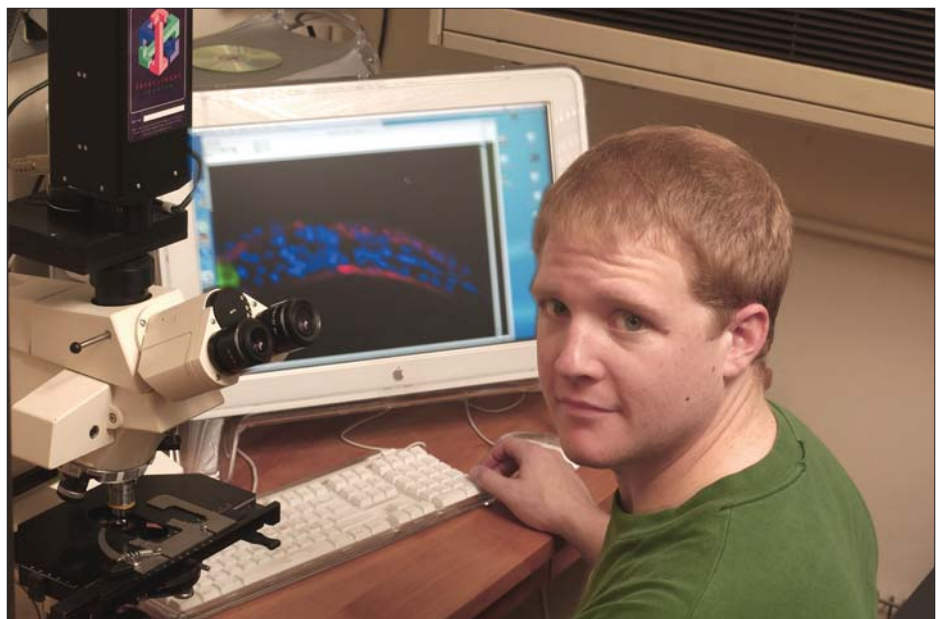
- A specific-pathogen-free mouse laboratory that produces genetically defined lines of mice for behavioral and pharmacological investigations;
- Biochemistry and pharmacology laboratories that are used in studies of neurotransmitter receptor regulation and function, enzyme mechanisms, alcohol and nicotine actions, learning and memory, and mechanisms of aging;
- Facilities for interviewing and testing subjects enrolled in family, twin, and adoption studies of personality traits, cognition, and reading abilities;
- A core genotyping and sequencing laboratory that is used for analysis of human, mouse, and invertebrate DNA.

These facilities house a wide variety of equipment that is used in a broad range of behavioral genetic, pharmacogenetic, neurobiological, and molecular genetic studies, for example:

- an autoradiographic image analyzer;
- chromatography (HPLC, FPLC, and GC) and electrophoresis systems;
- automated DNA sequencers;

- thermocyclers and a laboratory robot;
- centrifuges, ultracentrifuges, and cell harvesting systems;
- spectrophotometers, fluorometers, microplate readers, and scintillation and gamma counters;
- video-monitored and computerized behavioral testing apparatuses; and
- Nomarski Interference CDIC and fluorescent microscopes.

IBG maintains a heterogenous network of Unix, Windows, and Macintosh computers totalling approximately 150 machines across three subnets on the University of Colorado's network. The University of Colorado is connected to the Internet and Internet2 through multiple high speed connections. This provides ample bandwidth for IBG's web, e-mail, and file sharing facilities. IBG's central file server is a Compaq Alpha server with 400 gigabytes of RAID level 5 storage. All IBG users have access to the server's files from their desktop workstations. To insure data integrity, daily backups of the server are stored both onsite and offsite. Additionally, IBG makes available to users a color laser printer, scanners, digital cameras, and CD-ROM writing facilities.



Brian Hiester from the Link Lab.

# GRADUATE

## Graduate Training

IBG provides graduate training that interacts synergistically with the many research projects, both human and nonhuman, conducted under the auspices of its faculty. The research projects emphasize many areas related to behavioral genetics, including developmental psychology, neurobiology, neuropharmacology, pharmacogenetics, quantitative genetics, molecular biology, and evolutionary biology. Complementing intensive research training is a core program of courses in which students learn to apply the principles and techniques of behavioral genetics to the analysis of behavior.

The goal of this Graduate Interdisciplinary Certificate Program in Behavioral Genetics is to train scientists in the study of genetic and environmental contributions to individual differences in behavior. Because IBG is not a degree-granting unit of the Graduate School, each trainee must be a degree candidate in an academic department of the university. The institute has faculty and graduate student liaisons with several departments within the College of Arts and Sciences including the Department of Psychology, Department of Integrative Physiology, and the interdisciplinary Neuroscience program. The institute also has research and training links with the Department of Psychology at the University of Denver, and with both the School of Pharmacy and the Department of Pharmacology at the University of Colorado at Denver and Health Sciences Center.

The training program requires completion of four core courses (genetics, behavioral genetics, statistics, and scientific ethics) and three additional courses from electives including: quantitative genetics, molecular genetics and behavior, biometrical methods in behavioral genetics, bioinformatics and genomics, quantitative trait loci analysis, and concepts or seminar courses in behavioral genetics. All trainees and postdoctoral students are required to complete a course in scientific ethics and participate in the weekly journal club/colloquium series. Each trainee is expected to complete the requirements for the MA or MS degree near the end of year two.

Trainees are expected to serve as teaching assistants in a course judged by their advisory committee to be relevant to their professional specialty. This teaching requirement is usually completed during the second year of graduate training. All students are encouraged to ensure breadth of experience by becoming involved in the research of IBG faculty members in addition to that of their advisor. Trainees are expected to conduct their master's thesis and doctoral dissertation research on topics of direct relevance to animal or human behavioral genetics under the supervision of an IBG faculty member. Each trainee is expected to have completed the requirements for the PhD degree by the end of year four. Upon successful fulfillment of the requirements of the IBG training program, the student will receive a Certificate of Interdisciplinary Study in Behavioral Genetics.

Students wishing to become IBG trainees must submit an application for admission into the program to the director of the Behavioral Genetics Training Program. Excellence of record and promise are the principal criteria for selection of trainees. A further important consideration for acceptance is the diversity of background and training that is essential for the success of an interdisciplinary program.

Acceptance into the training program is contingent upon acceptance by the Graduate School and by an academic department of the university. Therefore, application must be made directly to the department of choice as well as to the institute. Information can be obtained at [ibgwww.colorado.edu](http://ibgwww.colorado.edu). Applicants are encouraged to write to the appropriate department for application information. For application forms for admission into the IBG training program, or for further information, write to: Director, Behavioral Genetics Training Program, Institute for Behavioral Genetics, 447 UCB, University of Colorado at Boulder, Boulder, CO 80309-0447. If you prefer to call, the telephone number is 303-492-7362.

# STUDENTS

## Graduate Students

**Oge Arum** (PhD program, Molecular, Cellular, and Developmental Biology). The molecular genetics of aging, with emphasis on the (oxidative) damage accumulation theory of aging, in the nematode *Caenorhabditis elegans*.

**L. Cinnamon Bidwell** (PhD program, Clinical Psychology). Ms. Bidwell is interested in the relationships between genetic and neuropsychological pathways in the etiology of attentional disorders, such as attention-deficit hyperactivity disorder and schizophrenia.

**Kimberly Brodsky** (PhD program, Psychology). After completing her undergraduate education at the University of California, Berkeley, Kim worked at the Henry H. Wheeler Brain Imaging Center on studies that applied functional magnetic resonance imaging techniques. For her master's project she is comparing the neurocognitive correlates of childhood ADHD and schizophrenia in collaboration with researchers at the Center for Schizophrenia Research at the University of Colorado at Denver and Health Sciences Center.

**Robert Buchwald** (PhD program, Ecology and Evolutionary Biology). Genetic diversity and evolution of nestmate recognition pheromones in bees.

**Victoria Cosgrove** (PhD program, Clinical Psychology). Ms. Cosgrove is interested in personality constructs and their genetic relationship to comorbidity between adolescent internalizing and externalizing disorders.

**Angela Friend** (PhD program, Psychology). Ms. Friend is interested in the genetic and environmental influences on reading and reading-related skills.

**Rebecca Gaffney-Brown** (PhD program, Psychology). Etiology and treatment implications for the comorbidity of attention deficit hyperactivity disorder, conduct disorder, and reading disability.

**Heather Gelhorn** (PhD program, Psychology). Defining a maximally heritable phenotype for conduct disorder, and aspects of adolescent drug and alcohol abuse as they relate to CD: Twin and family studies.

**Detre Godinez** (PhD program, Psychology). Genetic and environmental influences on the executive systems and its relationship with substance abuse and other comorbid disorders.

**Brett Haberstick** (PhD program, Psychology). Genetic and environmental etiologies for conduct disordered behaviors and substance experimentation in children and adolescents.

**Christie Hartman** (PhD program, Psychology). Ms. Hartman examines the genetic and environmental contributions to attention-deficit/hyperactivity disorder, conduct disorder, and their comorbidity.

**Jesse Hawke** (PhD program, Psychology). Differential genetic etiology of reading difficulties as a function of age and gender in the Colorado Twin Study of Reading Disability.

**Noa Heiman** (PhD program, Psychology). Genetic and environmental influences on personality dimensions in adolescence and later adulthood.

**Clarissa Parker** (PhD program, Neuroscience). The genetic and environmental determinants of substance abuse and related phenotypes such as impulsivity, aggression, and anxiety, with an emphasis on the interaction between alcohol and the HPA axis, and individual differences in response to alcohol and stress.

**Laura Sobik** (PhD program, Clinical Psychology). The genetic influences of cue-elicited craving for food.

## Visiting Student

**Cristian Zambran**, a PhD student in the biology department at the University of Chile in Santiago, visited IBG during the spring 2005 semester to test an experimental Alzheimer's drug for its actions at nicotinic receptors.



# COURSES

## Courses Taught by Faculty Fellows

### Fall 2004

Gregory Carey	PSYC 3102, UCB	Behavioral Genetics
Thomas Crowley	PSCH 8001/8610, UCDHSC	Big Six Substance Problems in Primary Care (Course Dir.)
	No course #, UCDHSC	Substance Use (for 3rd year Psychiatry Residents)
Marissa Ehringer	IPHY 2600, UCB	Introduction to Research Methods
Kenneth Krauter	MCDB 6000, UCB	Introduction to Lab Methods
	MCDB 4410, UCB	Human Molecular Genetics
	MCDB 7910, UCB	Seminar Practicum
Bruce F. Pennington	PSYC 4511, DU	Psychopathology
Dennis Petersen	PHRD 4710, UCDHSC	Integrated Organ Systems V: Cardiopulmonary
	TXCL 7322, UCDHSC	Principles of Toxicology 1 (2 lectures)
	PHSC/TXCL 7400, UCDHSC	Ethical Issues in Pharmaceutical Sciences & Toxicology (Course Dir. & 1 lecture)
	TXCL 7323, UCDHSC	Principles of Toxicology 2
James Sikela	DSBS 6600, UCDHSC	Dental Pharmacology (6 lectures)
	PHCL 7600, UCDHSC	Frontiers in Pharmacology (1 lecture)
	PHCL 7605, UCDHSC	Ethics in Research (1 lecture)
	HMGP 7600, UCDHSC	Survey of Human Genetics (2 lectures)
	HMGP 7620, UCDHSC	Genomics (12 lectures)
Michael Stallings	PSYC 5122, UCB	Quantitative Genetics
Jerry Stitzel	IPHY 6010, UCB	Seminar: Molecular Genetics Addiction
Boris Tabakoff	PHCL 6000, UCDHSC	Medical Pharmacology (4 lectures)
	PHCL 7600, UCDHSC	Frontiers in Pharmacology (1 lecture)
	PHCL 7605, UCDHSC	Ethics in Research (1 lecture)
	PHCL 7620, UCDHSC	Graduate Pharmacology (5 lectures)
	DSBS 6600, UCDHSC	Dental Pharmacology (2 lectures)
James Wilson	BIOL/PSYC 4104 UCDHSC	Behavioral Genetics (online course)

### Spring 2005

Mike Breed	EBIO 3240, UCB	Animal Behavior
Gregory Carey	PSYC 3102, UCB	Behavioral Genetics
Thomas Crowley	PSCH 8001/8610, UCDHSC	Big Six Substance Problems in Primary Care Medicine (Course Dir.)
Marissa Ehringer	IPHY 6010, UCB	Seminar, Bioinformatics & Genomics
John K. Hewitt	PSYC 7102, UCB	Seminar: Behavioral Genetics
Kent Hutchison	PSYC 5423, UCB	Research Problems in Clinical Psychology
Thomas E. Johnson	IPHY 6010, UCB	Seminar: Bioinformatics & Genomics
Kenneth Krauter	MCDB 7910, UCB	Seminar, Practicum
Richard Olson	PSYC 4001, UCB	Honors Seminar 2
	PSYC 4521, UCB	Critical Thinking: Genes & Environment
Dennis Petersen	PHRD 3700, UCDHSC	Integrated Organ Systems I: Physiology
	TXCL 7561, UCDHSC	Drug Metabolism and Pharmacogenetics
Richard Radcliffe	TXCL 7323, UCDHSC	Principles of Toxicology 2 (lectures)
	TXCL 7561, UCDHSC	Drug Metabolism and Pharmacogenetics (lectures)
	PHRD 3700, UCDHSC	Integrated Organ Systems I: Physiology
Soo Rhee	PSYC 7102, UCB	Seminar: Behavioral Genetics
Jerry Stitzel	IPHY 2600, UCB	Introduction to Research Methods
Erik Willcutt	PSYC 3313, UCB	Psychopathology
James Wilson	BIOL/PSYC 4104 UCDHSC	Behavioral Genetics (online course)

### Summer 2005

Michael Breed	EBIO 4350/5350, UCB	Biological Field Studies
Gregory Carey	PSYC 3102, UCB	Behavior Genetics

UCB: University of Colorado at Boulder

UCDHSC: University of Colorado at Denver and Health Sciences Center

DU: University of Denver



# COLLOQUIA

## Colloquia, Informal Talks, and Special Events ■ ■

### Fall 2004

**Allan Collins** (Professor of Psychology and Pharmacology, Department of Psychology, University of Colorado, Boulder). “Unfinished Business”

**Larry Gold** (Chief Science Officer & Chairman of the Board, SomaLogic, Inc., Boulder, Colorado). “Do Serum Protein Concentrations Reflect Behavior?”

**Leslie Morrow** (Professor of Psychiatry and Pharmacology, Associate Director, Bowles Center for Alcohol Studies, University of North Carolina School of Medicine, Chapel Hill, North Carolina). “The Role of GABAergic Neuroactive Steroids in Ethanol Action, Tolerance and Drinking Behavior”

**James Sikela** (Professor, Department of Pharmacology and Human Genetics Medical Program, University of Colorado at Denver and Health Sciences Center, Denver, Colorado). “Genome-Wide Identification of Great Ape and Human Lineage-Specific Genes”

### Spring 2005

**Marie Banich** (Director, Institute of Cognitive Science and Professor, Department of Psychology, University of Colorado, Boulder). “Neuroimaging of Attentional Control and its Potential Linkage to Genetics”

**Lon Cardon** (Professor of Bioinformatics, Wellcome Trust Centre for Human Genetics, University of Oxford, United Kingdom). “The Role of Linkage Disequilibrium in Identifying Complex Trait Genes in Humans”

**Karre Christensen** (MD, PhD, Dr. Medical Science, Professor of Epidemiology, Institute of Public Health, University of Southern Denmark and Senior Research Scientist, Terry Sanford Institute, Duke University, Durham, North Carolina). “Danish Twin Studies of Aging: Why Do We Age So Differently?”

**Tatiana Foroud** (Associate Professor, Department of Medical & Molecular Genetics and Department of Psychiatry, Indiana University School of Medicine). “Genetics of Alcoholism and the COGA Study”

**Matthew Stephens** (Associate Professor, Department of Statistics, University of Washington, Seattle, Washington). “Modelling Linkage Disequilibrium and Detecting Recombination Hotspots from SNP Data”

### Summer 2005

**Beth Corder** (Associate Research Professor, Center for Demographic Studies, Duke University, Durham, North Carolina). “Multilocus Risk Genotypes for Alzheimer’s Disease”

**Mike Edwards** (Postdoctoral Candidate, University of Wisconsin, Madison). “Characterization of Age-Related Effects on the Transcriptional Response to Oxidative Damage in Mouse Cardiac and Skeletal Muscle”

**Poster Day.** Faculty, researchers, and students display posters they presented at professional meetings during the previous year. This provides an opportunity to introduce the new members of the institute to the breadth of research at IBG.



IBG Orientation and Poster Day, Summer 2005.

# STAFF

## Research and Administrative Staff

### Research

Adrienn Albert  
Lindly Alston  
Raven Astrom  
Melissa J. Beckner  
Mary Beeson  
Stephanie Bogott  
Heather Bosler  
Matthew Bowker  
Alexis Bowles  
Josh Bricker  
Joshua Brooks  
Robert Brown  
Blake Buhlig  
Kathryn Bursleson  
Clint Carlson  
Phyllis Carosone-Link  
Rick Casey  
Matthew Cirbo  
Leza Clymer  
Rachael Cole  
Mark Conner  
Kimberly Corley  
June Crenshaw  
Vanessa Crittenden  
Robert Curtis  
Hilary Davis  
Patricia Davis  
Theresa DelVecchio  
Antonio DiLeo  
Jennifer Drapeau  
Chris Duffy  
Barbara Elliott  
Lauren Farnham  
Danelle Ferguson  
Jmil Ferguson  
Virginia Fonte  
Stephanie Foreman  
Elizabeth Freedman  
Anthony Giordano  
Elizabeth Glasser  
Christina Nelson-Goens  
Drew Goldberg  
Elizabeth Gooding  
Lena Gordon  
Andrew Gross  
Bonnie Gross  
Terry Grupp  
Melissa Harth  
Jonathan Hayes  
Heather Henderson  
Brian Hiester  
Sena Hitt-Lausten  
Bill Horton  
Dina Huber

Jacqueline Hulslander  
Eli Iacob  
George Jayne  
Anne Johnson  
Peter Jones  
Barbara Kase  
Jennifer Ziemba Keith  
Ashleigh Keller  
Jason Keller  
Nathan King  
David Kipp  
Colin Larson  
Amy Ledbetter  
Paula Lewis  
Sarah Lingafelter  
Carrie Liston  
Phil Livingstone  
Jacques Machol  
Christine Martin  
Tristan McClure-Begley  
Gregory McGinty  
Natalie Meinerz  
Lauren Milner  
Jill Miyamoto  
Donna Moore  
Ryan Morrow  
Sarah Moyle  
Lara Pallas  
Bradley Pemberton  
Nancy Phares-Zook  
Terry Plumlee  
Laurie Reitsema  
Sally Ann Rhea  
Taylor Roy  
Amy Rudolph  
Cathy Ruf

Daniel Ryan  
Scott Sabella  
Jerome Salazar  
Isabel Schlaepfer  
Christina Schmitz  
Jaquelyn Schon  
Robert Schroder  
Sean Shelby  
Ingrid Simecek  
Margaret Spring  
Justin Springett  
Gretchen Stein  
Cornell Strover  
Pat Tedesco  
Erin Thorpe  
Patricia Townsend  
Jennifer Tripodi  
Stephanie Tseeng  
William Van Morter  
Schuyler vanEngelenburg  
Rex Villanueva  
Elizabeth Johnson-Wold  
Corrine Wright  
John Yerg  
Jean Yu  
Joanna Sue Zeiger

### Student Hourly

Chelsie Ankler  
Norm Armstrong  
Kristin Becker  
Chris Bennett  
Gail Bleakney  
Megan Canon  
Sydni Edwards  
Melissa Barba-Espinoza

Kathy Fitzpatrick  
Mary Ellen Flynn  
Logan Fulcher  
Brittany Ganser  
Michael Gleason  
Angela Goldrick  
Benjamin Gurney  
Tamaru Hiromitsu  
Leslie Kaup  
Sweta KC  
Alison Kell  
Alexander Knuckles  
Rachel Kobza  
Jessica Kovats  
Marianne LaBorde  
Alex Lauderbaugh  
Estaban Loetz  
Ashley Lowe  
Michael Luckow  
Alison Mickiewicz  
Jennifer Mueller  
Sarah Nakata  
Diane Lesley-Neuman  
Jerilyn Phippeny  
Billie Riley  
Sam Severance  
Katherine Shaw  
Brice Young

### Administrative

Debbie Aguiar  
Bobbie Atkinson  
Dawn Caillouet  
Kathy Huckfeldt  
Kendra Locher  
Lee Ann Nickerson



Longitudinal Twin Study of Reading Disability. Back row, left to right: Sally Wadsworth, Dina Huber, Raven Astrom, Kathleen Fitzpatrick. Front row, left to right: Christy Nelson-Goens, Gail Bleakney.

# PUBLICATIONS

## Publications

### July 1, 2004–June 30, 2005

Azam, L., Dowell, C., Watkins, M., Stitzel, J.A., Olivera, B.M., & McIntosh, J.M. (2005). alpha-conotoxin BuIA, a novel peptide from *Conus bullatus* distinguishes among neuronal nicotinic acetylcholine receptors. *Journal of Biological Chemistry*, 280, 80–87.

Banaschewski, T., Hollis, C., Oosterlaan, J., Roeyers, H., Rubia, K., Willcutt, E., & Taylor, E. (2005). Towards an understanding of unique and shared pathways in the psychopathology of ADHD. *Developmental Science*, 8, 132–140.

Beresford, H.F., Deitrich, R., & Beresford, T.P. (2005). Cyclosporine discourages ethanol intake in C57bl/6j mice. *Alcoholism: Clinical and Experimental Research*, 29(Suppl. 5), #73, 19A. (Abstract)

Bhave, S.V., Grahame, N., Hoffman, P.L., & Tabakoff, B. (2005). "MAGIC-B" identifies candidate genes for alcohol preference in HAP and LAP mice. *Alcoholism: Clinical and Experimental Research*, 29(Suppl. 5), #499, 90A. (Abstract)

Bowers, B.J., Davis, H., & Ehringer, M.A. (2005). C57 female mice drink less alcohol when given access to a running wheel. *Alcoholism: Clinical and Experimental Research*, 29(Suppl. 5), #556, 100A. (Abstract)

Bowers, B.J., McClure-Begley, T.D., Keller, J.J., Paylor, R., Collins, A.C., & Wehner, J.M. (2005). Deletion of the  $\alpha 7$  nicotinic receptor subunit gene results in increased sensitivity to several behavioral effects produced by alcohol. *Alcoholism: Clinical and Experimental Research*, 29, 295–302.

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Bryan, A., Rocheleau, C.A., Robbins, R.N., Reuben, N., & Hutchison, K.E. (2005). Condom use among high-risk adolescents: Testing the influence of alcohol use on the relationship of cognitive correlates of behavior. *Health Psychology*, 24, 133–142.

Buchwald, R., Greenberg, A.R., & Breed, M.D. (2005). A biomechanical perspective on beeswax. *American Entomologist*, 51, 39–41.

Butt, C.M., King, N.M., Hutton, S.R., Collins, A.C., & Stitzel, J.A. (2005). Modulation of nicotine and ethanol preference by the mouse Chrna-4 A529T polymorphism. *Behavioral Neuroscience*, 119, 26–37.

Byrne, B., Wadsworth, S., Corley, R., Samuelsson, S., Quain, P., DeFries, J.C., Willcutt, E., & Olson, R.K. (2005). Longitudinal twin study of early literacy development: Preschool and kindergarten phases. *Scientific Studies of Reading*, 9, 219–235.

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Churchill, G.A., Airey, D.C., Allayee, H., Angel, J.M., Attie, A.D., Beatty, J., Beavis, W.D., Belknap, J.K., Bennett, B., et al. (2004). The Collaborative Cross, a community resource for the genetic analysis of complex traits. *Nature Genetics*, 36, 1133–1137.

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Crowley, T.J. (2005). Recent advances in psychosocial treatments for substance dependence: Relevance to opioid agonist maintenance treatment. In M. Rihs-Middel, R. Hammig, & N. Jacobshagen (Eds.), *Heroin-assisted treatment, work in progress* (pp. 167–189). Switzerland: Verlag Hans Huber.

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Deffenbacher, K.E., Kenyon, J.B., Hoover, D.M., Olson, R.K., Pennington, B.F., DeFries, J.C., & Smith, S.D. (2004). Refinement of the 6p21.3 quantitative trait locus influencing dyslexia: Linkage and association analyses. *Human Genetics*, 115, 128–138.

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CU-Boulder IBG Family Studies. Back row: Dan Ryan, Andy Gross, Corinne Wright, Jen Keith, Sally Ann Rhea, Annie Johnson, Rob Schroder, Clint Carlson, Matt Cirbo, Scott Sabella, Heather Bosler, Blake Buhlig. Middle row: Bonnie Gross, Erin Thorpe, Elizabeth Gooding, Margaret Spring, Patricia Townsend, Carrie Liston, Lauren Farnham. Front row: Leza Clymer, Donna Moore, Terry Plumlee, Alexis Bowles, Laurie Reitsema, Missy Beckner, Amy Ledbetter.

Lahey, B.B., Pelham, W.E., Loney, J., Kipp, H., Ehrhardt, A., Lee, S., Willcutt, E., Hartung, C., Chronis, A., & Massetti, G. (2004). Three-year predictive validity of DSM-IV Attention-Deficit/Hyperactivity Disorder in children diagnosed at 4–6 years of age. *American Journal of Psychiatry*, *161*, 2014–2020.

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Lee, M.J., Zolman, K.L., Lintz, L.C., & Radcliffe, R.A. (2005). Microarray analysis of transcription factor activation patterns in inbred long and short sleep mice during acquisition of rapid tolerance to ethanol. *Alcoholism: Clinical and Experimental Research*, *29*(Suppl. 5), #494, 89A. (Abstract)

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Li, X., Karadsheh, M., Jenkins, P., & Stitzel, J.A. (2005). Genetic correlation between alcohol and nicotine consumption in mice. *Behavioural Brain Research*, *157*, 79–90.

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Meinerz, N.M., Collins, A.C., & Marks, M.J. (2004). Partial deletion of nicotinic alpha4 and beta2 subunits differentially affects synaptosomal agonist-stimulated RB efflux. Program No. 624.18, *Society for Neuroscience*, (online). (Abstract)

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Meskew-Stacer, S., Ray, L., Marshall, E., Levin, M., & Hutchison, K. (2005). Subjective responses to alcohol and craving: Can participants accurately predict their craving for alcohol and subjective intoxication? *Alcoholism: Clinical and Experimental Research*, *29*(Suppl. 5), #126, 27A. (Abstract)

Metrik, J., McGeary, J., & Hutchison, K. (2005). Cannabinoid receptor gene (CNR1) polymorphism and expectancies in marijuana withdrawal among college drinkers. *Alcoholism: Clinical and Experimental Research*, *29*(Suppl. 5), #347, 65A. (Abstract)

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