Institute for Behavioral Genetics
University of Colorado at Boulder

Annual Report
July 1, 2001–June 30, 2002

John K. Hewitt, Director
Toni N. Smolen, Assistant Director

IBG Building

Table of Contents

Institute for Behavioral Genetics
University of Colorado at Boulder
447 UCB
Boulder, CO 80309-0447
Telephone 303-492-7362
Fax 303-492-8063

Mission

IBG is in many ways a unique facility, with a strong and very distinguished record. The IRC (Internal Review Committee) reports that the institute is truly outstanding. By any measure, it is one of the most successful and productive units on campus. The ERC (External Review Committee) concurs with the summary conclusion that IBG is a world-class operation with very few, if any, peers. (Program Review Panel Final Report, May 23, 1995.)

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.

Message from the Director

2001–02 marked my first year as new director of the Institute for Behavioral Genetics (IBG). What a pleasure and honor it is to be associated with such an outstanding group of faculty, staff, and students. The accomplishments of the whole institute are reflected in the publications, research projects, and training activities documented in this report as well as in honors bestowed on individuals.

Among these honors, our former director, Professor John DeFries, was awarded the 94th Distinguished Research Lectureship by the University of Colorado's Council on Research and Creative Work. This is the highest award that the faculty of the university gives to one of its members. The award was celebrated by a lecture, titled From Anxiety to Cognitive Disabilities: Adventures in Gene Localization, and delivered by John to a full house at the Fiske Planetarium in March.

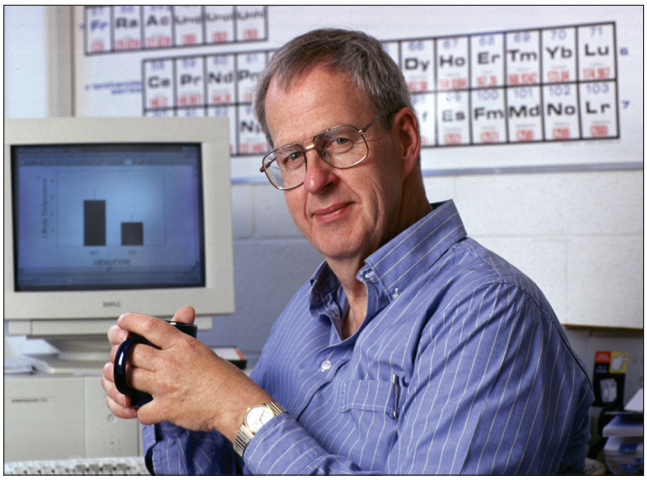
It was announced in February that Professor Allan Collins would be the recipient of the Langley Award from the Society for Research on Nicotine and Tobacco. This award honors scientists who have made ground-breaking advances in basic nicotine research in pharmacology, neuroscience, or genetics (Al made contributions in all three categories). The award is to be presented at the annual meeting in New Orleans, March 2003, and that event will appear in next year's annual report.

James Cypser and Professor Tom Johnson won the Sam Goldstein Award for the best paper published in the *Journal of Gerontology: Biological Sciences* between May 2001 and March 2002. Their paper was: Multiple stressors in *Caenorhabditis elegans* induce stress hormesis and extended longevity. *J. Gerontol.: A Biol. Sci. Med. Sci. 57*:B109-B114.

Professor Johnson was also given the 2002 Robert W. Kleemeier Award, from the Gerontological Society of America. This is the top research award given by the Gerontological Society, which includes 7,000 or so members and several times that many potential awardees. Tom receives the award in November and then will give a lecture and write an article for the *Journal of Gerontology* that will be published in 2003.

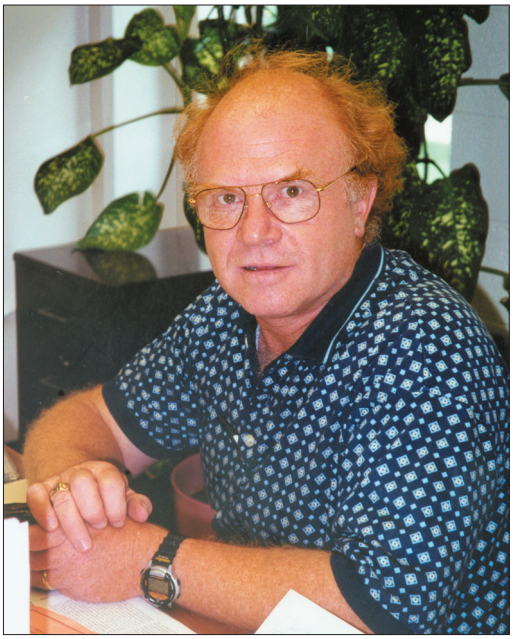
Two of our postdoctoral fellows won prestigious five-year early career development awards to study the relationships between drug abuse and mental health. Dr. Soo Rhee earned a K01 career development award from the National Institute on Drug Abuse to study causes of comorbidity among substance use disorder, attention deficit hyperactivity disorder, and conduct disorder. Dr. Susan Young received her K01 award from the National Institute on Mental Health to investigate the possible genetic link between executive cognitive function and clinical antecedents of substance use disorders such as attention deficit hyperactivity disorder and conduct disorder.

Two more of our postdoctoral researchers won independent Ruth L. Kirschstein National Research Service Awards, otherwise known as F32 postdoctoral fellow-



Professor Allan Collins received the Langley Award from the Society for Research on Nicotine and Tobacco for his ground-breaking research on nicotine.

Graduate student James Cypser, along with his advisor Professor Thomas Johnson, won the Sam Goldstein Award for best paper published in the Journal of Gerontology: Biological Sciences.



Professor Thomas Johnson received the 2002 Robert W. Kleemeier Award from the Gerontological Society of America for his ground-breaking work on aging.

ships. Dr. Christopher Butt was awarded his fellowship from the National Institute on Alcoholism and Alcohol Abuse to study the role of nicotine receptor polymorphisms in ethanol sensitivity. Dr. Sarah McCallum was awarded her fellowship from the National Institute on Drug Abuse to conduct genetic studies of nicotine tolerance and withdrawal using mouse strains that differ in sensitivity to nicotine administration.

One of our outstanding graduate students, Jeremy Owens, was awarded an F31 predoctoral fellowship from the National Institute on Alcoholism and Alcohol Abuse to pursue studies of genetic influences on differential ethanol sensitivity using congenic and mutant mouse models.

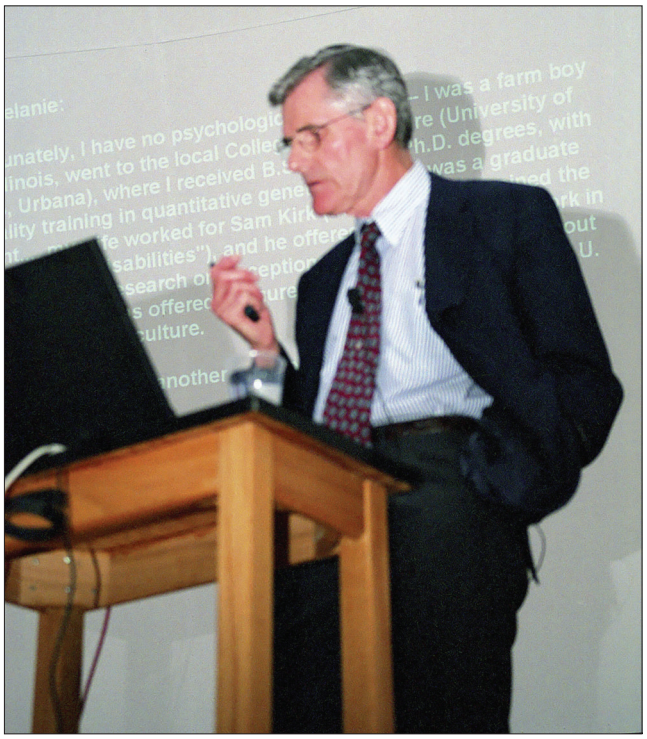
These individual awards underscore the world-class research and training achievements of the institute that are documented in the pages that follow. During 2001–02, IBG faculty published 75 research articles, 2 books, 10 book chapters and 64 abstracts. Our research was supported by 51 research grants and gifts, and our training activities by 3 training grants. Our total budget during this period was $11,270,803 (including general fund support, grants, and gifts), and we had a total of $50,654,383 in grant awards in place.

The executive editorship of the journal, *Behavior Genetics*, returned to IBG in July, after a brief hiatus, when I was invited by the Behavior Genetics Association to take over that role from Norman Henderson who wanted to step down. I was also pleased once again to host our annual week long Workshop on the Methodology of Twin and Family Studies in March. This year we had a record 95 registered 'students' (many are senior scientists) and 18 faculty. The 'students' represented nine different countries and 13 states within the USA.

As I said in my opening, it has been a real pleasure to be associated with these endeavors. I am especially looking forward to writing my introduction to next year's annual report, as I already know that it will include exciting news on new faculty appointments and important research accomplishments.

I want to thank all of the faculty, staff, and students of the institute for another year of stellar professional and scientific performance and, also, for the collegiality that pervades IBG. As an interdisciplinary institute, collegiality is an essential ingredient of our success. A special thanks goes to the assistant director, Dr. Toni Smolen, and to Ms. Debbie Aguiar for their work in preparing this report.

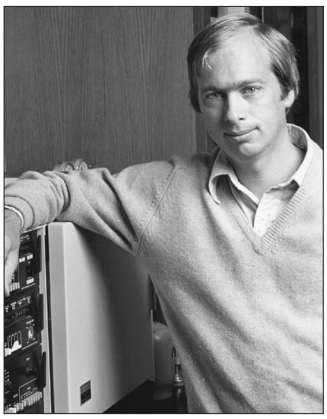
John K. Hewitt
Director



Professor John DeFries was awarded the 94th Distinguished Research Lectureship by the Council on Research and Creative Work. This is the highest award that the faculty of the university gives to one of its members. Following his award lecture to a full house at the Fiske Planetarium, a reception was held in his honor.

Faculty Fellows

Michael D. Breed

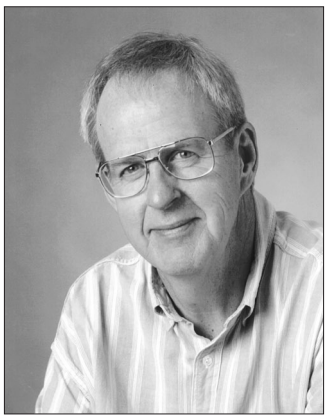


Professor, Department of Environmental, Population, and Organismic Biology; PhD, University of Kansas, Lawrence, 1977. Professor Breed's research emphasis is the genetics of social recognition systems in animals. His current interests include behavioral and genetic studies of the recognition cues used 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

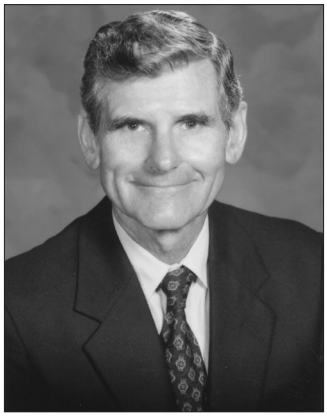
Associate Professor, Department of Psychology; PhD, University of Minnesota, 1978. Dr. Carey's research interests are in the areas of genetics and human psychopathology. Within these areas, his work concentrates on the anxiety disorders and on the development of externalizing behavior (antisocial tendencies, 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; 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 use of genetics as a tool to determine the mechanism of action of drugs.

John C. DeFries

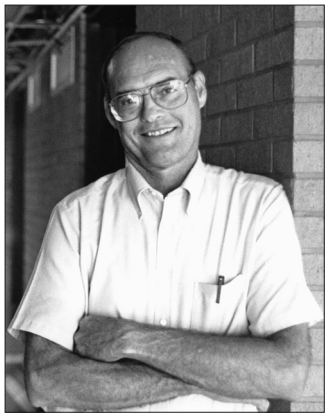


Professor, Department of Psychology; PhD, University of Illinois, 1961; President of the Behavior Genetics Association, 1982–83; Distinguished Research Lectureship, Council on Research and Creative Work, University of Colorado at Boulder, 2001–02. Professor DeFries's primary field of specialization is 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

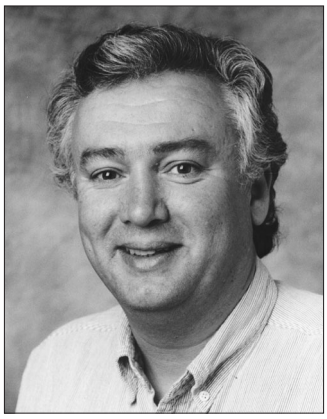
Professor, Department of Pharmacology, University of Colorado Health Sciences Center, Denver; PhD, University of Colorado, 1959; NIGMS Research Career Development Award, 1965–75; NIAAA Research Scientist Award, 1986–2001; President of the Research Society on Alcoholism, 1981–83; Co-Scientific Director 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.

V. Gene Erwin



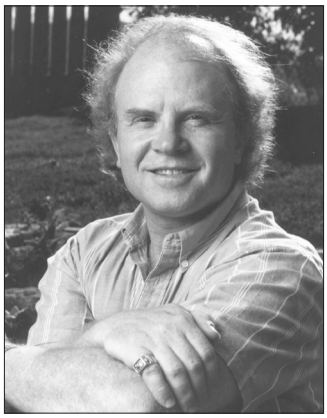
Professor of Pharmacology, School of Pharmacy; PhD, University of Colorado, 1965; Scientific Director of the University of Colorado Alcohol Research Center, 1992–present; Co-Scientific Director of the University of Colorado Alcohol Research Center 1977–92; NIAAA Research Career Award, 1984–94. Professor Erwin's research has been in biochemical neuropharmacology. Studies have focused on using pharmacogenetics as a tool for understanding the neuropharmacology and neurochemistry of alcohol and cocaine. Recent studies have focused on genetic correlations and quantitative trait locus analyses for alcohol- and cocaine-related behaviors and for brain neurotensin and dopamine receptors.

John K. Hewitt



Professor, Department of Psychology, and Director of IBG; PhD, University of London, 1978; President of the Behavior Genetics Association, 2000–01; Executive Editor of the journal *Behavior Genetics*. Professor Hewitt uses longitudinal and cross-sectional studies of twins and their 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; smoking, alcohol, and drug use and abuse; and genetics and behavioral medicine.

Thomas E. Johnson

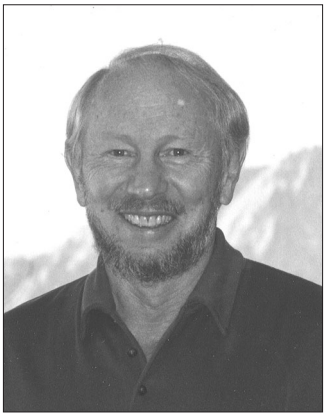


Professor of Behavioral Genetics, Department of Psychology; PhD, University of Washington, 1975; NIH Research Scientist Award, 1994–2004. Dr. Johnson is the discoverer of the first gerontogene, *age-1*, which doubles the life span of the round worm *C. elegans*. He is also cloning quantitative trait loci conferring sensitivity to alcohol and other anesthetic agents in mice. Several approaches, including behavioral and molecular genetic techniques, are used to analyze both aging and the action of genes leading to addiction. For more information, look at ibgwww.colorado.edu/tj-lab.

Carol B. Lynch

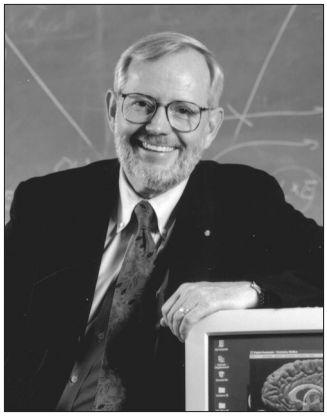
Professor, Department of Environmental, Population, and Organismic Biology; PhD, University of Iowa, 1971. Professor Lynch's research interests are the genetic basis of evolutionary adaptation and brain mechanisms underlying adaptive behaviors. Her current research uses a model system, which has been 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 60 generations for differences in nestbuilding. 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; 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

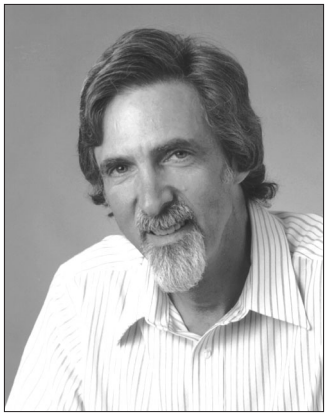


John Evans Professor, Department of Psychology, and Director of the Developmental Cognitive Neuroscience Program, University of Denver; PhD, Duke University, 1977. Professor Pennington is a developmental neuropsychologist whose research focuses on understanding disorders of cognitive development. The 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; 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.

Andrew Smolen

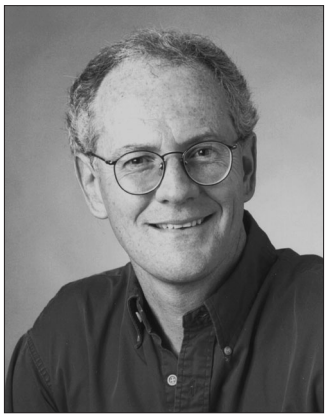


Research Associate, IBG; PhD, University of Colorado, 1979. Dr. Smolen is a pharmacologist whose primary interests are in the areas of neurochemistry and pharmacogenetics. His current research activities include the assessment of the contribution of specific candidate genes to complex behaviors such as substance abuse and attention deficit hyperactivity disorder.

Toni N. Smolen

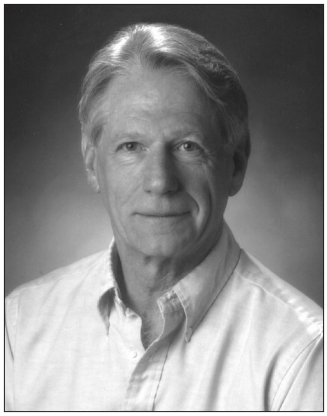
Research Associate, Assistant Director, IBG; PhD, University of Colorado, 1981. Dr. Smolen's research interests are in the areas of pharmacogenetics and neuropharmacology. Her current projects use genetically inbred and selected lines of mice in studies of biochemical and neurochemical mechanisms that 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, IBG and Department of Psychology; PhD, University of Southern California, 1993. Dr. Stallings's research interests include quantitative genetics, substance abuse, and personality. His current research uses biometrical modeling and quantitative trait loci (QTL) methodology to understand genetic and environmental influences on the development of substance use disorders and comorbid psychopathology.

Boris Tabakoff

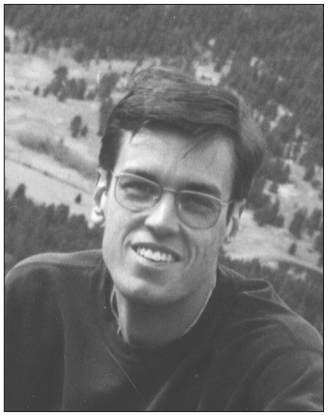


Professor and Chair, Department of Pharmacology, University of Colorado Health Sciences Center, Denver; PhD, University of Colorado, 1970; President of the Research Society on Alcoholism, 1983–85; President of the International Society for Biomedical Research on Alcoholism, 1986–90; RSA Award for Scientific Excellence in Alcohol Research, and Jellinek Award for alcoholism research, 1988; Florence Rena Sabin Award, 2002. 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 the brain.

Jeanne M. Wehner

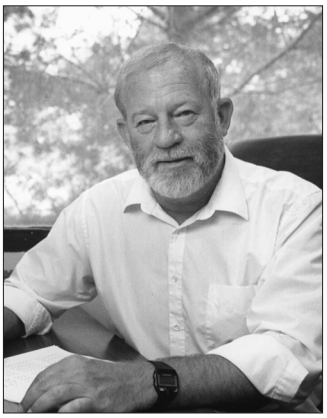
Professor of Psychology, PhD, University of Minnesota Medical School, 1976; NIAAA Research Scientist Development Award, 1991-96; 1997-2002. Professor Wehner is a biochemist whose primary research interests are pharmacogenetics and neurobiology. Current projects include biochemical and genetic studies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

Erik Willcutt



Assistant Professor of Clinical Psychology; 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 that increase susceptibility to these difficulties.

James R. Wilson



Professor Emeritus, Department of Psychology; 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. Recent work involves 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 for alleviation of migraine headaches.

Professional Research Assistant Taylor Roy, from the Smolen Laboratory, assists with molecular studies of candidate genes associated with risk for substance abuse.

Postdoctoral Fellows and Research Associates

Hannah C. Anchordoquy, PhD, University of Colorado, 1998. Genetic basis of behavior, including ADHD, reading disability, and substance abuse; development and generation of genotyping and QTL analyses.

Seth Balogh, PhD, University of Connecticut, 2000. Investigation of the genetic and molecular basis of learning and memory and interaction between nicotine and alcohol using transgenic and knockout mice.

Beth Bennett, PhD, University of Colorado, 1986. Molecular identification of genes underlying initial sensitivity to alcohol and alcohol preference.

Bo Bishop, PhD, Southern Illinois University at Carbondale, 1998. Genetic analyses of early indicators of social, cognitive, emotional, and behavioral problems in middle and late childhood and adolescence.

Massimiliano Bonafé, Visiting Scholar, MD, and Assistant Professor of Experimental Pathology, University of Bologne, Italy. The genetics of longevity.

Barbara Bowers, PhD, University of Colorado, 1990. Evaluation of the role of protein kinase C in sensitivity to ethanol and development of ethanol tolerance.

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.

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

Eduardo de Castro, PhD, University of Geneva, 1997. Identification of genes involved in oxidative stress response and aging in *C. elegans*.

Marissa Ehringer, PhD, University of Colorado Health Sciences Center, 2001. Investigation of genetic factors that contribute to nicotine, alcohol, and drug use problems.

Elise Eller, PhD, University of Utah, 2000. Genetic bases of complex traits such as alcoholism; developing statistical methods that incorporate population structure; anthropological genetics.

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.

Javier Gayán, PhD, University of Colorado, 2000. Behavior genetics of reading ability and disability using a variety of statistical methodology: Linear regression models, structural equation modeling, sib-pair linkage, and association analyses.

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.

Samuel Henderson, PhD, University of Chicago, 1992. Study of DAF-16 in regulating longevity and stress resistance in the nematode *C. elegans*.

Vadim Kapulkin, PhD, Warsaw University, 1999. Identification of molecules involved in cytotoxicity in invertebrates.

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.

Sarah McCallum, PhD, University of Pittsburgh, 1999. Examines behavioral and biochemical effects of nicotine in null mutant and transgenic animals; genetic basis of nicotine tolerance and withdrawal.

Richard Radcliffe, PhD, University of Colorado Health Sciences Center, 1996. Examination of gene expression effects on alcohol responses; development and testing of congenic mouse strains for quantitative trait loci related to anxiety, learning, and memory.

Shane Rea, PhD, University of Queensland, 2000. Demographics of aging in the nematode *Caenorhabditis elegans.* Identification of long-lived individuals in genetically homogeneous populations.

Soo Hyun Rhee, PhD, Emory University, 1999. Etiology of childhood disruptive disorders and substance use disorders.

Brad Rikke, PhD, University of Texas, 1992. Genetic mapping and identification of genes underlying dietary restriction's ability 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.

Christine Schreck, PhD, University of California, 1987. Neurochemical (serotonergic and dopaminergic) influences on differential alcohol preference and impulsivity behaviors across genetic strains of mice.

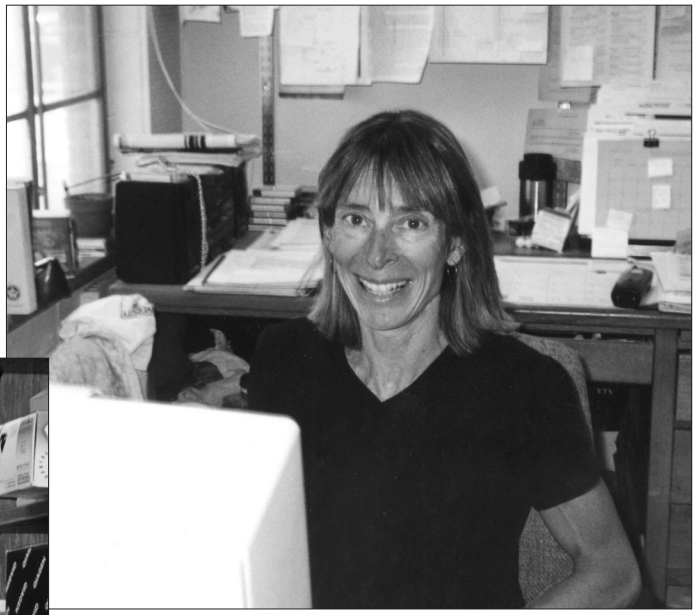
Shwu-Yar Tsai, PhD, Texas Technical University, 1993. Differential gene expression underlying QTL action in alcohol sensitivity in mice.

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, U.K., 1996. Molecular basis of nicotine's central effects, using a combined biochemical, receptor binding, and gene null mutation approach.

Deqing Wu, PhD, Peking University, 1995. Statistical and genetic analysis on 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.

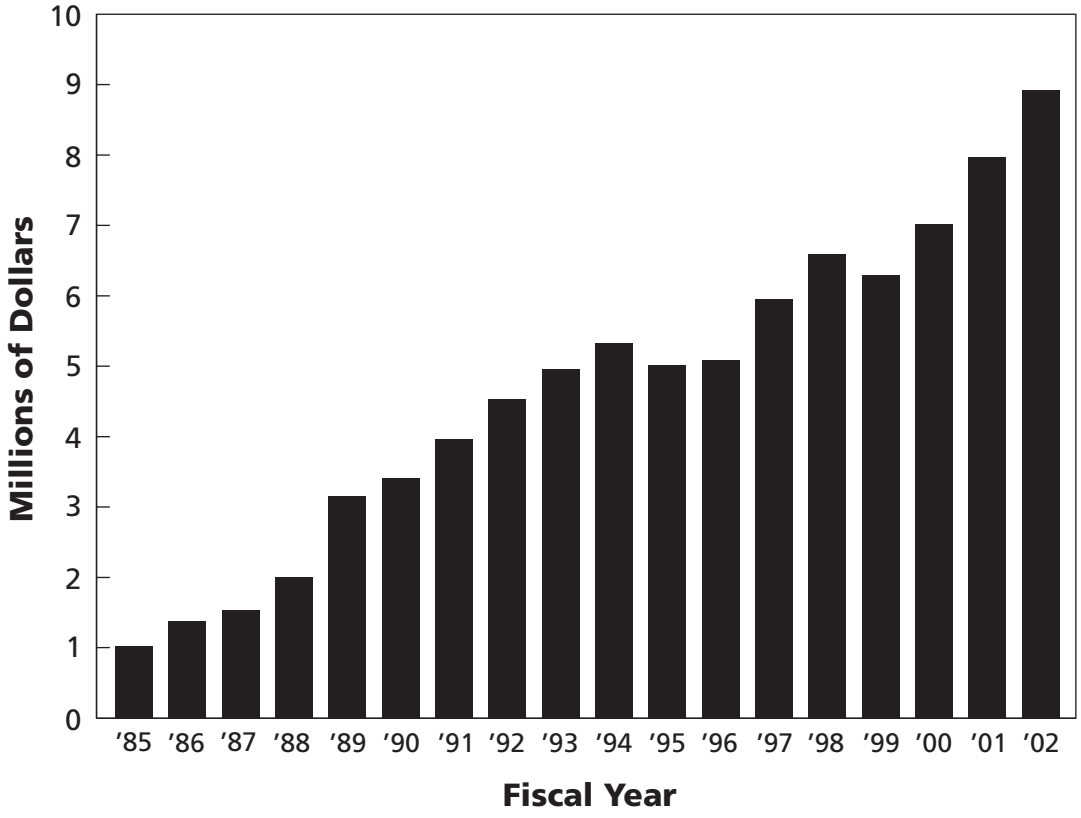


Drs. Beth Bennett (above) and Eduardo de Castro (left) from the Johnson Laboratory. Dr. Bennett's research uses mouse models to identify genes underlying alcohol sensitivity. Dr. de Castro is a visiting postdoctoral scholar from Geneva, Switzerland who is studying genes involved in the aging process of the roundworm C. elegans.

Research Support: 2001–02 Fiscal Year

Source of Funding	Number of Awards	Fiscal Year Dollars	Total Grant Dollars
Federal Agencies			
National Institute of Aging	4	972,267	3,243,991
National Institute on Alcohol Abuse and Alcoholism	12	2,136,228	12,188,193
National Institute of Child Health and Human Development	4	2,358,826	12,098,995
National Institute on Drug Abuse	10	1,692,137	10,749,125
National Institute of Mental Health	9	1,497,455	7,303,293
National Institute of General Medical Sciences	1	250,120	1,188,777
National Eye Institute	1	101,788	731,581
National Institute on Deafness and Other Communication Disorders	1	122,639	1,396,834
Other			
Abbott Laboratories	1	22,750	82,750
Alzheimer's Association	1	75,729	250,000
Binational U.S.–Israeli Science Foundation	1	8,625	69,950
MacArthur Foundation	1	14,000	42,000
W. T. Grant Foundation	1	115,292	363,394
The Ellison Medical Foundation	2	223,250	883,000
Polis-Schutz Research Gift	1	58,333	70,000
Nolop Research Gift	1	1,500	1,500
TOTAL	51	$9,650,939	$50,654,383

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 2001–02, p. 25

Research Activities

2001–2002 Fiscal Year

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

Aging

The Ellison Medical Foundation Senior Scholar Award–"Detection of Gerontogenes in Mice" ($873,000; $218,250), 1/1/99–12/31/03: These studies in mice aim to detect gerontogenes specifying life expectancy, rate of aging, and other life history traits using QTL mapping and mutagenic strategies.

Principal Investigator: Thomas E. Johnson

NIA (AG-12423)–"Transgenic *C. elegans* as Amyloid Disease Model" ($944,720; $347,289), 9/1/99–8/31/02: The formation of insoluble, fibrillar protein deposits, designated β amyloid, is central to the pathology of Alzheimer's disease. The major goal of this project is to investigate the biological factors involved in this formation and the toxicity of β amyloid, using *C. elegans* as a model system.

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

NIA (AG-16219)–"Molecular Genetics of Aging in *C. elegans*" ($1,347,387; $331,348), 8/1/99–7/31/03: The focus of this work is to extend and deepen our understanding of the mechanisms underlying the increased life expectancy of long-lived (Age) mutants in the nematode *Caenorhabditis elegans.*

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

NIA (AG-17949)–"Biometrical Analysis of Personality in Adulthood" ($277,872; $90,108), 4/1/00–3/31/03: The purpose of this study is to investigate the extent to which the relative contributions of genetic and environmental influences on adult personality may change as people age, and whether some traits, or levels of hierarchically organized traits, show more change than others.

Principal Investigator: Michael Stallings
Co-Investigators: John K. Hewitt, Scott Hofer

Alzheimer's Association (TLL-01-2752)–"Investigation of Proteins That Directly Interact with Intracellular Abeta Peptide" ($250,000; $75,729), 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 Aβ peptide in a transgenic *C. elegans* model.

Principal Investigator: Christopher D. Link

NIA (AG-08761)–"Oldest Old Mortality–Demographic Models and Analysis" ($10,635,276; $2,061,972), 1/1/99–12/31/03: The continuation of this program of demographic research on the oldest-old focuses on mechanisms and determinants of survival and longevity. The theoretical foundation that underlies the research and the conceptual framework that ties the various projects together are derived from the perspectives and methods of demography. The research program emphasizes demographic research on the genetic and non-determinants of longevity, including research on the interaction between fertility and mortality and research on why age-specific mortality decelerates with age.

"IBG Subcomponent" ($674,012; $203,522), 7/1/01–12/31/03: The major goal of this subproject is to examine mortality kinetics as a function of age in large populations of normal and mutant nematodes.

Alcohol

NIAAA (AA-03527)–"Genetic Approaches to the Neuropharmacology of Ethanol" ($8,290,175; $1,776,872), 12/1/97–11/30/02: The grant as a whole (Richard A. Deitrich, Principal Investigator) supports an Alcohol Research Center at the University of Colorado, with research being conducted at the Institute for Behavioral Genetics (IBG), the School of Pharmacy, and at the Departments of Pharmacology and Psychiatry at the University of Colorado Health Sciences Center in Denver. Subprojects administered through IBG are:

"Animal Production" ($1,380,548; $298,221): This subproject is devoted to the production and maintenance of mouse stocks useful in alcohol research.

Principal Investigator: Alan C. Collins

"QTL Mapping of Genes Associated with Ethanol Choice" ($468,831; $101,271): This subproject is mapping genes that are associated with choice versus avoidance for ethanol consumption.

Principal Investigator: Thomas E. Johnson

"Ethanol Effects on the GABAergic System" ($393,131; $94,297): These studies are being conducted to characterize the potential role of the GABA/benzodiazepine receptor complex in alcohol-related responses, and the effects of ethanol on this receptor complex, in order to test the hypothesis that a major gene (or genes) affecting responses to alcohol also regulates the function of the GABAergic system.

Principal Investigator: Jeanne M. Wehner

NIAAA (AA-11275)–"Ethanol's Actions in Gamma-PKC Null Mutants" ($754,092; $168, 625), 3/1/99–2/28/02: The goal of this research is to investigate the role of γ-PKC in determining behavioral responses to acute and chronic ethanol treatment.

Principal Investigator: Jeanne M. Wehner
Co-Investigator: Barbara J. Bowers

NIAAA (AA-11984)–"High Efficiency Mapping of Alcohol Sensitivity Genes" ($1,185,095; $365,356), 3/1/00–2/28/04: 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-08940)–"Mapping of Genes Predisposing to Alcohol Sensitivity" ($1,339,918; $21,046), 8/1/96–7/31/01: These studies will position quantitative trait loci (QTL) on the genetic map using a multipoint localization strategy.

Principal Investigator: Thomas E. Johnson

NIAAA (AA-12301)–"Identification of Genes Regulating Alcohol Consumption" ($662,550; $221,063), 7/1/01–3/31/04: The major goal of this study is to fine map alcohol avoidance behavior in congenic recombinant strains of mice carrying portions of the DBA Alcp1 QTL for alcohol avoidance on a 057 BL6 background.

Principal Investigator: Beth Bennett
Co-Investigator: Thomas E. Johnson

Anesthesia

NIGMS (GM-55635)–"QTLs Underlying Molecular Action of General Anesthesia" ($1,188,777; $250,129), 5/1/97–4/30/02: This grant aims to identify genetic differences that underlie QTL that have been associated with general anesthetic sensitivity in mice, focusing on a 250 Kb region containing a major gene involved in the action of propofol.

Principal Investigator: Thomas E. Johnson

Biotechnology

Abbott Laboratories–"Nicotinic Acetylcholine Receptor Collaboration" ($85,000; $12,151), 6/30/98–9/20/02: This collaborative project is testing novel nicotinic compounds for function at natural nicotinic receptors.

Principal Investigator: Michael Marks

Cold Adaptation and Nest Building

Binational Science Foundation–"The Genetics of Rapid Adaptation in the House Mouse" ($60,950; $8,625), 10/1/98–9/30/01: This joint United States-Israeli study is examining cold-adaptation in lines of mice genetically bred in the United States for high and low nest-building behavior and in two wild populations of the house mouse in Israel, one from a warm southern region and one from a colder northern region. The goals of this research include identifying genes that may be associated with cold adaptation in response to rapid environmental changes.

Principal Investigator: Carol B. Lynch
Co-Investigator: Uzi Ritle

The Colorado Adoption Project and Longitudinal Studies

NICHD (HD-10333)–"Determinants of Behavioral Development in Children" ($1,455,520; $336,363), 6/1/98–5/31/03: This award, a continuation of a previous grant from NICHD, provides funds to begin culmination of the Colorado Adoption Project. Adopted and control children are being interviewed at 13, 14, and 15 years of age; then, when they are l6 years old, these children are administered the same test battery that was completed by their parents more than a decade and a half earlier.

Principal Investigator: John C. DeFries
Co-Investigators: John K. Hewitt, Robert Plomin

William T. Grant Foundation–"Origins of Successful and Unsuccessful Transition to Adulthood: The Colorado Adoption Project" ($363,394; $115,292), 6/1/98–5/31/02: This grant combines longitudinal and behavioral genetic designs to provide the first prospective behavioral genetic study of the genetic and environmental origins of individual differences in transitions from adolescence to adulthood, through interviews with the CAP subjects at 19, 20, and 21 years of age.

Principal Investigator: John K. Hewitt
Co-Investigators: John C. DeFries, Robert Plomin

NICHD (HD-36773)–"Nature and Nurture in Social Demography: An Adoption Study" ($1,609,705; $382,709), 6/1/98–5/31/03: This project addresses familial influences on educational attainment, family formation choices of young adults, and how the quality of early family relationships shapes adult child-parent relationships.

Principal Investigator: John C. DeFries
Co-Investigators: Robert Plomin, Avshalom Caspi, Terrie E. Moffitt, John K. Hewitt

MacArthur Foundation–"Individual Differences in Adaptation Processes and Outcomes at Seven Years" ($42,000; $14,000), 10/1/99–12/31/01: The goal of this supplement is to identify the most promising variables indexing family influences and to estimate the likely importance of these variables on behavioral outcomes.

Principal Investigators: John K. Hewitt, Robert N. Emde, Jerome Kagan, Robert Plomin, J. Steven Reznick
Co-Investigators: Joseph Campos, David W. Fulker, John C. DeFries, Carolyn Zahn-Waxler

NIMH (MH-43899)–"Transition Into Early Adolescence: A Twin/Adoption Study" ($996,960; $134,653), 3/1/00–11/30/03: This grant continues support for testing

of adopted and nonadopted children in the Colorado Adoption Project, and twins in the Colorado Twin Study at ages 9 through 12, on a multidimensional battery of psychological measures.

Principal Investigator: John K. Hewitt
Co-Investigators: John C. DeFries, Robert Plomin

NIMH (MH-63207)–"Behavior Genetic Analyses of Executive Functions" ($1,133,060; $222,579), 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

Drug Abuse Vulnerability

NIDA (DA-11015)–"Antisocial Drug Dependence: Genetics and Treatment" ($7,399,816; $1,596,140), 8/1/97–6/30/02: This grant supports a Drug Abuse Research Center (Thomas J. Crowley, Principal Investigator). 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 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:

"Adolescent Drug/Alcohol Dependence: Chromosomal Loci" ($358,655; $75,501): This component is a whole-genome search for chromosomal loci containing genes influencing early-onset dependence on drugs.

Principal Investigator: Thomas J. Crowley
Co-Principal Investigator: John K. Hewitt
Co-Investigators: Michael C. Stallings, Stacey S. Cherny

"Familial Aggregation of Antisocial Substance Dependence" ($900,989; $173,253): The goal of this subproject is to expand a family study of adolescent boys who experience severe substance dependence/abuse and conduct disorder, allowing the research to move beyond descriptive models to the investigation of underlying mechanisms and mediating variables in SUD. The inclusion of female probands will allow generalizing the findings to female populations.

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

"A Longitudinal Adoption Study of Adolescent Substance Experimentation" ($624,409; $110,813): This component is designed to assess genetic and environmental influences on experimentation with tobacco, alcohol, marijuana, and other drugs using a longitudinal adoption design. It builds on more than 20 years of data collected by 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: John C. DeFries, Gregory Carey

"Heritable Early Indicators of Risk for Drug Dependence" ($1,191,610; $257,422): The goal of this study is to use an augmented twin study to understand how genes and environmental influences contribute to vulnerability to drug abuse and antisocial behavior.

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

"Administrative/Educational Core A" ($173,414; $36,488): The goal of the administrative/educational core component is to facilitate interactions among an interdisciplinary group of clinicians, behavioral geneticists, and molecular biologists at the Health Sciences Center and the Boulder campus of the University of Colorado.

Principal Investigator: Thomas J. Crowley
Co-Principal Investigator: John K. Hewitt
Co-Investigators: Robin Corley, Michael Stallings, Stacey Cherny, Greg Carey, Kenneth Krauter

"Assessment Core B" ($143,596; $29,305): The goal of this assessment core is to ensure that the phenotypic information from each of the components is collected, organized, and stored in a way that facilitates direct comparisons across components and combined analyses among components.

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

NIDA (DA-12845)–"Genetics of Adolescent Antisocial Drug Dependence" ($8,148,882; $1,496,154), 9/1/00–8/31/05: The purpose of this multisite project (Thomas Crowley, Principal Investigator) is to conduct a whole-genome search for chromosomal loci influencing early-onset antisocial drug dependence.

"IBG Subcomponent" ($576,655; $104,794): The primary roles of this subcomponent are data collection and monitoring of data collection efforts for the Colorado site, integration and management of the multisite data from Colorado, and data analysis and the reporting of scientific results.

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

NIAAA (AA-11949)–"NYS Family Study: Problem Alcohol Use and Problem Behavior" ($6,889,482; $2,218,269), 9/30/00-8/31/05: The proposed research (Delbert S. Elliott, Principal Investigator) 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" ($1,423,252; $303,751): 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: John DeFries, Michael Stallings, Andrew Smolen, Robin Corley, Susan Young

NIDA (DA-14642)–"Progression of Craving and Addiction: Genetic Factors" ($1,466,216; $290,216), 9/30/01–6/30/06 (Kent Hutchison, Principal Investigator): Our preliminary research 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" ($464,553; $73,078): 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

Learning

NIMH (MH-53668)–"QTL Mapping of Complex Learning in Mice" ($546,894; $150,134), 7/15/95–5/31/02: The major goals of this project are to map loci regulating hippocampal-dependent learning in the mouse, using quantitative trait loci (QTL) analysis.

Principal Investigator: Jeanne M. Wehner

Learning Disabilities

NICHD (HD-27802)–"Differential Diagnosis in Learning Disabilities" ($6,661,612; $1,282,895), 3/20/01–11/30/06: The long-range objectives of this Learning Disabilities Research Center (J.C. DeFries, Principal Investigator) 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; $174,605): 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 G. Wadsworth, Erik G. Willcutt

"Reading and Language Processes" ($1,481,997; $284,917): 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; $226,118): 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; $183,962): 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; $140,497): 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; $273,152): 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

NICHD (HD-38526)–"A Longitudinal Twin Study of Early Reading Development" ($2,372,158; $454,600), 3/1/99–2/28/05: 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: Sally Wadsworth, John C. DeFries, Erik G. Willcutt, Bruce F. Pennington, Brian Byrne

NIMH (MH-62120)–"DSM-IV ADHD in an Ethnically Diverse Community Sample" ($1,692,334; 368,417), 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: Andrew Smolen, John C. DeFries

NIMH (MH-62116)–"Behavior Genetics of Attentional and Co-Occurring Problems" ($147,383; $73,685), 8/1/00–7/31/02: This study is examining genetic and environmental contributions to aspects of attention problems and co-occurring behavior problems in children and adolescents.

Principal Investigator: Stephanie Schmitz

NIMH (MH-63941)–"Validity of DSM-IV ADHD Subtypes in a Community Sample" ($1,679,145; $266,721), 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, Andrew Smolen, John C. DeFries

NIDCD (DC-05190)–"Longitudinal Twin Study of Reading Disability" ($1,396,834; $122,639), 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

Nicotine

NIDA (DA-03194)–"Genetics of Nicotine Tolerance: Role of Receptors" ($1,417,325; $330,907), 9/1/99–8/31/04: This research is being conducted to test the hypothesis that hereditary differences in the number or affinity of receptors that bind nicotine account for differences in initial nicotine sensitivity and/or the development of tolerance.

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

NIDA (DA-12242)–"Alpha-Conotoxin MII: A Selective Nicotinic Receptor Probe" ($659,468; $124,801), 2/1/99–1/31/02: The objectives of this research proposal include thoroughly defining the binding of native and radioiodinated alpha-conotoxin MII to mouse brain preparations and model transfected HEK293 cells.

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

NIAAA (AA-11156)–"Ethanol, Nicotine, and Brain Nicotinic Receptors" ($1,106,231; $283,108), 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

NIDA (DA-12661)–"Analysis of Nicotinic Cholinergic Systems in Mutant Mice" ($134,587; $25,700), 7/1/99–6/30/04: This is a subcontract to perform studies for Baylor College of Medicine located in Houston, Texas. These studies use mice that have had specific nicotinic receptor subunit genes knocked out (so-called null mutants) to help identify whether specific receptor subtypes play critical roles in tolerance to nicotine.

Principal Investigator: John Dani
Co-Investigators: Richard Paylor, Allan C. Collins

NIAAA (AA-13018)–"Role of Nicotinic Receptors in Effects of Alcohol" ($2,371,673; $76,371), 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-Investigators: Allan C. Collins, Steve Heinemann

NIDA (DA-10156)–"Response to Nicotine: Molecular Studies of Murine nAChRs" ($2,970,804; $108,774), 9/30/95–8/31/01: This grant supports a program project (A.C. Collins, Principal Investigator) which investigates the role of nicotinic receptor subtypes in the regulation of response to nicotine after either acute or chronic exposure. The project has three subprojects and an administrative core:

"nAChR Subtypes and Responses to Nicotine" ($992,019; $35,284): The goal of this subproject is to define the role of receptor diversity in the development of tolerance to and dependence on nicotine.

Principal Investigator: Allan C. Collins
Co-Investigators: Michael J. Marks, Jerry A. Stitzel

"Regulation of nAChRs in Transfected Cells" ($1,256,937; $42,199): This component has as its goals to identify and clone members of the nicotinic acetylcholine gated ion channel receptor family in the mouse genome; to test the hypothesis, by gene knockout experiments, that specific nicotinic receptors mediate nicotine-induced nicotine tolerance and dependence in mice; and to test the hypothesis that knocking out or mutating a nicotinic receptor leads to a change in the regulation of another nicotinic receptor.

Principal Investigator: Stephen F. Heinemann

"Behavioral Studies of Nicotinic Receptor Null Mutants" ($182,410; $8,269): This research project investigates the role of specific nicotinic cholinergic receptors in learning and memory processes, and whether the cognitive

enhancing properties of nicotine are regulated by the activation of specific brain nicotinic receptors.

Principal Investigator: Jeanne M. Wehner

"Communication Core" ($438,056; $14,099): The main goal of the Communication Core is to bring together three research groups, that have had a long-standing interest in nicotine or nicotinic receptors, to investigate the role of nicotinic receptor subtypes in the regulation of dependence on nicotine.

Principal Investigator: Allan C. Collins

Statistical Models

NEI (EY-12562)–"Variance Components Models for Mapping QTLs" ($731,581; $101,788), 12/7/98–11/30/01: The major goal of this project is to expand research on variance components methods for mapping QTLs for human complex traits using both association and linkage approaches.

Principal Investigator: John K. Hewitt
Co-Investigators: John Williamson, Stacey Cherny, Pak Sham

NIMH (MH-19918)–"Workshop on Methodology of Twin and Family Studies" ($462,656; $85,220), 9/1/98–8/31/03: 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

Research Career Awards and Fellowships

NIDA (K05-DA-00197)–"Pharmacogenetic Regulation of Sensitivity to Nicotine" ($559,956; $119,990), 9/1/98–8/31/03: This award allows the principal investigator to pursue genetic strategies to study the development of tolerance to and physical dependence on nicotine.

Awarded to: Allan C. Collins

NIAAA (K02-AA-00195)–"Identifying Genes Predisposing to Alcoholism" ($510,575; $102,115), 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

NIAAA (K02-AA-00141)–"Ethanol's Actions in Gamma-PKC Null Mutants" ($491,918; $99,631), 8/1/97–7/31/02: This award allows the principal investigator to further her investigations into the role of γ-PKC in the development of alcohol dependence.

Awarded to: Jeanne M. Wehner

NIDA (K01-DA-13956)–"Causes of Comorbidity: Substance Use Disorder, ADHD & CD" ($498,497; $85,585), 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-01865)–"Executive Function: Links to Drug Use and Psychopathology" ($550,625; $62,669), 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

NIMH (F32-MH-12100)–"Behavioral and Molecular Genetic Study of ADHD" ($94,236; $6,253), 9/1/98–8/31/01: This postdoctoral fellowship award is for studies of attention deficit hyperactivity disorder and its association with other learning problems or psychiatric disorders.

Awarded to: Erik G. Willcutt

Ellison Foundation (F31-NO-0008)–"Using Micro Array Technology to Identify Genetic Factors Common to Multiple Forms of Life Extension in *C. elegans*" ($10,000; $5,000), 1/1/01–12/31/01: This study uses microarray technology and *C. elegans* mutants to discover candidate genes associated with life extension in the nematode.

Awarded to: James R. Cypser

NIDA (F32-DA-14152)–"Genetic Studies of Nicotine Tolerance-Withdrawal" ($75,028; $35,726), 5/1/01–4/30/03: This postdoctoral fellowship award is to examine genetic influences on effects of chronic nicotine in mice, including withdrawal and changes in nicotinic receptor function.

Awarded to: Sarah E. McCallum

NIAAA (F31-AA-13350)–"Pleiotropy for Alcohol-Related Phenotypes" ($47,886; $19,953), 9/1/01–8/31/03: This predoctoral fellowship will provide a better understanding of the genetic and neurological systems underlying alcohol abuse.

Awarded to: Jeremy C. Owens

NIAAA (F32-AA-13465)–"Nicotinic Receptor Polymorphisms and Ethanol Sensitivity" ($84,740; $6,387), 5/7/02–5/6/04: This project uses classical genetics, null-mutation technology, neurochemistry, and behavioral studies to assess the possible role of a genetic polymorphism in the nicotinic acetylcholine receptor in mechanisms of nicotine and alcohol abuse.

Awarded to: Christopher M. Butt

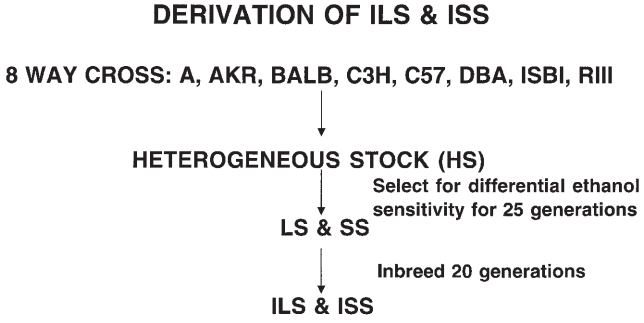
IBG Highlights

Mouse Models and Mapping Genes for Sensitivity to Ethanol

A large number of very specific strains of mice have been developed at the Institute for Behavioral Genetics (IBG). One of the most widely used and well characterized of these, the Long Sleep (LS) and Short Sleep (SS) lines, were developed by selection for differential sensitivity to the sedative/hypnotic effect of ethanol. LS are very sensitive, while SS are very resistant to the sedative effect. This behavioral response to ethanol may be similar to an important predictor of liability to alcoholism in humans: young men who are more resistant to the sedative/hypnotic effects of ethanol are more likely to become alcoholics. Hence, having an animal model, such as the LS and SS, is a valuable first step in determining the genetic and physiological basis underlying this link.

Eight commonly used inbred strains were crossed (this crossing took four generations; Figure 1) to produce a heterogeneous stock population (HS), which is still maintained at IBG. The HS provided the starting population for mass selection; mice were tested for loss of righting reflex (LORR; affectionately known to many labs as "sleep time") following an injection of ethanol intra-peritoneally. The dose, 3.3 g/kg, was standardized to their body weight. Duration of LORR was determined to be the time the animal stayed on its back in a V-shaped plexiglas tray, before righting itself three times within a minute. LORR is a good choice of behaviors for assessing the effect of ethanol in mice because this position, on their backs with their feet in the air, is a vulnerable one from which they will try to recover their normal posture unless extremely incapacitated.

Figure 1. The Heterogeneous Stock (HS) mice were developed by an 8-way cross among the inbred strains of mice listed at the top of the figure. HS mice have been used as the starting population for genetic selection on a wide variety of traits, including sensitivity to ethanol as measured by the loss of righting response following ethanol administration.



Mice were chosen for matings based on their LORR: those with the shortest LORR were the progenitors for the SS lines, while those with the longest LORR became the parents for the LS lines. Selection was initiated (G_0) in 1962 at the University of California at Berkeley where it continued from generation one (G_1) through generation three (G_3) when mice were moved to the Stanford Medical School. At G_5, the lines were moved to their present home at IBG at the University of Colorado in Boulder. Selection was resumed, and the dose of ethanol was increased to 3.5 g/kg at G_8 and to 4.2 g/kg at G_9 because many of the SS mice were not losing the righting response at the original dose. Selection was suspended from G_{19}-G_{24} and resumed at G_{25}, when the SS selection dose was further increased to 4.7 g/kg and the LS dose reduced to 3.8 g/kg. These doses were maintained through G_{33} when selection was terminated. At this time, the SS mice slept about 10 minutes and the LS over two hours, given the same dose of ethanol. These selected lines have been maintained as 10 families, each of which is propagated by duplicate sets of matings between nonsiblings. The point of a selection such as this is to concentrate genes associated with ethanol sensitivity in one line (LS) and those associated with resistance in the other (SS). All other nonethanol sensitivity genes are approximately the same in both lines of mice. Following selection, the LS showed greater sensitivity than the SS to the depressant effects of a variety of alcohols, barbiturates, anesthetics, and nicotine. Interestingly, LS and SS do not differ very much in the rate at which they metabolize ethanol; SS mice regain their righting response at a much higher blood ethanol concentration (BEC) than LS, indicating that central nervous system differences underlie the differential sensitivity to ethanol. LS and SS also show a variety of behavioral differences, both in response to ethanol and other drugs, as well as in underlying physiological measures. For example, SS show higher ethanol preference, tolerance, ethanol-induced activity, and withdrawal seizures than LS. Also the Purkinje cells, a type of brain cell that may be involved in the differential sensitivity to ethanol, of LS are more responsive to ethanol than those of SS.

For some genetic studies it is important that all of the genes in the animals be fixed, not just those involved in ethanol sensitivity. Fixation of all loci, or genes, is most readily accomplished by systematically mating close relatives for a number of generations. To this end, 20 generations of brother-sister (referred to as sib, for sibling) mating in the LS and SS lines produced the

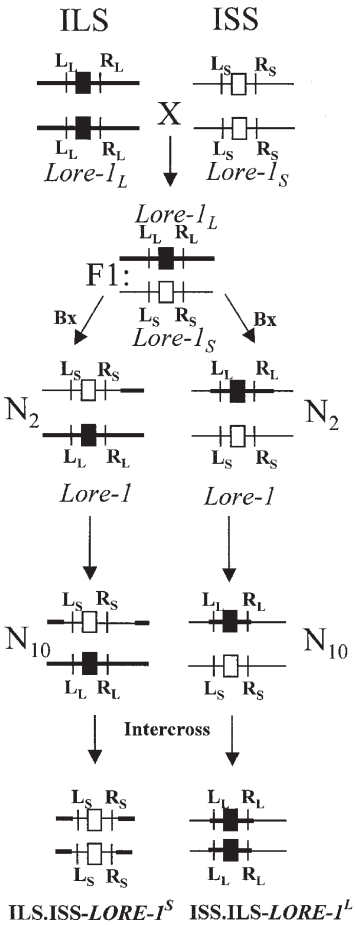
Inbred Long Sleep (ILS) and Inbred Short Sleep (ISS) strains, which are maintained in the IBG specific-pathogen-free, or so-called SPF colony (Figure 1). These mice retain the loss of righting response, the blood ethanol concentration at regaining their righting response, and most of the other behavioral and pharmacological differences found in LS and SS mice.

Various crosses using the ILS and ISS have enabled researchers at IBG to map genes associated with differential sensitivity to ethanol, and other traits as well. The idea underlying this approach is that an inbred selected strain, such as the ILS has only one form of each gene, called an allele, which contributes to a trait such as LORR. The ISS would be likely to have a different form, or different allele, of the gene contributing to LORR. When the inbred strains are crossed, the alleles are shuffled in all the offspring and by correlating the trait such as LORR with the alleles present in each mouse (the mouse's genotype), it is possible to identify regions on each chromosome associated with long or short LORR. These chromosomal regions are called quantitative trait loci, or QTLs.

It takes two generations of cross-mating, called an F_2, for the genes to be shuffled. For example, in a large F_2 cross between ILS and ISS, over 1,000 mice were tested for LORR, and almost 200 mice were genotyped for over 100 genetic markers evenly distributed over the 20 mouse chromosomes. Analysis of these results yielded four QTLs that together accounted for about 60% of the LORR difference between ILS and ISS, or about 70 minutes of "sleep time."

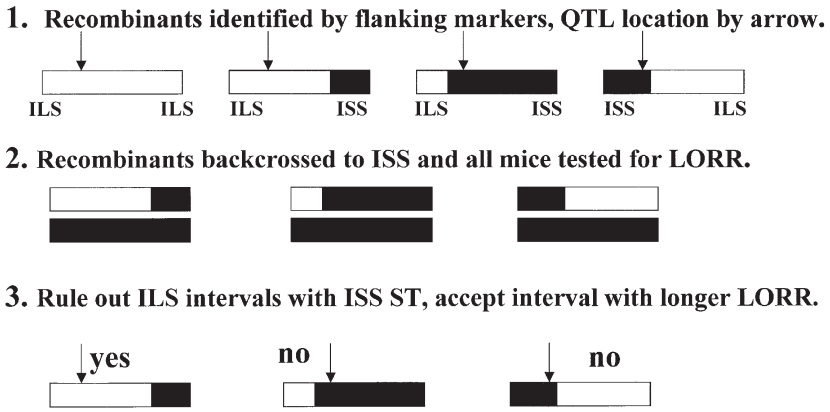
Each of these four QTLs, which are referred to as Lore1, Lore2, Lore4, and Lore5, have been "moved" individually using genetic breeding techniques onto the opposite mouse strain background to produce

Figure 2. Production of Congenic Strains. A region of interest on the chromosome can be moved from one strain of mouse to the other by crossing a number of generations. In each generation, the cross (F1) is tested, and those with the ILS (▮) characters are mated to ISS (□). Those F1 with ISS characters are mated to ILS to produce the N2 generation. Repeating this mating scheme for several generations (N10) and intercrossing the resulting animals, produces an ILS strain that contains the selected portion of the ISS DNA, and an ISS strain that has the corresponding ILS DNA material inserted into its genome.



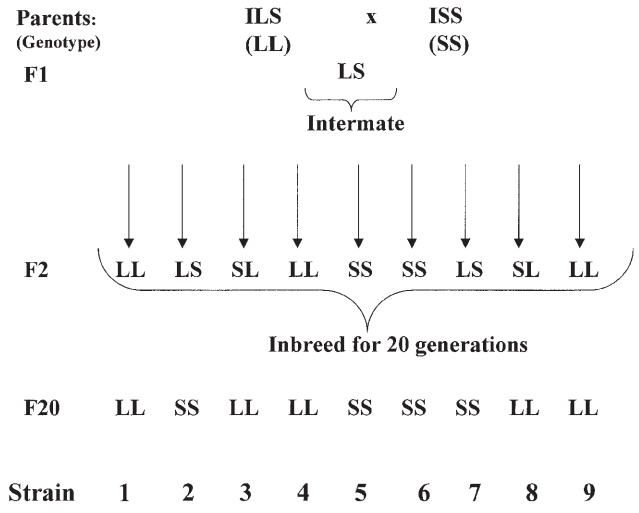
The LS and SS mice were developed by genetic selection for differential sensitivity to the sedative/hypnotic effects of ethanol. Following administration of ethanol, the mice lose their righting reflex and can be placed on their backs in a V-shaped plexiglas tray. After a period of time, referred to as "sleep time," they regain their ability to stand up. LS mice, such as the one shown, are sensitive to ethanol and will "sleep" longer than SS mice, which are very resistant to the sedative/hypnotic effects of ethanol. The mice are identified by red ink markings on their tails.

Figure 3. Progeny testing to localize a QTL to a reduced chromosomal region. The ILS region in blue on the left illustrates the congenic region described in Figure 2. During the backcrossing, crossing over in meiosis will produce smaller ILS regions (ISS regions are red). 1. The extent of the ILS region is identified by genotyping. 2. Mice with the indicated recombinant chromosomes are backcrossed to ISS. Populations of these chromosomal types are tested for sensitivity to ethanol (duration of LORR); mice with the recombinant chromosome are compared to their littermates that are homozygous ISS. 3. ILS chromosomal regions that also show a longer LORR indicate the QTL for LORR is in this smaller area.



reciprocal congenic strains of mice (Figure 2). Congenic strains allow researchers to do two things: first, the effect of each QTL can be confirmed, by behavioral and physiological testing, as the QTL from one strain (e.g., the ILS Lore 1) is isolated in an otherwise entirely ISS genome. Second, the chromosomal region can be narrowed by testing the offspring of mice with gene crossovers in that region (Figure 3). If the ILS LORR persists in mice with the narrowed ILS region, then the QTL is mapped to the reduced interval.

Figure 4. Production of Recombinant Inbred (RI) Strains. Two parental strains of mice are mated together to produce an F1 generation. Two F1 offspring are mated to produce F2 mice, which are bred together. The offspring of F2 matings are inbred by successive brother-sister matings for an additional 18 generations to produce a series of RI strains each with a unique genotype consisting of one or the other parental alleles (e.g., LL or SS).



Successive iterations of this mating strategy, coupled with testing of the offspring, can fine-map the QTL to a region small enough to sequence. This can result in the identification of candidate genes that may affect this behavioral and physiological response to ethanol. Other behavioral and physiological responses to ethanol, or to other drugs, can be tested in these congenic mice to determine if genes found in the same area influence them as well.

Another type of cross, shown in Figure 4, produces a recombinant inbred (RI) series of mice. In these mice, the genes from the two parent strains (e.g., ILS and ISS) are shuffled, much as in an F_2 cross. The key difference is that in the production of the RI, mice in the F_2 generation are intermated and a number of independent strains are produced by brother-sister inbreeding for 20 additional generations. This process results in a number of inbred strains, each with a unique genotype consisting of only ILS or ISS alleles in varying combinations. Unlike an F_2 where each mouse is unique genetically, in a single RI strain all the mice are genetically identical. Thus, a given genotype can be tested repeatedly for a single trait such as LORR, giving much more accurate measurement. Alternatively, RI strains can be tested for a variety of different traits, each of which can be mapped on the strain genotype, making the RI panel a powerful gene mapping tool. The LXS RIs (Figure 1), with 79 strains fully inbred, is the largest RI series in existence. This series, and the earlier LSXSS RIs, have been used to map genes for a number of traits including sensitivity to ethanol and other sedative/hypnotic drugs, brain receptor densities and binding characteristics for neurotransmitters, and ethanol consumption.

Dr. Beth Bennett
Research Associate

Twin Study of Early Reading Development

A new international twin study of early reading development is underway in Australia (directed by Brian Byrne at the University of New England), in Norway (directed by Stefan Samuelsson at Stavanger College), and at the Institute for Behavioral Genetics (directed by Richard Olson, with co-investigators John DeFries, Sally Wadsworth, and Erik Willcutt). This new longitudinal research with twins from preschool through the second grade is motivated by results from other research at IBG with older twins from the third through twelfth grades. The studies with older children have revealed strong genetic influences on a group reading deficit as well as on individual differences in reading throughout the normal range. In addition, there are strong genetic influences on an oral language skill called phoneme awareness that are largely shared with individual differences and deficits in word reading. However, the research with older children does not tell us about the genetic and environmental etiology of phoneme awareness and other important reading related skills *prior* to formal reading instruction, or how these skills are related to genetic and environmental influences on reading, during the critical period of formal reading instruction in the first and second grades. Our international longitudinal research project is designed to answer these important questions from both a cross-cultural and cross-language perspective.

Preliminary results from 250 preschool twin pairs, including 73 from Australia, 35 from Norway, and 142 from the U.S., have recently been reported by Byrne et al. (2002). Significant genetic influence (h^2 = .52) and nonsignificant shared environmental influence (c^2 = .16) were found for individual differences in the twins' phoneme awareness measured in standard tests of their current skills. Moreover, we found very similar results for preschoolers' ability to *learn* about phoneme-level language skills during "dynamic" training/testing sessions (h^2 = .50, c^2 = .22). Thus, it seems that individual differences in this important reading-related language skill reflect learning differences *prior* to reading instruction that have significant genetic etiology. Interestingly, phoneme awareness was not the only learning skill that showed significant genetic etiology. A composite measure of visual-spatial, story, and sound-symbol learning also showed significant genetic influence (h^2 = .47, c^2 = .00). Of equal importance are the findings of significant shared environmental influences for individual differences in grammar (h^2 = .22, c^2 = .43), vocabulary (h^2 = .18, c^2 = .49), and print knowledge (h^2 = .28, c^2 = .55). These skills are also known to be related to individual differences in early reading development.

As we enlarge the sample of preschool twins, we will be able to address questions about the degree of shared genetic and environmental etiology for the different learning skills, and whether results may vary across the different countries and languages. At present, the pattern of results seems quite similar across the three countries. Some of the most exciting results will come from longitudinal analyses of genetic and environmental influences as we follow the children from preschool through kindergarten, first grade, and second grade. These analyses will clarify for the first time how important reading related skills, prior to formal reading instruction, are causally linked through genes and environment to individual differences in early reading development. This knowledge is of critical importance, since reading skills at the end of second grade are highly correlated with reading skills in the later grades and in adults.

Reference

Byrne, B., Delaland, C., Fielding-Barnsley, R., Quain, P., Samuelsson, S., Hoien, T., Corley, R., DeFries, J.C., Wadsworth, S., Willcutt, E., & Olson, R.K. (2002). Longitudinal twin study of early reading development in three countries: Preliminary results. *Annals of Dyslexia*, 52, 49-73.

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 bred at IBG.

Ongoing selection studies include various lines of mice that differ in sensitivity to alcohol (projects supported by NIAAA grants to Dr. V. Gene Erwin and the University of Colorado Alcohol Research Center), and the development of congenic lines by intergressing various QTLs on LS or SS inbred backgrounds (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, and 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&2)
- Low Acute Functional Tolerance (LAFT 1&2)
- Congenic ILS.Lore Short and ISS.Lore Long Bilineal Selection
- B6.D2 Congenic for voluntary ethanol consumption
- D2.H2 Congenics
- Nicotinic Knockouts

Faculty Director
Allan C. Collins

Lab Supervisor
Jerry Salazar

Staff
Mark Conner
Colin Larson
Ryan Morrow
William van Morter
Jean C. Yu

Professional Research Associates
Matt Battaglia
Jessica Hall
Christine Martin
Justin Springett

Student Assistants
Kelsey Cain
Vishwas Ganesan
Anthony Giordano
Christopher Leeds
Jessica Michael
Erin Nix
Julia Rifkin
Amit Singh

Laboratory Supervisor Jerry Salazar.

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 interview and testing of 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, scintillation and gamma counters
- video monitored and computerized behavioral testing apparatuses
- Nomarski Interference CDIC and fluorescent microscopes

IBG maintains a heterogeneous network of Unix, Windows, and Macintosh computers totaling 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 on site and off site. Additionally, IBG makes available to users a color laser printer, scanners, digital cameras, and CD-ROM writing facilities.

Professional Research Assistant Chinatsu McGeary loads subject samples into the ABI automated DNA sequencer located in the IBG Molecular Biology Core Facility.

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 newly established PhD program in neuroscience. The institute also has research and training links with the Department of Psychology at the Univer-sity of Denver, and with both the School of Pharmacy and the Department of Pharmacology at the University of Colorado Health Sciences Center in Denver.

The following course requirements are in addition to those that may be imposed by the department in which the trainee is enrolled: Behavioral Genetics, Genetics, Quantitative Genetics, Molecular Genetics and Behavior, Biometrical Methods in Behavioral Genetics, Statistics, Concepts in Behavioral Genetics, Research in Behavioral Genetics, and Seminar in Behavioral Genetics. At least three of the first four courses listed must be taken, and at least six courses from this list must be taken to complete the training program. All trainees and postdoctoral students are required to complete a course in scientific ethics. Each trainee is expected to complete the requirements for the MA or MS degree near the end of year two.

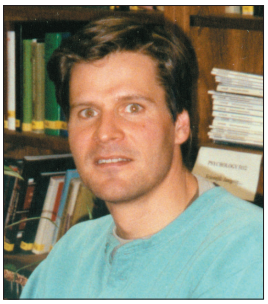
Trainees are expected to serve as teaching assistants in a course judged by their advisory committee to be relevant to their professional specialty. This teaching requirement is usually completed during the second year of graduate training. All students are encouraged to ensure breadth of experience 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 proper functioning 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. Applicants are encouraged to write also 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, University of Colorado at Boulder, 447 UCB, Boulder, CO 80309-0447. If you prefer to call, the telephone number is 303-492-7362.

Visiting Student

Visiting student scholar Mats Larsson from the University of Orebro, Orebro, Sweden. In Sweden Mats studied iris patterns and their relationship to personality using the Reyid Method of iris interpretation. His research interests include using both a map of the DNA sequences that are responsible for the fiber patterns in the iris, as well as iris patterns as a methodology to identify candidate genes related to personality. While at IBG Matts worked under the direction of Dr. Michael Stallings and was involved in association studies of personality, in particular novelty seeking and dopamine receptor polymorphisms in adolescents.



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.*

Rebecca Cross (PhD program, psychology). Differential genetic etiology of reading disability as a function of processing speed.

Jim Cypser (PhD program, psychology). Examination of the relationship between stress resistance and life expectancy as mediated by hormesis (induced stress resistance) and single-gene mutants.

Chayna Davis (PhD program, psychology). Etiology of reading difficulties and rapid naming: Bivariate twin and genetic linkage analysis.

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

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). Genetic and environmental contributions to externalizing behavior, cognitive ability, and the relationship between the two.

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

Denise Hix (PhD program, psychology). Genetic regulation of initial sensitivity and tolerance development to alcohol.

John McGeary (PhD program, psychology). Genetic and environmental influences on the interaction of stress and the effects of alcohol.

Jeremy Owens (PhD program, psychology). The role of the neuronal nicotinic receptor system in differential response to ethanol.

Amy Smith (PhD program, psychology). Microarray analysis of gene expression differences in gamma-PKC null mutant mice compared with their wild type littermates; examination of strain differences in GluR2 AMPA-type glutamate receptors.

Steven Wilson (PhD program, psychology). Longitudinal changes in genetic influence on general intelligence; genetic and environmental influences on alcohol-related problems.

Graduate students left to right: Heather Gelhorn, Dietre Godinez and Noa Heiman.

Graduate student Jeremy Owens preparing a research poster presentation.

Courses Taught

Fall 2001

Michael D. Breed	EPOB 5310, UCB	Environmental Biology Core
	EPOB 2650, UCB	Honors Environmental Biology
Gregory Carey	PSYC 3102/5102, UCB	Behavioral Genetics
Allan C. Collins	PSYC 4132/5132, UCB	Behavioral Neuropharmacology
Richard A. Deitrich	PHCL 7605, UCHSC	Ethics in Research
John K. Hewitt	PSYC 5242, UCB	Biometrical Methods in Behavioral Genetics
Thomas E. Johnson	PSYC 7102, UCB	Behavioral Genetics
Bruce F. Pennington	PSYC 4525, DU	Developmental Neuropsychology
Michael C. Stallings	PSYC 5112, UCB	Concepts in Behavior Genetics QTL Methodology
Boris Tabakoff	DSBS 6600, UCHSC	Dental Pharmacology
	PHCL 7600, UCHSC	Frontiers in Pharmacology
	PHCL 7605, UCHSC	Ethics in Research
Jeanne M. Wehner	PSYC 5102, UCB	Behavioral Genetics
Erik Willcutt	PSYC 3313, UCB	Psychopathology

Spring 2002

Michael D. Breed	EPOB 3240, UCB	Animal Behavior
Gregory Carey	PSYC 5741, UCB	General Statistics
Richard Olson	PSYC 4521, UCB	Critical Thinking: Genes and Environment
	PSYC 4001, UCB	Honors Seminar
Toni Smolen	PSYC 5112, UCB	Concepts in Behavioral Genetics
Michael C. Stallings	PSYC 3102, UCB	Behavioral Genetics
	PSYC 5112, UCB	Concepts in Behavioral Genetics
Boris Tabakoff	PHCL 6000, UCHSC	Medical Pharmacology
	PHCL 7620, UCHSC	Graduate Pharmacology
Jeanne M. Wehner	PSYC 7012, UCB	Research in Behavioral Genetics
Erik Willcutt	PSYC 3313, UCB	Psychopathology

Summer 2002

Michael D. Breed	EPOB 4630, UCB	Field Techniques in Environmental Science
Gregory Carey	PSYCH 3102, UCB	Behavioral Genetics

Colloquia and Informal Talks

Fall 2001

Avshalom Caspi (Professor, Social, Genetic, Developmental Psychiatry Research Centre, Institute of Psychiatry, London, United Kingdom and Department of Psychology, University of Wisconsin-Madison). The Child is the Father of the Man: Personality Development from Childhood to Adulthood.

Marissa Ehringer (Postdoctoral Fellow, University of Colorado, Center on Antisocial Drug Dependence, Institute for Behavioral Genetics). Identification of Gene Coding Variants in Alcohol-Related QTLs.

Soo Rhee (IBG Research Associate, University of Colorado, Boulder, Colorado). Examining the Causes of Comorbidity: Current Approaches Using Family Studies and Future Directions.

Spring 2002

Tracy Bale (Postdoctoral Fellow, Peptide Biology Laboratories, Salk Institute, La Jolla, CA). The Role of Corticotropin-Releasing Factor Receptors in Anxiety and Stress. (co-sponsored with the Department of Molecular, Cellular and Developmental Biology)

Alan Baddeley (Professor of Experimental Psychology, University of Bristol, United Kingdom). What's New in Working Memory? (co-sponsored with Department of Psychology)

Massimiliano Bonafé (Visiting Scholar, MD and Assistant Professor of Experimental Pathology, University of Bologna, Italy). What Centenarians Tell Us about the Genetics of Longevity.

James Cypser (Graduate Student, Institute for Behavioral Genetics, University of Colorado, Boulder, Colorado). Characterization and Genetics of Induced Stress Resistance and Life Extension in *C. elegans*.

Jonathan Flint (Wellcome Trust Senior Clinical Fellow, Wellcome Trust Centre for Human Genetics, University of Oxford, UK). Molecular Genetic Approaches to Psychiatric Disease. (co-sponsored with the Department of Molecular, Cellular and Developmental Biology)

Pauline Gee (President and CEO, Xenometrics, Inc., a Division of Discovery Partners International, Inc.). Alternative Careers: Transitioning from Academia to Industry.

Hui-Fu Guo (Postdoctoral Fellow, Cold Spring Harbor Laboratory, New York). Essential Role of Neuro-fibromatosis 1-Regulated Pathway for *Drosophila* Learning. (co-sponsored with the Department of Molecular, Cellular and Developmental Biology)

Alison Shaw (Professor of Human Sciences, Brunel University, Middlesex, United Kingdom). Migration and Consanguinity Marriage Trends Among British Pakistanis. (co-sponsored with Department of Anthropology)

Jerry Stitzel (Assistant Research Scientist, Department of Pharmacology, University of Michigan Medical School, Ann Arbor). From Genome to Phenome: Identifying Molecular Variations That Underlie Heritable Phenotypic Diversity in Mice. (co-sponsored with the Department of Molecular, Cellular and Developmental Biology)

Anatoli Yashin (Head of the Laboratory of Advanced Statistical Methods, Max Plank Institute of Demographic Research, Rostock, Germany). Survival Models in Genetic Epidemiology: The Results of Genetic Studies of Human Aging and Longevity Using Data from Three Scandinavian Twin Registers.

Sige Zou (Postdoctoral Fellow, Howard Hughes Medical Institute, University of California, San Francisco). A Genomic Approach Toward Understanding Longevity in *Drosophila melanogaster*. (co-sponsored with the Department of Molecular, Cellular and Developmental Biology)

IBG Colloquium. Guest speaker Dr. Avsholam Caspi.

Research and Administrative Staff

Research

Lindly Alston
Angela Austin
Sara Bailey
Matthew Battaglia
Mary Beeson
Helen Bishop
Todd Bizzigotti
Adrienne Blackwood
Bryan Blakely
Alexander Boal
Stephanie Bogott
Robert Brown
James Campbell
Phyllis Carosone-Link
Nomita Chhabildas
Leza Clymer
Rachael Cole
Mark Conner
Justina Cooley
Kimberly Corley
Helen Datta
Patricia Davis
Sarah de Castro
Michele DeFilippis
Brendan DePue
Antonio DiLeo
Athena Dodd
Linda Drullinger
Barbara Elliott
Katherine Elliott
Margaret Fatovic
David Fennimore
Danelle Ferguson
Virginia Fonte
Kari Gilmore
Lena Gordon
James Goss
Kari Gottschling
Andrew Gross
Terry Grupp
Jessica Hall
Jacqueline Hulslander
Scott Hutton
George Jayne
Melissa Jimenez
Anne Johnson
Elizabeth Johnson-Wold
Nicole Kandel
Billy Keith
Corey King
Colin Larson
Amy Ledbetter
Elizabeth Legg
Caren Lowe
Christine Martin
Brook McClintic
Chinatsu McGeary
Natalie Meinerz
Jill Miyamoto
Ryan Morrow
Kelsy Moses
Christina Nelson-Goens
Cyrus Peterson
Erik Peterson
Nancy Phares-Zook
Sally-Ann Rhea
Julia Rifkin
Taylor Roy
Amy Rudolph
Sherri Ruggiero
Daniel Ryan
Scott Sabella
Jerome Salazar
Elizabeth Siewert
Isaac Sisneros
Abigail Smith
Justin Springett
Tara Stahla
Gretchen Stein
Andrew Taft
Pat Tedesco
Jacey Tramutt
Ingrid Ullring
William Van Morter
Nathan Vellinga
Angela Villella
Satori Waddle
Laurel Wade
Corrine Wright
Jerald Young
Jean Yu
Jennifer Ziemba

Student Hourly

Sierra Atkinson
Armando Avila
Kelsy Lee Cain
Jerod Cox
Kevin Cox
Robert Curtis
Jennifer Drapeau
Victoria Dubiel
Margaret Enion
Julie Ernisse
Jaclyn Francese
Vishwas Ganesan
Anthony Giordano
Sybil Greenberg
Lesley Hueman
Donald Hyppolite
Jason Keller
Nathan King
Eric Laudenslager
Sena Hitt-Laustsen
Christopher Leeds
Michael Luckow
Sarah Magill
Gwendolyn Marks
Erin Marshall
Tristan McClure-Begley
Jessica Michael
Lauren Milner
Brigid Moriarty
Sarah Nakata
Erin Nix
Isaac Newland
Zach Noteman
Trent Paradis
Theodore Pokrywka
Benjamin Pressley
Jaime Rogers
Renee Schmitz
Amit Singh
Tricia Torgensen
Chelsea Trinka
Ari Van Schilfgaarde
Eric Wagner
Sarah Walters
Mark Windland

Administrative

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

Publications

July 1, 2001–June 30, 2002

Adams, C.E., Stitzel, J.A., Collins, A.C., & Freedman, R. (2001). α7-Nicotinic receptor expression and the anatomical organization of hippocampal interneurons. *Brain Research*, *922*, 180-190.

Adams, C.E., Stitzel, J.A., Collins, A.C., & Freedman, R. (2001). α7-Nicotinic receptor expression and the anatomical organization of hippocampal interneurons. *Society for Neuroscience Abstracts, 27,* Program No. 145.3. (Abstract)

Balogh, S.A., Owens, J.C., Butt, C.M., Labarca, C., Lester, H.A., Picciotto, M.R., Collins, A.C., & Wehner, J.M. (2002). Nicotine and ethanol-induced hypothermia in α4 and β2 nicotinic receptor subunit mutant mice. *Alcoholism: Clinical and Experimental Research, 26*, 142A. (Abstract)

Balogh, S.A., & Wehner, J.M. (2001). Long-term contextual fear memories in C57 and DBA mice. *Society for Neuroscience Abstracts, 27,* Program No. 955.13. (Abstract)

Bennett, B., Beeson, M., Gordon, L., & Johnson, T.E. (2002). Reciprocal congenics defining individual quantitative trait loci for sedative/hypnotic sensitivity to ethanol. *Alcoholism: Clinical and Experimental Research, 26,* 149-157.

Beresford, C.A., Siewert, E., Wilson, S., Corley, R., & Beresford, T. (2001). Correlated eating and drinking behavior in adult females: Does the relationship change? *Alcoholism, Clinical and Experimental Research, 25,* 138A. (Abstract)

Beresford, C.A., Siewert, E., Wilson, S., Corley, R., & Beresford, T. (2001). Eating behavior correlates with drinking behavior in adolescent females. *Alcoholism, Clinical and Experimental Research, 25*, 86A. (Abstract)

Bhave, S.V., Kirstein, S., Wu, P.H., Hoffman, P.L., & Tabakoff, B. (2002). Gene expression patterns in selectively bred lines of mice differing in acute functional tolerance to ethanol. *Alcoholism: Clinical and Experimental Research, 26*, 54A. (Abstract)

Bhave, S.V., Tabakoff, B., & Hoffman, P.L. (2001). Acute and chronic effects of ethanol on apoptosis in cerebellar granule neurons: Signal transduction pathways. *Alcoholism: Clinical and Experimental Research, 25*, 31A. (Abstract)

Bhave, S.V., Yoshimura, M., Hoffman, P.L., & Tabakoff, B. (2001). DNA microarray analysis of gene expression in brains of selected lines of mice and transgenic mice that differ in responses to ethanol. *Alcoholism: Clinical and Experimental Research, 25,* 71A. (Abstract)

Bhave, S.V., Yoshimura, M., Wu, P.H., Hoffman, P.L., & Tabakoff, B. (2002). Overexpression of adenylyl cyclase Type VII in the brain and development of tolerance to ethanol and drugs of abuse. *Alcoholism: Clinical and Experimental Research, 26,* 54A. (Abstract)

Blumenthal, T., Evans, D., Link, C.D., Guffanti, A., Lawson, D., Thierry-Mieg, J., Thierry-Mieg, D., Chiu, W.L., Duke, K., Kiraly, M., & Kim, S.K. (2002). A global analysis of *Caenorhabditis elegan*s operons. *Nature*, 417, 851-854.

Bowers, B.J., Elliott, K.J., & Wehner, J.M. (2001). Differential sensitivity to the anxiolytic effects of ethanol and flunitrazepam in PKCγ null mutant mice. *Pharmacology, Biochemistry and Behavior, 69,* 99-110.

Bowers, B.J., & Wehner, J.M. (2001). Ethanol consumption and behavioral impulsivity are increased in PKCγ null mutant mice. *Journal of Neuroscience*, *21*, RC180 (1-5).

Bryan, A.D., Hutchison, K.E., & Smolen, A. (2001). Indirect effects of the DRD4 VNTR polymorphism on sexual desire. *Behavior Genetics, 31,* 448. (Abstract)

Butov, A.A., Johnson, T.E., Cypser, J.R., Sannikov, I.A., Volkov, M.A., Sehl, M.E., & Yashin, A.I. (2001). Hormesis and debilitation effects in stress experiments using the nematode worm *C. elegans*: The model of balance between cell damage and HSP levels. *Experimental Gerontology, 37,* 57-66.

Butt, C.M., Hutton, S.R., King, N.M., Balogh, S.A., Owens, J.C., Marks, M.J., & Collins, A.C. (2002). Potential association of a nicotinic receptor polymorphism with mouse strain differences in ethanol sensitivity and withdrawal. *Alcoholism: Clinical and Experimental Research, 26,* 100A. (Abstract)

Butt, C.M., Pauly, J.R., Wilkins, L.H., Dwoskin, L.P., & Debski, E.A. (2001). Pharmacology, distribution, and development of muscarinic acetylcholine receptor subtypes in the optic tectum of *Rana pipiens*. *Neuroscience*, 104, 161-179.

Butt, C.M., Zhao, B., Duncan, M.J., & Debski, E.A. (2002). Sculpting the visual map: The distribution and function of serotonin-1a and serotonin-1b receptors in the optic tectum of the frog. *Brain Research, 931,* 21-31.

Cardoso-Martins, C., & Pennington, B.F. (2001). What is the contribution of rapid serial naming to reading and spelling ability? Evidence from children and adolescents with and without reading difficulties. *Psicologia, Reflexão e Crítica, 14,* 387-397.

Carey, G. (2002). *Human genetics for the social sciences*. Thousand Oaks, CA: Sage Publications.

Carpenter, M., Pennington, B.F., & Rogers, S.J. (2001). Understanding of other's intentions in children with autism. *Journal of Autism and Developmental Disorders, 31,* 589-599.

Chhabildas, N.A., Pennington, B.F., & Willcutt, E.G. (2001). A comparison of the neuropsychological profiles of the DSM-IV subtypes of ADHD. *Journal of Abnormal Child Psychology, 29,* 529-540.

Collins, A.C., Marks, M.J., McCallum, S.E., Peterson, C.G., Beaudet, A.L., & Paylor, R. (2001). High and low-affinity [^{3}H]epibatidine binding reveals differences in nAChR upregulation following chronic nicotine treatment in beta2 null mutant mice. *Society for Neuroscience Abstracts, 27,* Program No. 807.3. (Abstract)

Compton, D.L., Davis, C.J., DeFries, J.C., Gayán, J., & Olson, R.K. (2001). Genetic and environmental influences on reading and RAN: An overview of results from the Colorado Twin

Study. In M. Wolf (Ed.), *Dyslexia, fluency, and the brain* (pp. 277-303). Timonium, MD: York Press.

Compton, D.L., DeFries, J.C., & Olson, R.K. (2001). Are RAN- and phonological awareness-deficits additive in children with reading disabilities? *Dyslexia*, 7, 125-149.

Conigrave, K.M., Degenhardt, L., Whitfield, J.B., Saunders, J.B., Helander, A., & Tabakoff, B. on behalf of the WHO/ISBRA study group (2002). CDT, GGT and AST as markers of alcohol use: The WHO/ISBRA collaborative project. *Alcoholism: Clinical and Experimental Research, 26,* 332-339.

Cross, R.J., Gayán, J., DeFries, J.C., & Olson, R.K. (2001). Differential genetic etiology of reading disability as a function of processing speed. *Behavior Genetics, 31,* 450. (Abstract)

Cypser, J.R., & Johnson, T.E. (2002). Multiple stressors in *Caenorhabditis elegans* induce stress hormesis and extended longevity. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences, 57*, B109-B114.

Davis, C.J., Gayán, J., Knopik, V.S., Smith, S.D., Cardon, L.R., Pennington, B.F., Olson, R.K., & DeFries, J.C. (2001). Etiology of reading difficulties and rapid naming: The Colorado Twin Study of Reading Disability. *Behavior Genetics, 31,* 625-635.

Davis, C.J., Gayán, J., Knopik, V.S., Smith, S.D., Cardon, L.R., Pennington, B.F., Olson, R.K., & DeFries, J.C. (2001). Reading difficulties and rapid naming: Bivariate twin and genetic linkage analyses. *Behavior Genetics, 31,* 451. (Abstract)

Davis, C.J., Knopik, V.S., Olson, R.K., Wadsworth, S.J., & DeFries, J.C. (2001). Genetic and environmental influences on rapid naming and reading ability: A twin study. *Annals of Dyslexia, 51,* 231-247.

Deffenbacher, K.E., Hoover, D.M., Kenyon, J.B., Olson, R.K., DeFries, J.C., & Smith, S.D. (2001). Mutation screening of the SynGAP gene in patients with dyslexia. *American Journal of Human Genetics, 69,* 538. (Abstract)

Dermine, J.F., Duclos, S., Garin, J., St-Louis, F., Rea, S., Parton, R.G., & Desjardins, M. (2001). Flotillin-1-enriched lipid raft domains accumulate on maturing phagosomes. *Journal of Biological Chemistry, 276,* 18507-18512.

Dobelis, P., Collins, A.C., & Dunwiddie, T.V. (2001). Effects of nicotinic cholinergic transmission on seizure sensitivity. *Society for Neuroscience Abstracts, 27,* Program No. 377.3. (Abstract)

Draski, L.J., Bice, P.J., & Deitrich, R.A. (2001). Developmental alterations of ethanol sensitivity in selectively bred high and low alcohol sensitive rats. *Pharmacology, Biochemistry and Behavior, 70,* 387-396.

Dukat, M., Damaj, I.M., Young, R., Vann, R., Collins, A.C., Marks, M.J., Martin, B.R., & Glennon, R.A. (2002). Functional diversity among 5-substituted nicotine analogs; in vitro and in vivo investigations. *European Journal of Pharmacology, 435,* 171-180.

Ehringer, M.A., Thompson, J., Conroy, O., Xu, Y., Yang, F., Canniff, J., Beeson, M., Gordon, L., Bennett, B., Johnson, T.E., & Sikela, J.M. (2001). High-throughput sequence identification of gene coding variants within alcohol-related QTLs. *Mammalian Genome, 12,* 657-663.

Eisenman, L.M., Donovan, H.S., & Johnson, T.E. (2001). Effect of alcohol on c-fos expression in hypothalamus of LS and SS mice. *Society for Neuroscience Abstracts, 27,* Program No. 572.6. (Abstract)

Erwin, V.G., Gehle, V.M., Davidson, K.L., & Radcliffe, R.A. (2001). Correlations and common quantitative trait loci between neurotensin receptor density and hypnotic sensitivity to ethanol. *Alcoholism: Clinical and Experimental Research, 25,* 1699-1707.

Erwin, V.G., Radcliffe, R.A., & Deitrich, R.A. (2001). Neurotensin levels in specific brain regions and hypnotic sensitivity to ethanol and pentobarbital as a function of time after haloperidol administration in selectively-bred rat lines. *Journal of Pharmacology and Experimental Therapeutics, 29,* 698-704.

Fisher, S.E., Francks, C., Marlow, A.J., MacPhie, L., Newbery, D.F., Cardon, L.R., Ishikawa-Brush, Y., Richardson, A.J., Talcott, J.B., Gayán, J., Olson, R.K., Pennington, B.F., Smith, S.D., DeFries, J.C., Stein, J.F., & Monaco, A.P. (2002). Independent genome-wide scans identify a chromosome 18 quantitative-trait locus influencing dyslexia. *Nature Genetics, 30,* 86-91.

Fonck, C.I., Damaj, M.I., Deshpande, P., Bowers, B.J., Wehner, J.M., Nashmi, R., Khakh, B.S., Schwarz, J., Lester, H.A., & Labarca, C. (2001). Knock-in mice carrying hypersensitive α4 nicotinic receptors: Nicotine responses. *Society for Neuroscience Abstracts, 27,* Program No. 808.6. (Abstract)

Francks, C., Fisher, S.E., Olson, R.K., Pennington, B.F., Smith, S.D., DeFries, J.C., & Monaco, A.P. (2002). Fine mapping of the chromosome 2p12-16 dyslexia susceptibility locus: Quantitative association analysis and positional candidate genes SEMA4F and OTX1. *Psychiatric Genetics, 12,* 35-41.

Gayán, J., & Olson, R.K. (2001). Genetic and environmental influences on orthographic and phonological skills in children with reading disabilities. *Developmental Neuropsychology, 20,* 487-511.

Gelhorn, H.L., Stallings, M.C., Young, S.E., Corley, R.P., Hewitt, J.K., & Crowley, T.J. (2002). Substance use patterns and antisocial behavior in clinical family pedigrees. *Drug and Alcohol Dependence, 66,* S63. (Abstract)

Grady, S.R., McCallum, S.E., Murphy, K.L., McIntosh, J.M., Beaudet, A.L., Paylor, R., Marks, M.J., & Collins, A.C. (2001). Effects of the nicotinic acetylcholine receptor α4 subunit null mutation on synaptosomal neurotransmitter release. *Nicotine and Tobacco Research*. (Abstract)

Grady, S.R., Murphy, K.L., Cao, J., Marks, M.J., McIntosh, J.M., & Collins, A.C. (2002). Characterization of nicotinic agonist-induced [^{3}H]dopamine release from synaptosomes prepared from four mouse brain regions. *Journal of Pharmacology and Experimental Therapeutics, 301,* 651-660.

Grady, S.R., Murphy, K.L., Marks, M.J., & Collins, A.C. (2001). Uptake and release of [^{3}H]-dopamine from synaptosomes of mouse frontal cortex, striatum, nucleus accumbens, and olfactory tubercle. *Society for Neuroscience Abstracts, 27,* Program No. 377.12. (Abstract)

GuhaThakurta, D., Palomar, L., Stormo, G.D., Tedesco, P., Johnson, T.E., Walker, D.W., Lithgow, G., Kim, S., & Link,

C.D. (2002). Identification of a novel cis-regulatory element involved in the heat shock response in *Caenorhabditis elegans* using microarray gene expression and computational methods. *Genome Research, 12,* 701-712.

Heiman, N., Stallings, M.C., Hewitt, J.K., & Hofer, S.M. (2001). Investigating age differences in the genetic and environmental structure of the TPQ in later adulthood. *Behavior Genetics, 31,* 454-455. (Abstract)

Hekimi, S., Benard, C., Branicky, R., Burgess, J., Hihi, A.K., & Rea, S. (2001). Why only time will tell. *Mechanisms of Ageing and Development, 122,* 571-594.

Henderson, S.T., & Johnson, T.E. (2001). daf-16 integrates developmental and environmental inputs to mediate aging in the nematode *Caenorhabditis elegans*. *Current Biology, 11,* 1975-1980.

Hopfer, C., Stallings, M.C., Crowley, T.J., & Hewitt, J.K. (2002). Family transmission of marijuana use, abuse, and dependence. *Drug and Alcohol Dependence, 66,* S81. (Abstract)

Hopfer, C.J., Stallings, M.C., & Hewitt, J.K. (2001). Common genetic and environmental vulnerability for alcohol and tobacco use in a volunteer sample of older female twins. *Journal of Studies on Alcohol, 62,* 717-723.

Hutchison, K.E., LaChance, H., Niaura, R., Bryan, A.D., & Smolen, A. (2001). The DRD4 VNTR polymorphism influences reactivity to smoking cues. *Behavior Genetics, 31,* 455. (Abstract)

Hutchison, K.E., LaChance, H., Niaura, R., Bryan, A.D., & Smolen, A. (2002). The DRD4 VNTR polymorphism influences reactivity to smoking cues. *Journal of Abnormal Psycohology, 11,* 134-143.

Hutchison, K.E., McGeary, J., Smolen, A., Bryan, A.D., & Swift, R.M. (2002). The DRD4 VNTR polymorphism moderates craving after alcohol consumption. *Health Psychology, 21,* 139-146.

Johnson, T.E., Wu, D., Tedesco, P., Dames, S., & Vaupel, J.W. (2001). Age-specific demographic profiles of longevity mutants in *Caenorhabditis elegans* show segmental effects. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences, 56,* B331-B339.

Kaplan, D.E., Gayán, J., Ahn, J., Won, T.-W., Pauls, D., Olson, R.K., DeFries, J.C., Wood, F., Pennington, B., Page, G., Smith, S.D., & Gruen, J.R. (2002). Evidence for linkage and association with reading disability, on 6P21.3-22. *American Journal of Human Genetics, 70,* 1287-1298.

Kodata, Y., & Tabakoff, B. (2001). Search for ethanol-responsive domains in adenylyl cyclase using a chimeric approach. *Alcoholism: Clinical and Experimental Research, 25,* 59A. (Abstract)

Krystal, J.H., & Tabakoff, B. (2002). Ethanol abuse, dependence, and withdrawal: Neurobiology and clinical implications. In K.L. Davis, D. Charney, J.T. Coyle, & C. Nemeroff (Eds.), *Neuropsychopharmacology: The fifth generation of progress* (pp. 1425-1443). Philadelphia: Lippincott, Williams & Wilkins.

Lessem, J.M., Cherny, S.S., Abecasis, G.R., Sham, P.C., & Purcell, S. (2001). An overview of regression methods of linkage analysis in selected samples. *Behavior Genetics, 31,* 458. (Abstract)

Lessem, J.M., Stallings, M.C., Young, S.E., Hewitt, J.K., & Crowley, T.J. (2002). Family transmission of alcohol use, abuse, and dependence in the CADD sample. *Drug and Alcohol Dependence, 66,* S101. (Abstract)

Link, C.D. (2001). Transgenic invertebrate models of age-associated neurodegenerative diseases. *Mechanisms of Ageing and Development, 122*, 1639-1649.

Link, C.D., & Johnson, C.J. (2002). Reporter transgenes for the study of oxidant stress in *Caenorhabditis elegans*. *Methods in Enzymology, 352*, 497-505.

Luckey, S., & Petersen, D.R. (2001). Activation of Kupffer cells during the course of carbon tetrachloride-induced liver injury and fibrosis in rats. *Experimental and Molecular Pathology, 71,* 226-240.

Luckey, S.W., Vasiliou, V., & Petersen, D.R. (2001). 4-Hydroxynonenal inhibits IL-6 production in rat Kupffer cells. *The Toxicologist, 55,* #204. (Abstract)

Malkinson, A.M., Radcliffe, R.A., & Bauer, A.K. (2002). Quantitative trait locus (QTL) mapping of susceptibilities to butylated hydroxytoluene (BHT)-induced lung tumor promotion and pulmonary inflammation in CXB mice. *Carcinogenesis, 23,* 411-417.

Marks, M.J., & Collins, A.C. (2001). Mouse models to evaluate genetic influences on responses to nicotine. In E.D. Levin (Ed.), *Frontiers and methods in neuroscience series: Nicotinic receptors in the nervous system* (pp. 143-166). New York: CRC Press.

Marks, M.J., Grady, S.R., McCallum, S.E., Peterson, C.G., Whiteaker, P., McIntosh, J.M., Beaudet, A.L., Paylor, R., & Collins, A.C. (2001). The beta4 null mutation differentially affects biochemical measures of nicotinic receptor function. *Society for Neuroscience Abstracts, 27,* Program No. 808.5. (Abstract)

Marks, M.J., Whiteaker, P., Grady, S.R., Picciotto, M.R., McIntosh, J.M., & Collins, A.C. (2002). Characterization of [^{125}I]epibatidine binding and nicotine agonist-mediated 86Rb+ efflux in interpeduncular nucleus and inferior colliculus of β2 null mutant mice. *Journal of Neurochemistry, 81,* 1102-1115.

Martinez, L., & Tabakoff, B. on behalf of the WHO/ ISBRA Collaborative Study Investigators (2001). Microsatellite polymorphism of the adenylyl cyclase type IX gene and association with alcohol-related traits in the WHO/ISBRA Study subjects. *Alcoholism: Clinical and Experimental Research, 25,* 69A. (Abstract)

Martinez, L., & Tabakoff, B. on behalf of the WHO/ ISBRA Collaborative Study Investigators (2002). Genetic and functional association of adenylyl cyclase (AC7) with alcoholism and depression. *Alcoholism: Clinical and Experimental Research, 26,* 8A. (Abstract)

Martinic, M. (Prepared on behalf of symposium participants: Diamond, I., Grant, M., Greenfield, T., Hacker, G., Lewis, D.,

Nadeau, L., Riley, E., & Tabakoff, B.) (2001). The research community and the private sector: A hands-on or hands-off relationship? *Alcoholism: Clinical and Experimental Research, 25*, 1801-1804.

McBride, W.J., Li, T.K., Deitrich, R.A., Zimatkin, S., Smith, B.R., & Rodd-Henrichs, Z.A. (2002). Involvement of acetaldehyde in alcohol addiction. *Alcoholism: Clinical and Experimental Research, 26*, 114-119.

McCallum, S.E., Hutton, S.R., & Collins, A.C. (2001). Nicotine-stimulated [^{3}H]GABA release from mouse thalamic synaptosomes is modulated by ethanol. *Society for Neuroscience Abstracts, 27*, Program No. 377.4. (Abstract)

Mihalek, R.M., Bowers, B.J., Wehner, J.M., Kralic, J.E., VanDoren, M.J., Morrow, A.L., & Homanics, G.E. (2001). Neurosteroid resistant $GABA_A$-receptor δ subunit knockout mice also have multiple defects in behavioral responses to ethanol. *Alcoholism: Clinical and Experimental Research, 25*, 1708-1718.

Mogg, A.J., Whiteaker, P., McIntosh, J.M., Marks, M., Collins, A.C., & Wonnacott, S. (2002). Methyllycaconitine is a potent antagonist of α-conotoxin-MII-sensitive presynaptic nicotinic acetylcholine receptors in rat striatum. *Journal of Pharmacology and Experimental Therapeutics, 302,* 197-204.

Murakami, S., & Johnson, T.E. (2001). The OLD-1 positive regulator of longevity and stress resistance is under DAF-16 regulation in *Caenorhabditis elegans*. *Current Biology, 11,* 1517-1523.

Nelson, E.J., Debeer, T., & Tabakoff, B. (2001). Functional and structural characteristics of an ETOH-sensitive cyclase. *Alcoholism: Clinical and Experimental Research, 25,* 106A. (Abstract)

Nelson, E.J., & Tabakoff, B. (2002). Computational and biochemical analysis of the interaction between the ethanol-sensitive Type VII adenylyl cyclase (AC7) and PKC delta. *Alcoholism: Clinical and Experimental Research, 26,* 11A. (Abstract)

Nunley, K., Bhave, S.V., Tabakoff, B., & Hoffman, P.L. (2001). Altered cellular localization of NMDA receptor subunits after chronic ethanol exposure. *Alcoholism: Clinical and Experimental Research, 25*, 8A. (Abstract)

Olson, R.K., & Datta, H. (2002). Visual-temporal processing in reading-disabled and normal twins. *Reading and Writing, 15,* 127-149.

Owens, J.C., Balogh, S.A., Butt, C.M., Labarca, C., Lester, H.A., Picciotto, M.R., Wehner, J.M., & Collins, A.C. (2002). The effects of ethanol on acoustic startle are modulated by the neuronal nicotinic receptor α4 subunit. *Alcoholism: Clinical and Experimental Research, 26*,142A. (Abstract)

Owens, J.C., Bennett, B., & Johnson, T.E. (2001). Differential responses to ethanol-induced activity and ethanol-induced hypothermia in the ILS.ISS.Lore congenics. *Society for Neuroscience Abstracts, 27,* Program No. 572.14. (Abstract)

Owens, J.C., Bennett, B., & Johnson, T.E. (2001). Evidence that the Lore-1 region specifies ethanol-induced activation in addition to sedative/hypnotic sensitivity to ethanol. *Alcoholism: Clinical and Experimental Research, 25,* 1551-1557.

Pearce, A.N., Huang, Z.-Y., & Breed, M.D. (2001). Genetic and endocrine correlations of aggressive behavior in honey bees. *Journal of Insect Physiology, 47,* 1243-1247.

Pennington, B.F. (2001). Genetic methods. In C.A. Nelson & M. Luciana (Eds.), *The handbook of developmental cognitive neuroscience* (pp. 149-158). Cambridge, MA: MIT Press.

Pennington, B.F. (2002). *The development of psychopathology: Nature and nurture*. New York: Guilford Press.

Pennington, B.F., Cardoso-Martins, C., Green, P.A., & Lefly, D.L. (2001). Comparing the phonological and double deficit hypotheses for developmental dyslexia. *Reading and Writing: An Interdisciplinary Journal, 14*, 707-755.

Pennington, B.F., & Lefly, D.L. (2001). Early reading development in children at family risk for dyslexia. *Child Development, 72,* 816-833.

Petersen, D.R., Sampey, B.P., Ronis, M.J., & Badger, T.M. (2001). Immunohistochemical characterization of hepatic 4-HNE and MDA-adducted proteins following chronic intragastric ethanol administration. *The Toxicologist, 55*, #1615. (Abstract)

Petrakis, I.L., Tabakoff, B., & Krystal, J.H. (2001). Alcohol abuse and dependence: Neurobiology and clinical implications. *The Economics of Neuroscience, 3,* 29-36.

Piper, J.T., Luckey, S.W., & Petersen, D.R. (2001). Mechanisms of 4-HNE adduction using model polypeptides. *The Toxicologist, 55,* #212. (Abstract)

Prescott, C.A., Cross, R., Horn, J.L., & Kendler, K.S. (2001). Sources of covariance between alcoholism and motivations for drinking. *Behavior Genetics, 31,* 465. (Abstract)

Rabbani, M., & Tabakoff, B. (2001). Chronic ethanol treatment reduces adenylyl cyclase activity in human erythroleukemia cells. *European Journal of Pharmacology, 430,* 19-23.

Rea, S. (2001). CLK-1/Coq7p is a DMQ mono-oxygenase and a new member of the di-iron carboxylate protein family. *FEBS Letters, 509*, 389-394.

Reichard, J.F., Petersen, D.R., & Luckey, S.W. (2001). 4-HNE increases mRNA levels of enzymes responsible for maintaining redox equilibrium in rat hepatocytes. *The Toxicologist, 55,* #211. (Abstract)

Rhea, S.A., & Corley, R.P. (2001). Family history influences on adopted adolescents' substance experimentation. *Behavior Genetics, 31,* 466. (Abstract)

Rhee, S.H., Feigon, S.A., Bar, J.L., Hadeishi, Y., & Waldman, I.D. (2001). Behavior genetics in psychopathology. In H.E. Adams & P.B. Sutker (Eds.), *Comprehensive handbook of psychopathology* (3rd ed, pp. 53-84). New York: Plenum.

Rhee, S.H., Hewitt, J.K., Young, S.E., Corley, R.P., Crowley, T.J., & Stallings, M.C. (2001). The etiology of comorbidity between substance dependence and conduct disorder in adolescents. *Behavior Genetics, 31*, 466-467. (Abstract)

Rhee, S.H., Stallings, M.C., Corley, R.P., Young, S.E., Crowley, T.J., & Hewitt, J.K. (2002). Test of alternative hypotheses

explaining the relation between marijuana use and other illicit drug initiation in adolescents. *Drug and Alcohol Dependence, 66,* S145. (Abstract)

Rhee, S.H., & Waldman, I.D. (2002). Genetic and environmental influences on antisocial behavior: A meta-analysis of twin and adoption studies. *Psychological Bulletin, 128,* 490-529.

Rhee, S.H., Waldman, I.D., Hay, D.A., & Levy, F. (2001). Aetiology of the sex difference in the prevalence of DSM-III-R attention-deficit hyperactivity disorder: A comparison of two models. In F. Levy & D.A. Hay (Eds.), *Attention, genes, and ADHD* (pp. 139-156). East Sussex, England: Brunner-Routledge.

Sakai, J., Stallings, M.C., Mikulich, S.K., Corley, R.P., Young, S.E., & Crowley, T.J. (2002). Family studies of substance dependence and antisocial personality disorder: A potential selection bias. *Drug and Alcohol Dependence, 66,* S154. (Abstract)

Schmitz, S. (2001). Attention problems and emotionality at ages 7 and 12. *Behavior Genetics, 31,* 468. (Abstract)

Schmitz, S., & Mrazek, D.A. (2001). Genetic and environmental influences on the associations between attention problems and other problem behaviors. *Twin Research, 4,* 453-458.

Shah, I., Tabakoff, B., Bhave, S., Taylor, R., Phang, T., Gabow, A., Cohen, K., Dolbey, A., Outteridge, D., Acquaah-Mensah, G., & Hunter, L. (2002). Interactive workbench for integrative neuroscience research on alcoholism. *Alcoholism: Clinical and Experimental Research, 26,* 56A. (Abstract)

Simon, J.A., Keenan, J.M., Pennington, B.F., Taylor, A.K., & Hagerman, R.J. (2001). Discourse processing in women with Fragile X syndrome: Evidence for a deficit establishing coherence. *Cognitive Neuropsychology, 18,* 1-18.

Smith, S.D., Gilger, J.W., & Pennington, B.F. (2002). Dyslexia and other specific learning disorders. In D.L. Rimoin, J.M. Conner, & R.E. Pyeritz (Eds.), *Emery and Rimoin's principles and practice of medical genetics* (4th ed., pp. 2827-2865). New York: Churchill Livingstone.

Smith, S.D., Kelley, P.M., Askew, J.W., Hoover, D.M., Deffenbacher, K.E., Gayán, J., Brower, A., & Olson, R.K. (2001). Reading disability and chromosome 6p21.3: Evaluation of MOG as a candidate gene. *Journal of Learning Disabilities, 34*, 512-519.

Smith, A.M., Powers, P.A., Gregg, R.G., & Wehner, J.M. (2001). A role for the β_1 subunit of neuronal calcium channels in anxiety and ataxia. *Society for Neuroscience Abstracts, 27*, Program No. 151.24. (Abstract)

Smith, A.M., & Wehner, J.M. (2002). Aniracetam improves contextual fear conditioning and increases hippocampal γ-PKC activation in DBA/2J mice. *Hippocampus*, *12*, 76-85.

Snell, L.D., Glanz, J., Hoffman, P.L., & Tabakoff, B. (2002). Effects of smoking, gender and alcohol dependence on platelet monoamine oxidase-B: Activity, protein and affinity labeling measurements. *Alcoholism: Clinical and Experimental Research, 26*, 52A. (Abstract)

Snell, L.D., Hoffman, P.L., & Tabakoff, B. (2001). Platelet monoamine oxidase activity: Associations with alcohol dependence, smoking and other measures in the WHO/ISBRA Collaborative Study. *Alcoholism: Clinical and Experimental Research, 25*, 86A. (Abstract)

Soriano, B., Diener, K., Gaydos, J., Johnson, G., & Tabakoff, B. (2002). Gene array expression core for research on alcoholism. *Alcoholism: Clinical and Experimental Research, 26*, 56A. (Abstract)

Stallings, M.C., Corley, R.P., Hewitt, J.K., Krauter, K.S., Lessem, J.M., Mikulich, S.K., Rhee, S.H., Smolen, A., Young, S.E., & Crowley, T.J. (2002). A genome-wide search for quantitative trait loci influencing substance dependence vulnerability. *Drug and Alcohol Dependence, 66*, S170. (Abstract)

Stallings, M.C., Hewitt, J.K., Lessem, J.M., Young, S.E., Corley, R.P., Mikulich, S.K., & Crowley, T.J. (2001). Modeling the familial transmission of alcohol dependence symptoms in clinical and control family pedigrees. *Behavior Genetics, 31*, 470. (Abstract)

Stevens, K.E., Bullock, A.E., & Collins, A.C. (2001). Chronic corticosterone treatment alters sensory gating in C3H mice. *Pharmacology, Biochemistry and Behavior, 69*, 359-366.

Stevens, K.E., Stitzel, J.A., Jimenez, M., & Collins, A.C. (2001). Transferring the α7 nicotinic receptor between different mouse backgrounds alters auditory gating. *Society for Neuroscience Abstracts, 27*, Program No. 145.4. (Abstract)

Tabakoff, B. (2001). Can one tell a book by its cover? *Addiction, 96*, 1667-1668.

Tabakoff, B., Helander, A., Conigrave, K., Martinez, L.D., Hoffman, P.L., Whitfield, J., Degenhardt, L., Saunders, J., Barón, A., Glanz, J., & members of the WHO/ISBRA Study Group (2001). WHO/ISBRA study on state and trait markers in alcoholism. *Alcoholism: Clinical and Experimental Research, 25*, 99S-103S.

Tabakoff, B., Yoshimura, M., Wu, P.H., & Hoffman, P.L. (2002). Adenylyl cyclase and nmda signaling in ethanol action on apoptosis. *International Journal of Neuropsychopharmacology, 5*, S10. (Abstract)

Takacs, C.D., Ehringer, M., Favre, R., Cermola, M., Eggertsson, G., Palsdottir, A., & Reysenbach, A. (2001). Phylogenetic characterization of the blue filamentaous bacterial community from an Icelandic geothermal spring. *FEMS Microbial Ecology, 35,* 123-128.

Tecott, L.H., & Wehner, J.M. (2001). Mouse molecular genetic technologies: Promise for psychiatric research. *Archives of General Psychiatry, 58*, 995-1004.

Tritto, T., Marley, R.J., Bastidas, D., Stitzel, J.A., & Collins, A.C. (2001). Potential regulation of nicotine and ethanol actions by α4-containing nicotinic receptors. *Alcohol, 24*, 69-78.

Tritto, T., Stitzel, J.A., Marks, M.J., Romm, E., & Collins, A.C. (2002). Variability in response to nicotine in the LSxSS RI strains: Potential role of polymorphisms in α4 and α6 nicotinic receptor genes. *Pharmacogenetics, 12*, 197-208.

Turri, M.G., Henderson, N.D., DeFries, J.D., & Flint, J. (2001). Quantitative trait locus mapping in laboratory mice derived from a replicated selection experiment for open-field activity. *Genetics Society of America, 158*, 1217-1226.

Van Orden, G.C., Pennington, B.F., & Stone, G.O. (2001). What do double dissociations prove? *Cognitive Science, 25*, 111-172.

Wadsworth, S.J., Corley, R.P., Hewitt, J.K., & DeFries, J.C. (2001). Stability of genetic and environmental influences on reading performance at 7, 12, and 16 years of age in the Colorado Adoption Project. *Behavior Genetics, 31*, 353-359.

Wadsworth, S.J., Corley, R., Hewitt, J.K., Plomin, R., & DeFries, J.C. (2001). Reading performance at 7, 12, and 16 years of age in the Colorado Adoption Project: Parent-offspring analyses. *Behavior Genetics, 31*, 473. (Abstract)

Wadsworth, S.J., Davis, C.J., Knopik, V.S., Willcutt, E.G., & DeFries, J.C. (2002). Genetics of reading disabilities. In I. Arcolini & G. Zardini (Eds.), *I disturbi di apprendimento della lettura e della scrittura* (pp. 23-35). Milano: FrancoAngeli.

Waldman, I.D., Rhee, S.H., Levy, F., & Hay, D.A. (2001). Causes of the overlap among symptoms of ADHD, oppositional defiant disorder, and conduct disorder. In F. Levy & D.A. Hay (Eds.), *Attention, genes, and ADHD* (pp. 115-138). East Sussex, England: Brunner-Routledge.

Wehner, J.M., & Radcliffe, R.A. (2001). Cued and contextual fear conditioning in mice (Unit 8.5C). In J. Crawley, G. Gerfen, M. Rogawski, D. Sibley, P. Skolnick, S. Wray, & R. McKay (Eds.), *Current protocols in neuroscience 2001* (pp. 1-12). New York: John Wiley & Sons.

Wehner, J.M., Radcliffe, R.A., & Bowers, B.J. (2001). Quantitative genetics and mouse behavior. *Annual Reviews of Neuroscience 2001*, 24, 845-867.

Whiteaker, P., Peterson, C.B., Xu, W., McIntosh, J.M., Paylor, R., Beaudet, A.L., Collins, A.C., & Marks, M.J. (2002). Involvement of the α3 subunit in central nicotinic binding populations. *Journal of Neuroscience, 22*, 2522-2529.

Whiteaker, P., Xu, W., McIntosh, J.M., Paylor, R., Beaudet, A.L., Collins, A.C., & Marks, M.J. (2001). Most mouse-brain [125]alpha-conotoxin MII-binding sites are unaffected by alpha 3 nicotinic subunit-null mutation. *Nicotine and Tobacco Research*. (Abstract)

Willcutt, E.G., Pennington, B.F., Smith, S.D., Cardon, L.R., Gayán, J., Knopik, V.S., Olson, R.K., & DeFries, J.C. (2002). Quantitative trait locus for reading disability on chromosome 6p is pleiotropic for attention-deficit/hyperactivity disorder. *American Journal of Medical Genetics (Neuropsychiatric Genetics), 114*, 260-268.

Wu, P.H., Bhave, S.V., Yoshimura, M., & Tabakoff, B. (2001). Development of tolerance to cataleptic effects of cannabinoid in mice overexpressing Type VII adenylyl cyclase in the brain. *Society for Neuroscience Abstracts, 27*, Program No. 805.1. (Abstract)

Wu, P.H., Yoshimura, M., Hoffman, P.L., & Tabakoff, B. (2001). Development of tolerance to ethanol in mice overexpressing adenylyl cyclase type VII in the brain. *Alcoholism: Clinical and Experimental Research, 25*, 112A. (Abstract)

Wu, P.H., Yoshimura, M., Hoffman, P.L., & Tabakoff, B. (2002). Enhanced development of chronic tolerance to ethanol, cannabinoid and morphine in mice over-expressing Type VII adenylyl cyclase in the brain. *Alcoholism: Clinical and Experimental Research, 26*, 144A. (Abstract)

Yashin, A.I., Cypser, J.R., Johnson, T.E., Michalski, A.I., Boyko, S.I., & Novoseltsev, V.N. (2001). Ageing and survival after different doses of heat shock: The results of analysis of data from stress experiments with the nematode worm *Caenorhabditis elegans*. *Mechanisms of Ageing and Development, 122*, 1477-1495.

Yashin, A.I., Cypser, J.R., Johnson, T.E., Michalski, A.I., Boyko, S.I., & Novoseltsev, V.N. (2002). Heat shock changes the heterogeneity distribution in populations of *Caenorhabditis elegans*: Does it tell us anything about the biological mechanism of stress response? *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences, 57*, B83-B92.

Yoshimura, M., Jones, S.M., Snyder, E.Y., Krushel, L.A., Zahniser, N.R., Tabakoff, B., & Zawada, W.M. (2002). Neural stem cells with a regulatable dopamine transporter for alcohol studies. *Alcoholism: Clinical and Experimental Research, 26*, 58A. (Abstract)

Yoshimura, M., & Tabakoff, B. (2001). Generation of type 7 adenylyl cyclase knockout mice. *Alcoholism: Clinical and Experimental Research, 25*, 120A. (Abstract)

Young, S.E., Rhee, S.H., Stallings, M.C., Corley, R.P., Crowley, T.J., & Hewitt, J.K. (2002). Genetic and environmental links between tobacco, alcohol, and marijuana problem use in adolescence. *Drug and Alcohol Dependence, 66*, S200. (Abstract)

Young, S.E., Smolen, A., Corley, R.P., Krauter, K.S., DeFries, J.C., Crowley, T.J., & Hewitt, J.K. (2002). Dopamine transporter polymorphism associated with externalizing behavior problems in children. *American Journal of Medical Genetics (Neuropsychiatric Genetics), 114*, 144-149.

Young, S.E., Smolen, A., Stallings, M.C., Corley, R.P., Crowley, T.C., & Hewitt, J.K. (2001). Candidate gene studies in substance-dependent adolescents, their siblings and controls. *Behavior Genetics, 31*, 474-475. (Abstract).

Zimatkin, S.M., Liopo, A.V., Slychenkov, V.S., & Deitrich, R.A. (2001). Relationship of brain ethanol metabolism to the hypnotic effect of ethanol. I: Studies in outbred animals. *Alcoholism: Clinical and Experimental Research, 25*, 976-981.

Zimatkin, S.M., Liopo, A.V., Slychenkov, V.S., Bardina, L.R., & Deitrich, R.A. (2001). Relationship of brain ethanol metabolism to the hypnotic effect of ethanol. II: Studies in selectively bred rats and mice. *Alcoholism: Clinical and Experimental Research, 25*, 976-981.

Many thanks to:

Debbie Aguiar
Kathy Huckfeldt
Kendra Locher

for their assistance in the preparation of this Annual Report.