Institute for Behavioral Genetics
University of Colorado at Boulder

Annual Report

July 1, 2003–June 30, 2004

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

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Institute for Behavioral Genetics
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Mission

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

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

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

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

DIRECTOR

From the Director

The Institute had another year of outstanding accomplishments during 2003–2004 and made significant contributions to graduate education, research training, and the creation of new research knowledge about genetic influences on behavior.

During the past year IBG faculty published 85 journal articles, 1 book, 12 book chapters and 73 abstracts. In addition, 58 research grants and 3 training grants provided support for IBG research and training activities. The total IBG budget during 2003–2004 (including general fund support, grants and gifts), was $12,451,052 which represents a 6.4% increase over the previous fiscal year. Of that amount, $11,123,126 came from research and training grant awards.

Especially gratifying was the appointment of two new tenure-track Assistant Professors and Faculty Fellows. We congratulate them and welcome them into the Institute and their academic department.

At the beginning of the academic year, Marissa Ehringer was appointed as Assistant Professor of Integrative Physiology and Faculty Fellow of the Institute, the first appointment linking the Institute with the newly reorganized and renamed Department of Integrative Physiology. Dr. Ehringer earned her PhD in Human Medical Genetics, from the University of Colorado Health Sciences Center in 2001. Her doctoral research focused on identification of gene-coding variants within alcohol-related QTLs in mice and her postdoctoral and current research applies molecular genetics and bioinformatics to the study of human drug abuse. Her first funded grant this year was to study variations in single nucleotide polymorphisms (SNPs) in two candidate genes (the alpha4 nicotinic receptor and protein kinase C gamma) in relation to human tobacco smoking. Her expertise in molecular genetics and bioinformatics will greatly enhance the Institute's commitment to interdisciplinary translational research.

In January, Jerry Stitzel joined us as our second Assistant Professor of Integrative Physiology and Faculty Fellow of the Institute. Dr. Stitzel obtained his PhD in Molecular Biology from Johns Hopkins University in 1992 for his work on inducible transcription of replication by RNA polymerase in mammalian cells. After that, he conducted postdoctoral research on nicotinic receptors, and held the position of Assistant Research Scientist in the Department of Pharmacology at the University of Michigan Medical School. His research utilizes genetic strategies in rodents to determine neurobiological bases of the behavioral and physiological actions of nicotine. His broad expertise in molecular biology and genetics will further strengthen the Institute's program of research on the genetics of addiction.

The appointment of these new tenure-track faculty continues our commitment to invigorate the Institute's program of interdisciplinary behavior genetics research, and graduate and postdoctoral training.

The graduate and postdoctoral training mission was given renewed and expanded impetus during this year with the renewal of our grant for Research Training in Biological Sciences supported by the National Institute on Mental Health (PI: Jeanne Wehner), and the award of a new grant for Research Training in the Genetics of Substance Abuse supported by the National Institute on Drug Abuse (PI: Al Collins). Together with our training support from the National Institute of Child Health and Human Development for Research Training in Developmental Behavior Genetics (PI: John Hewitt), these awards allow the Institute to fully support thirteen graduate students and 5 postdoctoral trainees in behavior genetics. We are especially proud of the external recognition of the value of our graduate training program that flourishes as an integral part of the mission of the Institute.

Another significant development this year was the initiation of work on a new wing of the main Institute building to accommodate improved animal testing and holding facilities as well as faculty offices and meeting space. This is part of an upgrade of the Institute's facilities that we are undertaking to ensure our continued ability to conduct state-of-the-art animal model and human research. I am especially grateful for the efforts of Drs. Andy Smolen and Toni Smolen, along with Mr. Sean Shelby, in working with University staff, as well as with architects and construction companies, to ensure the success of this project. The project will be completed in 2005.

We congratulate John DeFries who began his University of Colorado Council on Research and Creative Work (CRCW) Faculty Fellowship during the summer of 2004.

Success in interdisciplinary research requires something beyond individual accomplishment; it requires the kind of collegial interactions and collaborative efforts that are engendered and facilitated by the Institute. I thank all of the faculty, staff, and students who contribute to this. A special thanks goes to the Assistant Director, Dr. Toni Smolen, and to Ms. Debbie Aguiar, Mr. Sean Shelby, Ms. Rachel Kobza, and Ms. Dawn Caillouet for their work in preparing this report.

John K. Hewitt
Director

Faculty Fellows

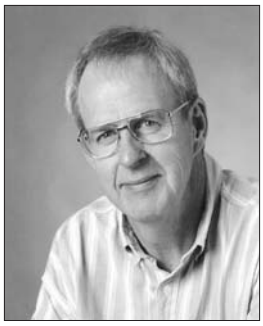
Michael D. Breed

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

Gregory Carey

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

Allan C. Collins

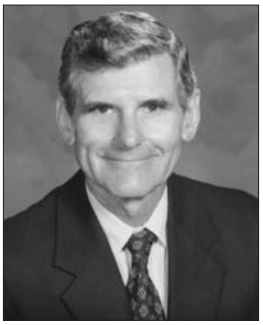


Professor of Psychology and Pharmacology, Department of Psychology, University of Colorado at Boulder; PhD, University of Wisconsin, 1969; NIAAA Research Scientist Award, 1978–83; NIDA Level V Research Scientist Award, 1993–2003. Professor Collins is a biochemical pharmacologist whose primary research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

Thomas Crowley

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

John C. DeFries



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

Richard A. Deitrich

Professor, Department of Pharmacology, University of Colorado 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.

Marissa A. Ehringer

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

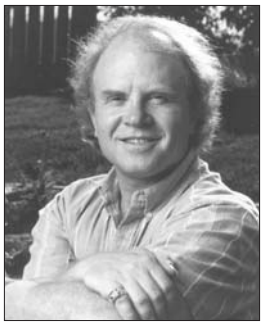
John K. Hewitt

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

Kent Hutchison

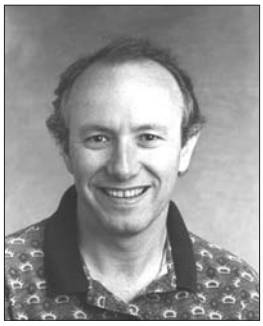
Associate Professor, Department of Psychology, University of Colorado at Boulder; PhD, Oklahoma State University, 1995. Dr. Hutchison is a clinical psychologist whose research examines mechanisms that underlie substance abuse and dependence (e.g., craving and drug reinforcement), individual difference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

Thomas E. Johnson



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

Kenneth Krauter



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

Carol B. Lynch

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

Richard K. Olson

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

Bruce F. Pennington

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

Dennis R. Petersen

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

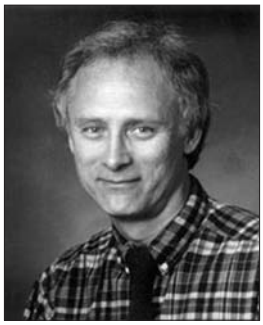
Richard A. Radcliffe

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

Soo Rhee

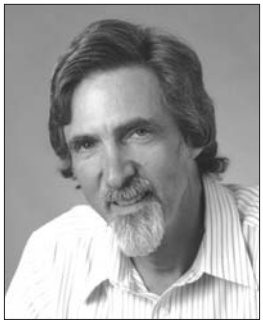
Assistant Professor of Psychology, Department of Psychology, University of Colorado at Boulder; PhD, Emory University, 1999. Dr. Rhee's primary research interests are the etiology and development of childhood disruptive disorders, the etiology and development of substance use disorders, the causes of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

James Sikela



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

Andrew Smolen



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

Toni N. Smolen

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

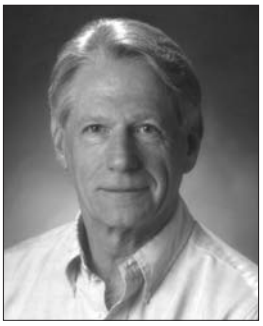
Michael Stallings

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

Jerry A. Stitzel

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

Boris Tabakoff

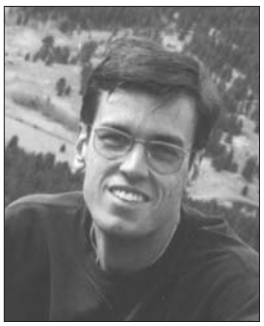


Professor and Chair, Department of Pharmacology, University of Colorado Health Sciences Center, Denver; PhD, University of Colorado, 1970; President of the Research Society on Alcoholism, 1983–85; President of the International Society for Biomedical Research on Alcoholism, 1986–90; RSA Award for Scientific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

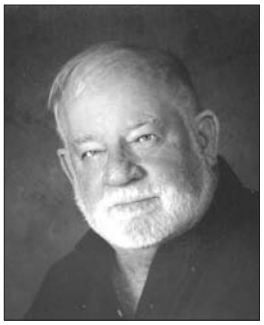
Jeanne M. Wehner

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

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



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



POSTDOCS & ASSOCIATES

Postdoctoral Fellows, Senior Research Associates and Research Associates

Seth Balogh, PhD, University of Connecticut, 2000. Investigation of the genetic and molecular basis of learning and memory, and the 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; development and characterization of the largest existing panel of murine RI strains.

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

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

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

Christopher Downing, PhD, State University of New York at Albany, 2001. Classical and molecular genetic methods, such as QTL analysis, congenic and transgenic mice, and gene expression techniques to identify and evaluate genes mediating drug-related phenotypes.

Naomi Friedman, PhD, University of Colorado, 2002. Working memory and executive functions, including individual differences and behavioral genetic analyses of executive functions such as inhibition.

Sharon Grady, PhD, University of Michigan, 1973. Function of nicotine in the central nervous system of mice, specifically, nicotine-stimulated release of neurotransmitters from synaptosomes.

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

Nate Kahn, PhD, University of Denver, 1999. Molecular genetics of stress resistance and aging, using transgenic C. elegans for analysis of loci and molecular mechanisms involved in stress responses and longevity.

Jeffrey Lessem, PhD, University of Colorado, 1999. Research into the methodology for detecting quantitative trait loci; particularly in relation to substance use disorders and conduct disorders.

Christopher Link, PhD, University of Massachusetts, 1981. Molecular genetics; modeling of neurodegenerative diseases using transgenic *C. elegans*.

Michael Marks, PhD, University of Michigan, 1974. Genetic influences on molecular, biochemical, physiological, and behavioral factors mediating the responses to nicotine in mice.

Shane Rea, PhD, University of Queensland, 2000. Demographics of aging in the nematode *C. elegans*. Identification of long-lived individuals in genetically homogeneous populations. Elucidation of the molecular basis of life extension in the mitochondrial Mit mutants of *C. elegans*.

Brad Rikke, PhD, University of Texas, 1992. Genetic mapping and identification of genes underlying 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, their correlates, antecedents, and possible outcomes.

Amy Smith, PhD, University of Colorado, 2003. 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.

Gary Stetler, PhD, University of Utah, 1980. The application and development of high-throughput methods for the identification of genes involved in human behavior and learning.

David Timberlake, PhD, University of California, San Diego, 2003. Investigations of heritability of tobacco use and associations between nicotine dependence and candidate genes.

Rolando Tiu, Jr., PhD, Case Western Reserve University, 2003. Exploration of the relationships between general and specific cognitive abilities and achievement.

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

Deqing Wu, PhD, Peking University, 1995. Statistical and genetic analysis of aging in *C. elegans*.

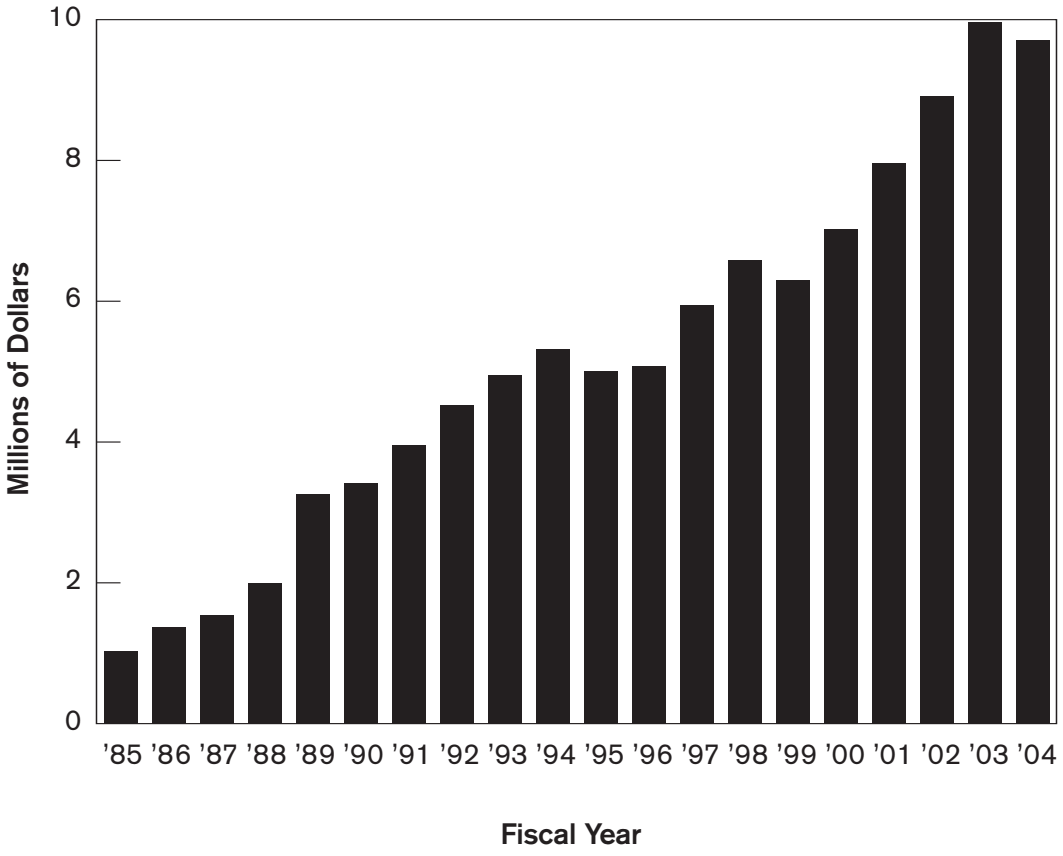
Susan Young, PhD, University of Colorado, 1998. Genetic and environmental factors underlying the development of conduct disorder, ADHD and substance use problems; links between executive cognitive function and developmental psychopathology.

Postdocs David Timberlake (L) and Joe Tiu (R) exchange ideas in the IBG Library.

Research Support: 2003–2004 Fiscal Year

Source of Funding	Number of Awards	Fiscal Year Dollars	Total Grant Dollars
Federal Agencies			
National Institute on Aging	6	904,578	6,089,726
National Institute on Alcohol Abuse and Alcoholism	16	2,444,622	15,933,545
National Institute of Child Health and Human Development	5	2,693,844	12,117,065
National Institute on Drug Abuse	10	2,046,947	10,260,868
National Institute of Mental Health	8	1,240,125	6,966,972
National Eye Institute	1	311,506	1,620,719
National Institute on Deafness and Other Communication Disorders	1	257,250	1,396,834
National Institute of Neurological Disorders and Stroke	1	25,000	100,000
Other			
Abbott Laboratories	1	6,115	85,000
Alzheimer's Association	1	85,223	250,000
American Cancer Society	1	120,214	347,807
Butcher Foundation	1	16,433	16,433
Colorado Tobacco Research Program	4	485,153	863,543
The Ellison Medical Foundation	1	50,000	200,000
Polis-Schutz Research Gift	1	15,207	70,000
TOTAL	58	$10,702,217	$56,318,512

Expenditures



"The most accurate way to make year-to-year comparisons of data on research and other sponsored project activitiy is to look at actual expenditures"

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

Research Activities For Fiscal Year 2003–2004

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

Aging

NIA (AG-008761)-"Oldest Old Mortality–Demographic Models and Analysis" ($10,635,276; $1,148,982), 1/1/99–12/31/03: This program of research (J. Vaupel, PI) 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 research on genetic and non-genetic determinants of longevity, including the interaction between fertility and mortality, and research on why age-specific mortality decelerates with age.

"IBG Subcomponent" ($674,012; $133,485), 9/1/01–12/31/03: The major goal of this subproject is to examine mortality kinetics as a function of age in large populations of normal and mutant nematodes.

Principal Investigator: Thomas E. Johnson

NIA (AG-008761)-"Oldest Old Mortality–Demographic Models and Analysis" ($8,574,896; $289,188), 5/15/04–4/30/09: Renewal of previous grant. The research proposed in this P01 (J. Vaupel, PI) is driven by the concepts and methods of demography. All six projects focus on research on exceptional longevity. Longevity has proven to be remarkably plastic: Environmental and genetic alterations can produce large increases in longevity. Our overarching goal is to explore the nature of and limits to this plasticity.

"IBG Subcomponent" ($1,251,584; $33,249): The major goal of this subproject is to examine mortality kinetics as a function of age in large populations of normal and mutant nematodes.

Principal Investigator: Thomas E. Johnson

NIA (AG-016219)-"Molecular Genetics of Aging in *C. elegans*" ($1,347,387; $28,510), 8/1/99–7/31/04: 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-017949)-"Biometrical Analysis of Personality in Adulthood" ($277,872; $67,238), 4/1/00–3/31/04: 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; $85,223), 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
Co-Investigator: Thomas E. Johnson

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

Principal Investigator: Brad A. Rikke

NIA (AG-012423)-"Transgenic *C. elegans* as Amyloid Disease Model" ($1,388,497; $357,463), 5/1/03–3/31/07: The goal of this project is to understand the cellular and molecular basis of β-amyloid peptide (Aβ) toxicity using genetic and molecular genetic analysis of transgenic *C. elegans* animals expressing the human Aβ peptide.

Principal Investigator: Christopher D. Link

NIA (AG-021037)-"Comparative Modeling of Neurodegenerative Diseases" ($1,150,374; $284,633), 6/1/03–5/31/07: The goal of this project is to use transgenic *C. elegans* models to investigate whether age-associated neurodegenerative diseases (other than Alzheimer's Disease) have a common underlying toxic mechanism.

Principal Investigator: Christopher D. Link

NIA (AG-016219)-"Molecular Genetics of Aging in *C. elegans*" ($1,347,387; $28,510), 9/15/04–7/31/09: The main goal of this project is to extend the understanding of mechanisms underlying the increased life expectancy of long-lived (Age) mutants in the nematode *Caenorhabditis elegans*, these mutants having revealed the relationship between increased longevity and increased ability to respond to stress.

Principal Investigator: Thomas E. Johnson
Co-Investigator: Samuel Henderson

Alcohol

NIAAA (AA-03527)-"Genetic Approaches to the Neuropharmacology of Ethanol" ($8,900,388; $254,255), 12/1/97–11/30/03: 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" ($1,640,957; $108,505): 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" ($507,891; $16,275): 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" ($444,549; $21,424): 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-011984)-"High Efficiency Mapping of Alcohol Sensitivity Genes" ($1,185,095; $120,815), 3/1/00–2/28/05: These studies will complete the construction of a large number of recombinant inbred strains from the inbred Long Sleep (ILS) and the inbred Short Sleep (ISS) strains of mice and will map, genetically, eight traits involved in the actions of alcohol.

Principal Investigator: Thomas E. Johnson

NIAAA (AA-012301)-"Identification of Genes Regulating Alcohol Consumption" ($662,550; $165,375), 7/1/01–3/31/05: 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 C57 BL6 background.

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

NIAAA (AA-008940)-"Mapping of Genes Predisposing to Alcohol Sensitivity" ($2,803,556; $421,535), 5/1/03–4/30/08: The major goals of this project are to continue fine-scale mapping of quantitative trait loci that specify sensitivity to the anesthetic effects of alcohol and to use gene sequence data available for both mice and humans to identify candidate genes in these QTL regions. We also will test the hypotheses that these candidates differ between ILS and ISS and map to the defined Lore interval.

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

NIAAA (AA-013901)-"5HT2 and 5HT1A Receptors in PKC-gamma Null Mutant Mice" ($445,500; $148,000), 7/1/03–6/30/06: The goal of this project is to elucidate the specific role of PKCγ in complex behaviors associated with alcohol dependence.

Principal Investigator: Barbara J. Bowers

NIAAA (AA-014250)-"Genetic Association and Stratification: Alcoholism" ($631,479; $154,253), 9/30/03–8/31/06: The main goal of this project is to test for association between three phenotypes related to alcohol dependence and abuse and seven candidate genes while controlling for the effects of population stratification in a nationwide probability sample.

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

NIAAA (AA-014666)-"Mouse Models of Alcohol Induced Behavior" ($1,674,563; $83,461), 4/1/04–3/31/09: This project will provide support for the maintenance and production of mouse stocks that are valuable for alcohol related research.

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

NIAAA (AA-014425)-"Genetic Analysis of Ethanol-Mediated Stress Reduction" ($2,127,480; $33,837), 6/1/04–5/31/09: The major goal of this proposal (L. Lu, PI) is to extend transcriptome QTL mapping and trait association in RI strains to the hippocampus of the LXS mice under alcohol and stress exposure to test the role of shared genetic mediation of responses to both treatments.

"IBG Subcomponent" ($427,817; $6,069): The genetic specification of anxiety and aggression will be examined using the LXS RI mouse panel.

Principal Investigator: Beth Bennett

Drs. Outi Salminen, Sharon Grady, and Mike Marks from the Collins Lab.

The Colorado Adoption Project and Longitudinal Studies

NIMH (MH-043899)-"Transition Into Early Adolescence: A Twin/Adoption Study" ($996,960; $75,271), 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-063207)-"Behavior Genetic Analyses of Executive Functions" ($1,133,060; $219,181), 6/1/01–5/31/06: The goal of this project is to conduct the first behavioral genetic study of individual differences in executive functions in a genetically informative twin sample already characterized for general and specific cognitive abilities.

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

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

"IBG Subcontract: Behavioral Genetic Analysis of Adolescent Health Risk" ($237,824; $87,551), 7/1/02–10/31/04: This study focuses on the pairs sample of MZ twins, DZ twins, full-siblings, half-siblings, and unrelated children reared together, for the purposes of conducting behavior genetic analyses of health risks and outcomes.

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

NICHD (HD-010333)-"Determinants of Behavioral Development in Children" ($1,192,034; $353,588), 6/1/03–5/31/07: The broad purpose of this component of the Colorado Adoption Project is to investigate the genetic and environmental etiologies of individual differences in psychological development during late adolescence in the context of a longitudinal prospective "full" adoption, sibling, and twin study spanning 16 years. The continuation to project Years 27 through 30 will complete testing of 405 pairs of twins aged 13 through 16, previously tested at 1, 2, 3, 4, 7, 9, 10, 11 and 12 years of age, using many of the same measures as the CAP adoptive and nonadoptive participants.

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

NICHD (HD-036773)-"Nature and Nurture in Social Demography: An Adoption Study" ($1,653,437; $330,453), 8/6/03–5/31/08: This project addresses familial influences on educational attainment, family determinants of union- and family-formation choices of young adults, and how the quality of early family relationships shapes adult child-parent relationships.

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

Drug Abuse Vulnerability

NIDA (DA-012845)-"Genetics of Adolescent Antisocial Drug Dependence" ($8,148,882; $817,909), 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" ($471,861; $54,278): The primary roles of this subcomponent are data collection and monitoring of data collection efforts for the Colorado site, integration and management of the multi-site data from Colorado, and data analysis and the reporting of scientific results.

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

NIAAA (AA-011949)-"NYS Family Study; Problem Alcohol Use and Problem Behavior" ($6,889,482; $997,473), 9/30/00–8/31/05: The proposed research (Scott Menard, 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" ($1,388,480; $309,304): 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-011015)-"Antisocial Drug Dependence: Genetics" ($8,823,379; $2,048,950), 8/15/03–4/30/08: This grant supports the Center on Antisocial Drug Dependence (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: Genetics and Treatment" ($64,863; $14,342): The major goal of this component is a whole-genome search for chromosomal loci containing genes influencing early-onset dependence on drugs and antisocial behavior.

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

"Familial Aggregation of Antisocial Substance Dependence" ($1,314,485; $306,268): The goal of this component is a 5-year follow-up assessment of 285 families of subjects formerly in treatment for substance use disorder (SUD) and conduct disorder (CD) as adolescents and 200 community control families. The study will provide important information regarding family influences underlying SUD and CD, the generality versus specificity of familial influences on these behaviors, and the identification of family factors that differentiate persistent versus adolescent-limited problem behavior.

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

"A Longitudinal Adoption Study of Adolescent Substance Experimentation" ($772,661; $180,458): The major goal of this component is to assess genetic and environmental influences on experimentation with tobacco, alcohol, marijuana, and other drugs using a longitudinal adoption design. This study builds on more than 20 years of data collected as part of the Colorado Adoption Project (CAP), and focuses on the transmission of substance use and antecedent behaviors such as conduct disorder symptoms, other behavioral problems, and academic achievement difficulties.

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

"Heritable Early Indicators of Risk for Drug Dependence" ($1,118,759; $260,607): The major goal of Component 4 is to use an augmented twin study to understand how genes and environmental influences contribute to vulnerability to drug abuse and antisocial behavior as they develop during adolescence. A second wave of assessments will be conducted with 1300 pairs of twins and their siblings 5 years after the initial interview.

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

"Administrative/Educational Core A" ($261,419; $60,797): The major goal of the administrative and educational core is to facilitate interactions among an interdisciplinary group of clinicians, behavioral geneticists, and molecular biologists at the Health Sciences Center and Boulder campus of the University of Colorado.

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

"Assessment Core B" ($250,694; $58,443): The major goal of this assessment core is to ensure that the genetic phenotypic information from each of these components is collected, organized, and stored in a way that facilitates direct comparisons across components and combined analyses among components.

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

"Pilot Project" ($20,000; $20,000), 8/15/03–4/30/04: The focus of this pilot project is to investigate polymorphisms in the cannabinoid receptor gene for their possible functional importance in the etiology of marijuana use in a young adult sample.

Principal Investigator: Marissa A. Ehringer

NIDA (DA-014642)-"Progression of Craving and Addiction: Genetic Factors" ($1,466,216; $294,000), 9/30/01–6/30/06: Our preliminary research (Kent Hutchison, Principal Investigator) 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; $92,782): 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

Marissa Ehringer and Isabel Schlaepfer discuss genetic data.

Colorado Learning Disabilities Research Center staff (L to R): June Crenshaw, Terry Grupp, Mary Ellen Flynn, Elizabeth Johnson-Wold, Melissa Barba-Espinosa

NIDA (DA-015522)-"A Family Study of Substance Use and Conduct Disorder" ($2,643,042; $418,224), 9/10/03–6/30/08: This family study of adjudicated adolescent boys and girls with Substance Use and Conduct Disorder (Christian J. Hopfer, Principal Investigator) has two primary goals. The first is to test competing models of the comorbidity between Substance Use and Conduct Disorder and the second is to examine the familial transmission of these disorders.

"IBG Subcomponent" ($135,001; $21,628): This study examines the familial transmission of risk for substance dependence and antisocial behavior and investigates whether common risk factors may account for the co-aggregation of these problem behaviors in families.

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

Learning Disabilities

NICHD (HD-038526)-"A Longitudinal Twin Study of Early Reading Development" ($2,372,158; $570,961), 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-62116)-"Behavior Genetics of Attentional and Co-Occurring Problems" ($147,383; $6,140), 8/1/00–7/31/03: 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-062120)-"DSM-IV ADHD in an Ethnically Diverse Community Sample" ($1,581,867; 333,813), 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

NICHD (HD-027802)-"Differential Diagnosis in Learning Disabilities" ($6,661,612; $1,351,291), 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; $184,738): The objectives of this research project are to collect psychometric test data from twin pairs. The data will be used to assess the genetic and environmental etiologies of reading deficits, ADHD, and their comorbidity, as well as their covariation with measures of other psychopathologies, reading and perceptual processes, mathematics performance, and executive functions.

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

"Reading and Language Processes" ($1,481,997; $301,539): 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; $249,584): 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; $189,442): 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; $136,989): 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; $288,999): This unit is responsible for coordinating the four research projects as well as maintaining communication among them, ascertaining and scheduling subjects, obtaining questionnaire data, managing a master file of combined data sets, and administering the center budget and other fiscal matters.

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

NIMH (MH-063941)-"Validity of DSM-IV ADHD Subtypes in a Community Sample" ($1,679,145; $340,397), 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; $257,250), 2/15/02–1/31/07: This project will initiate the first longitudinal twin study of reading disability and its relation with ADHD and other psychopathology.

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

Linguistics

Butcher Foundation-"Linguistic and Genetic Relationships in Northern Cameroon (Central Africa)" ($98,598; $16,433), 5/1/04–4/30/05: The purpose of this interdisciplinary study is to examine the correlation between linguistic sub-grouping and genetic makeup of selected populations in the extreme north province of Cameroon.

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

Nicotine

NIDA (DA-003194)-"Genetics of Nicotine Tolerance: Role of Receptors" ($1,417,325; $281,420), 9/1/99–6/30/04: 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

Colorado Tobacco Research Program (2R-033)-"Nicotinic Receptor Mediation of Anxiety and Cognition" ($514,500; $257,250), 7/1/00–06/30/05: The goal of the studies is to support research that will help us understand the biology of nicotine addiction.

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

NIAAA (AA-011156)-"Ethanol, Nicotine, and Brain Nicotinic Receptors" ($1,106,231; $282,030), 9/1/00–8/31/04: The goal of this project is to study alcohol and nicotine interactions, focusing on ethanol effects on brain nicotinic receptors.

Principal Investigator: Allan C. Collins

NIAAA (AA-013018)-"Role of Nicotinic Receptors in Effects of Alcohol" ($2,371,673; $462,787), 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

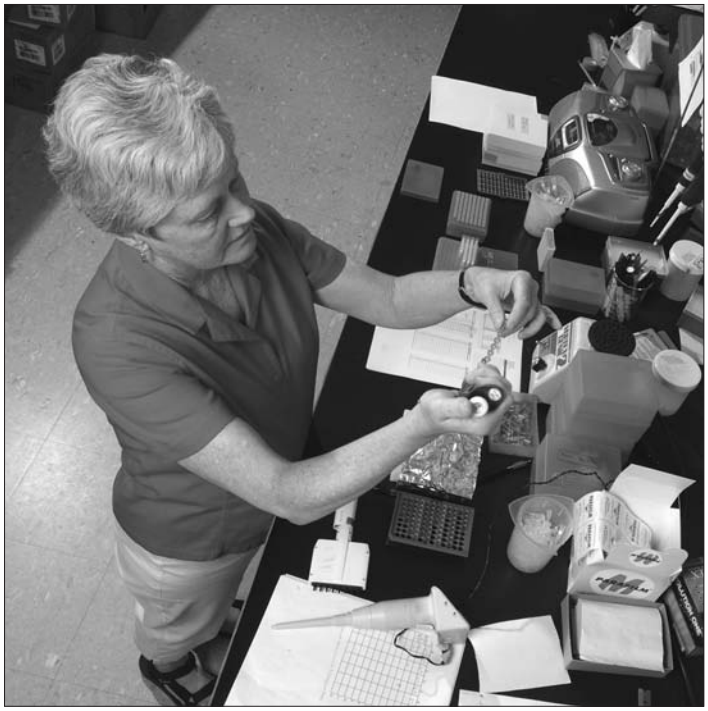
NIDA (DA-012242)-"Alpha-Conotoxin MII: A Selective Nicotinic Receptor Probe" ($1,310,348; $260,160), 7/1/02–6/30/07: The goal of this project is to investigate the nicotinic receptors that interact with α-conotoxins.

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

NIDA (DA-012661)-"Analysis of Nicotinic Cholinergic Systems in Mutant Mice" ($126,279; $25,700), 7/1/02–6/30/04: 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

Jay Yerg (Link Laboratory) is preparing samples for microarray analysis.



Mary Beeson (Johnson Laboratory) is preparing samples for polymerase chain reactions (PCR), which make millions of copies of a small sequence of DNA for analysis.

Colorado Tobacco Research Program (2I-034)-"Candidate Genes for Tobacco Use and Nicotine Dependence" ($110,250; $35,250), 7/1/02–12/31/04: The focus of this CTRP grant is to investigate single nucleotide polymorphisms within two candidate genes that may be involved in smoking and nicotine dependence. The two candidates, the alpha4 subunit of neuronal nicotinic acetylcholine receptor and the protein kinase C gamma genes, have been strongly implicated in pharmacological and behavioral responses to nicotine in mouse models.

Principal Investigator: Marissa A. Ehringer

NIDA (DA-015663)-"Studies with Nicotinic Null Mutant Mice" ($1,474,167; $289,243), 5/1/03–6/30/07: This is a Program Project which provides support for the production and maintenance of multiple nicotine receptor knockout mouse strains.

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

NINDS (NS-042196)-"Cognitive Dysfunction after TBI: Role of alpha7 nAChrs" ($1,092,310; $825,000), 4/1/02–3/31/06: The focus of this study (J. Pauly, Principal Investigator) is the role of nicotinic receptors in responses of the brain to head injury.

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

Principal Investigator: Michael Marks

Colorado Tobacco Research Program (3I-030)-"Immunochemical Protocols for Nicotinic Receptors" ($146,565; $146,565), 7/1/03–9/30/04: The aim of this project is to develop antibody-based protocols for isolating nicotinic receptors on the basis of their subunit composition.

Principal Investigator: Paul Whiteaker

Colorado Tobacco Research Program (3F-034)-"Presynaptic Nicotinic Receptor Subtypes in Dopamine Neurons" ($92,228; $46,088), 7/1/03–6/30/05: The goal of this project is to determine which is (are) the subunit composition(s) of nicotinic acetylcholine receptor(s) mediating the dopamine release in brain dopaminergic terminal areas in naive and nicotine-treated animals. This will eventually add to our understanding of nicotine addiction.

Principal Investigator: Outi Salminen

American Cancer Society (RSG-01-139-01-CNE)-"Genetic Analysis of Nicotine Preference in Mice" ($347,807; $120,214), 1/1/04–6/30/05: The goal of this project is to perform QTL (quantitative trait locus) analysis and subsequently fine map genes that influence nicotine oral self-selection in mice.

Principal Investigator: Jerry Stitzel

Schizophrenia

NIMH (MH-066115)-"Abnormal Eye Movement in Schizophrenia: Genome-wide Scan" ($1,672,187; $278,698), 1/9/04–12/31/08: The aims of the proposal (Randal Ross, Principal Investigator) are to perform a genome-wide scan looking for a linkage to a schizophrenia-associated endophenotype, an elevated frequency of leading saccades during a smooth pursuit eye movement (SPEM) task. SPEM abnormalities have been associated with schizophrenia for almost 100 years, and have been suggested as a potential marker of genetic risk for over 20 years.

"IBG Subcomponent" ($122,377; $11,463): The purpose of this subcontract is to assist Dr. Randal Ross in conducting extended pedigree and sibling-pair linkage analyses to detect quantitative trait loci that increase risk for schizophrenia.

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

Statistical Models

NEI (EY-012562)-"Variance Components Models for Mapping QTLs" ($1,620,719; $311,506), 9/1/02–8/31/07: The goal of this project is to further extend the methodology of variance components analysis to accommodate more general data structures and models that are of practical importance to the design and analysis of modern genetic studies, and to integrate these into a comprehensive software package.

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

NIMH (MH-019918)-"Workshop on Methodology of Twin and Family Studies" ($755,555; $142,313), 7/1/03–6/30/08: The major goal of this project is to hold a series of international workshops on the methodology of twin studies at the Institute for Behavioral Genetics in Boulder, Colorado.

Principal Investigator: John K. Hewitt

Research Career Awards and Fellowships

NIDA (K05-DA-000197)-"Pharmacogenetic Regulation of Sensitivity to Nicotine" ($559,956; $19,998), 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-000195)-"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

NIDA (K01-DA-013956)-"Causes of Comorbidity: Substance Use Disorder, ADHD & CD" ($498,497; $100,823), 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

NIAAA (F31-AA-13350)-"Plieotropy for Alcohol-Related Phenotypes" ($47,886; $3,991), 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

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

Awarded to: Susan E. Young

NIAAA (F32-AA-013465)-"Nicotinic Receptor Polymorphisms and Ethanol Sensitivity" ($84,740; $38,683), 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

Seventeenth International Workshop on Methodology of Twin and Family Studies held at the Millennium Harvest House Hotel, Boulder, Colorado.

Research Highlights

The Neurobiology of Nicotine: Gaining Insight Through Genetics

Nicotine is a molecule of great biomedical interest. As the addictive substance in tobacco, it is responsible for over 450,000 premature deaths per year and approximately $75 billion in annual health care costs. On the other hand, nicotine has been found to possess intriguing therapeutic properties. For example, nicotine has been shown to normalize a neurophysiological information processing deficit common among schizophrenics, function as an effective co-treatment for haloperidol-resistant Tourette's Syndrome patients and act as a cognitive enhancer. In addition, nicotine exhibits neuroprotective properties and may be responsible for the reported delayed onset in smokers of familial forms of Parkinson's and Alzheimer's disease. The biological bases for these wide-ranging actions of nicotine are not well understood. Consequently, it is the long term objective of my research program to elucidate the biological bases for a variety of behavioral and physiological effects of nicotine using the mouse as a model system. The mouse is well suited for this purpose as nicotine exhibits effects in mice that are quite similar to those observed in humans, including cognitive enhancement, normalization of information processing deficits, and neuroprotection. Aspects of nicotine addiction, including tolerance development and self-administration also can be evaluated in mice. The information obtained from this research not only will lead to a greater appreciation for the biological mechanisms underlying these wide-ranging responses to nicotine, but also should provide knowledge that will be invaluable for the development of new strategies for the prevention and/or treatment of myriad diseases and disorders.

Since the 1950s, genetic strategies have been utilized successfully to identify the biological bases for heritable differences in drug sensitivity and disease. Genetic approaches can be employed to test hypotheses; if a protein is critical to the biological process then genetic polymorphisms that affect the expression or function of the protein should affect the biological process. Moreover, genetic approaches are valuable in generating new hypotheses to explain the action of a drug and/or a biological process; for example, when a phenotype is significantly impacted by a polymorphism in a gene whose protein product was not previously thought to be critical for the phenotype. Both hypothesis testing and hypothesis generating genetic strategies are valuable methods for establishing the biological mechanisms of poorly understood biological processes such as those leading to the wide ranging effects of nicotine on behavior and physiology. In the attempt to unravel the biological bases for nicotine's many effects, our laboratory employs an integrative strategy that is based on genetic methodologies but also incorporates molecular, cellular, biochemical, pharmacological, behavioral and physiological methods.

Currently, there are two main projects in our lab. The first project employs a candidate gene strategy to identify and assess the potential role of naturally occurring genetic variants of members of the nicotinic receptor subunit gene family in modulating the behavioral and physiological effects of nicotine. Most of the laboratories efforts on this project are focused on genetic variation in two nicotinic receptor subunit genes, Chrna4 and Chrna7. A polymorphism in Chrna4, which leads to an amino acid substitution in the nicotinic receptor $\alpha 4$ subunit, has been shown to be associated with a range of responses to nicotine as well as mouse strain differences in nicotinic receptor

function. Using a series of genetically modified mice, we now are attempting to more definitively establish which responses to nicotine are influenced by the Chrna4 polymorphism and to determine which neuronal pathways are important for the influence of the Chrna4 polymorphism on the behavioral and physiological effects of nicotine. Studies to establish the cellular and molecular mechanisms through which the Chrna4 polymorphism affects nicotinic receptor function also are being conducted. The results of these studies should improve our understanding of how a polymorphism that modestly affects nicotinic receptor function influences nicotine sensitivity. Because a recent report has shown that polymorphisms in the human gene for the α4 subunit, Chrna4, are associated with smoking, our studies may be particularly relevant to understanding the genetics of smoking.

Studies on Chrna7, the gene that encodes the nicotinic receptor α7 subunit, have shown that variability in this gene is linked to mouse strain differences in the level of expression of α7- containing nicotinic receptors. In collaboration with Dr. Cathy Adams and Dr. Karen Stevens at the University of Colorado Health Sciences Center, we also have found that the Chrna7 variants in mice are linked to altered development and neuroanatomy of the hippocampus and deficits in measures of information processing that are thought to be mediated, in part, by the hippocampus. Presently, we are characterizing polymorphisms in the promoter and other parts of Chrna7 in an attempt to establish the molecular mechanism through which the variants of Chrna7 affect receptor expression and neuroanatomy. We also plan to assess what influence the Chrna7 variants have on other responses to nicotine and alcohol.

The second project in our lab is focused on identifying genetic loci that influence individual differences in nicotine consumption in mice. The first phase of the project involves the identification of genetic loci that influence free-choice nicotine consumption in a genetic cross between two mouse strains, C3H/HeJ and C57BL/6J. These mouse strains were chosen due to large differences in their desire/willingness to consume nicotine. This part of the project has been completed and we have identified two major loci, one on chromosome 1 and another on chromosome 4, that contribute significantly to individual differences in nicotine consumption. Interestingly, both of these loci map over chromosomal regions previously identified by others that influence alcohol consumption in mice. Therefore, these regions of the mouse genome may contain genes that contribute to both nicotine and alcohol consumption. Identification of these genes may help to explain the high co-morbidity between smoking and alcoholism in humans. We currently are in the second phase of the project which involves fine mapping of the nicotine-consumption loci using heterogeneous stock (HS) mice and single nucleotide polymorphism (SNP)-based genotyping. The goal of this phase of the project is to narrow the region associated with nicotine consumption to a small enough area to be able to identify potential candidate genes for further analysis.

Jerry A. Stitzel, PhD
Assistant Professor and Faculty Fellow
(*The Stitzel lab is pictured on the inside back cover*)

The Application of Genomic Technology to Human Disease and Evolution

Our laboratory is interested in the development and application of advanced genome technologies, particularly as they apply to our understanding of human disease and human evolution. Areas of special interest include the identification of genetic factors involved in neurogenetic diseases such as alcohol and drug abuse, mental retardation, and cognitive disability, and the use of novel evolutionary genomics approaches to identify genes unique to the human and great ape lineages. Technologies that are used include high throughput DNA sequencing, gene expression profiling using high density DNA chip technologies, cDNA array-based comparative genomic hybridization (aCGH), and novel bioinformatics tools for the rapid in silico discovery of genes underlying QTLs for complex traits.

The following are a number of areas of particular interest to our laboratory.

Alcohol and drug abuse: We are using mouse models of alcohol action to identify genes that underlie alcohol-related processes and pathways as a first step toward identifying human genes that contribute to predisposition to develop alcoholism and alcohol abuse. High throughput genomic approaches, mentioned above, are also being used to search for gene coding or regulatory region sequence variations that underlie QTLs for a number of alcohol- or drug-related phenotypes.

Identification of gene copy number variants related to human genetic diseases and traits: Novel genome-wide and gene-based approaches, such as cDNA aCGH, are being used in human studies to search for gene copy number changes within the human population and especially for those involved in mental retardation, birth defects and other human genetic diseases and traits.

Evolutionary genomics of human cognition: To gain insights into the evolutionary genomics of human and great ape lineages, we are using cDNA aCGH to identify lineage-specific gene duplications or losses that have occurred between these lineages. Of particular interest are those human lineage-specific genes that underlie the cognitive abilities unique to the human brain, and how such genes, when defective, lead to cognitive disability.

James Sikela, PhD
Professor and Faculty Fellow
(*See an image from this research on the inside front cover*)

Laura Dumas (Sikela Laboratory) preparing DNA for analysis.

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 which 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, & 129 Svev/Taconics inbred strains, C58/J
- Heterogeneous Stock (HS)
- Open-field Activity lines
- Long-Sleep (LS) and Short-Sleep (SS) selected lines
- ILS and ISS inbred strains
- LSXSS recombinant inbred strains
- Nesting behavior lines
- PKC null mutants
- ISS X ILS recombinant inbred strains
- High Acute Functional Tolerance (HAFT 1) &
- Low Acute Functional Tolerance (LAFT 1)
- Congenic ILS.Lore Short & ISS.Lore Long Bilineal Selection
- B6.D2 Congenic for voluntary ethanol consumption
- D2.H2 Nicotinic Congenics
- Nicotinic Knockouts

Faculty Directors:
Allan C. Collins
Jerry Stitzel

Lab Supervisor:
Jerry Salazar

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

Professional Research Associates:
Hilda Rowena Clark
Vanessa Crittenden
Heather Henderson
Christine Martin
Cathy Ruf

Student Assistants:
Yoo Jung Choi
Anthony Giordano
John Hays

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

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; and
- Nomarski Interference CDIC and fluorescent microscopes.

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

Stephanie Tseeng, Marissa Ehringer, Hilary Davis, and Isabel Schlaepfer analyze results from DNA genotyping assays.

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 University 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 and participate in the weekly journal club/colloquium series. Each trainee is expected to complete the requirements for the MA or MS degree near the end of year two.

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

Students wishing to become IBG trainees must submit an application for admission into the program to the director of the Behavioral Genetics Training Program. Excellence of record and promise are the principal criteria for selection of trainees. A further important consideration for acceptance is the diversity of background and training that is essential for the 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. Information can be obtained at ibgwww.colorado.edu. Applicants are encouraged to write to the appropriate department for application information. For application forms for admission into the IBG training program, or for further information, write to: Director, Behavioral Genetics Training Program, Institute for Behavioral Genetics, 447 UCB, University of Colorado at Boulder, Boulder, CO 80309-0447. If you prefer to call, the telephone number is 303-492-7362.

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*.

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

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

Victoria Cosgrove (PhD program, Clinical Psychology). Ms. Cosgrove is interested in personality constructs and their genetic relationship to comorbidity between adolescent internalizing and externalizing disorders. She is currently a second-year graduate student in the Clinical Psychology training program.

Rebecca Gaffney-Brown (PhD program, Psychology). Etiology and treatment implications for the comorbidity of Attention Deficit Hyperactivity Disorder, Conduct Disorder, and Reading Disability.

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

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

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

Christie Hartman (PhD program, Psychology). Christie Hartman examines the genetic and environmental contributions to Attention Deficit/ Hyperactivity Disorder, Conduct Disorder, and their comorbidity.

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

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

Jeannine M. Moineau (PhD program, Psychology/ Neuroscience). Investigating protein aggregates in neurodegenerative diseases using *C. elegans*.

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

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.

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

Visiting Students

Norman Armstrong, undergraduate student, Dillard University. Mr. Armstrong was working with Beth Bennett in the Johnson Lab on the effects of alcohol on aggressive behavior in mice.

Rohan Palmer, undergraduate student, William Paterson University. Mr. Palmer was working in the Smolen Lab on the stability, yield, and quality assessment of DNA collected from a Scope® mouthwash sampling procedure.

Courses Taught by Faculty Fellows

Fall 2003

Mike Breed	EPOB 6100, UCB	Graduate Seminar-Social Evolution
Gregory Carey	PSYC 3102, UCB	Behavioral Genetics
Allan Collins	PSYC 7102, UCB	Seminar: Behavioral Genetics
Thomas Crowley	PSCH 6000, UCHSC	Human Behavior in Health and Illness (2 lectures)
	PSCH 8001/8610, UCHSC	Big Six Substance Problems in Primary Care Medicine (Course Dir.)
John C. DeFries	PSYC 7012, UCB	Research in Behavioral Genetics
John K. Hewitt	PSYC 5242, UCB	Biometrical Methods in Behavioral Genetics
Kenneth Krauter	MCDB 4410, UCB	Human Molecular Genetics
Bruce F. Pennington	PSYCH 4525, DU	Developmental Neuropsychology
James Sikela	HMGP 7620, UCHSC	Genomics (15 lectures)
	HMGP 6000, UCHSC	Survey of Human Genetics (2 lectures)
	DSBS 6600, UCHSC	Dental Pharmacology (7 lectures)
	PHCL 7605, UCHSC	Ethics in Research (1 lecture)
	PHCL 7600, UCHSC	Frontiers in Pharmacology (1 lecture)
	PHCL 7611, UCHSC	Introduction to Bioinformatics (1 lecture)
Boris Tabakoff	PHCL 6000, UCHSC	Medical Pharmacology
	PHCL 7620, UCHSC	Graduate Pharmacology
Jeanne M. Wehner	PSYC 5102, UCB	Behavioral Genetics
Erik Willcutt	PSYC 7713, UCB	Practicum – Clinical Psychology
James Wilson	BIOL/PSYC 4104, UCD	Behavioral Genetics (On-Line Course)

Spring 2004

Mike Breed	EPOB 3240, UCB	Animal Behavior
Gregory Carey	PSYC 5741, UCB	General Statistics
Allan Collins	PSYC 7102, UCB	Seminar: Behavioral Genetics
Thomas Crowley	PSCH 8001/8610, UCHSC	Big Six Substance Problems in Primary Care Medicine (Course Dir.)
Marissa Ehringer	KAPH 6010, UCB	Seminar, Bioinformatics and Genomics
Kent Hutchison	PSYC 5423, UCB	Research Problems in Clinical Psychology
Thomas E. Johnson	PSYC 5112, UCB	Concepts in Behavioral Genetics: Genetics of Aging
Kenneth Krauter	MCDB 7910, UCB	Seminar Practicum
Richard Olson	PSYC 4001, UCB	Honors Seminar 2
	PSYC 4521, UCB	Critical Thinking: Genes and Environment
Dennis Petersen	PHRD 3750, UCHSC	Integrated Organ Systems I: Physiology
	PHSC 3410, UCHSC	Physiology/Pathophysiology II (12 lectures)
Richard Radcliffe	PHRD 3750, UCHSC	Physiology (20 lectures)
	PHRD 4740, UCHSC	CNS Pharmacology (6 lectures)
	TXCL 7326/27, UCHSC	Physiology I & II (Graduate Course Dir.)
	PHSC 7353, UCHSC	Drug Metabolism & Pharmacogenetics (2 lectures)
	TXCL 7323, UCHSC	Principles of Toxicology II: Nervous System Toxicology (2 lectures)
Soo Rhee	PSYC 3102, UCB	Introduction to Behavioral Genetics
Toni Smolen	PSYC 5112, UCB	Concepts in Behavioral Genetics: Scientific Integrity
Michael Stallings	PSYC 3101, UCB	Statistics/Research Methods
	PSYC 5112, UCB	Concepts in Behavioral Genetics: QTL Methodology
Boris Tabakoff	PHCL 7620, UCHSC	Graduate Pharmacology
	NRSC 7614, UCHSC	Alcoholism

Summer 2004

Michael Breed	EBIO 4350, UCB	Field Studies/Field Biology

Colloquia, Informal Talks, and Special Events

Fall 2003

Robin Corley (Senior Research Associate, Institute for Behavioral Genetics, University of Colorado, Boulder). "The Colorado Preschool Reading Study: Where Are These Twins Coming From—and Where Are They Headed?"

Chris Downing (Research Associate, Institute for Behavioral Genetics, University of Colorado, Boulder). "Effects of the Metabotropic Receptor Subtype 5 (mGluR5) on the Sedative Properties of Ethanol"

John K. Hewitt (Director, Institute for Behavioral Genetics and Professor, Department of Psychology, University of Colorado, Boulder). "Genetic and Family Influences on Adolescent Problem Behavior"

Michael Marks (Senior Research Associate, Institute for Behavioral Genetics, University of Colorado, Boulder). "Exploring the Complexities of Nicotine Responses: Genetic, Biochemical and Pharmacological Studies"

Spring 2004

Connie Ho (Associate Professor, Department of Psychology, Chinese University of Hong Kong). "Dyslexia in China"

Mark P. Mattson (Chief, Laboratory of Neurosciences, National Institute on Aging, Washington, DC, and Professor, Department of Neuroscience, Johns Hopkins University School of Medicine, Baltimore, Maryland). "Neurohormesis: Implications for Aging and Neurodegenerative Disorders"

Sharon Mexal (Postdoc, Human Medical Genetics Program, University of Colorado Health Sciences Center, Denver). "Gene Expression Profiling of Cigarette Smoking and Schizophrenia in Postmortem Brain: Interactions Between Substance Use and Psychopathology"

Michael Miles (Associate Professor, Department of Pharmacology and Toxicology, Virginia Commonwealth University, Richmond, Virginia). "Genetics, Drugs, and Chips: Molecular Triangulation on CNS Plasticity"

Richard Miller (Professor, Department of Pathology, and Associate Director, Geriatrics Center, University of Michigan, Ann Arbor). "Genetic Analysis of Aging and Disease in Mice"

Marina Picciotto (Associate Professor, Department of Psychiatry, Yale University School of Medicine, New Haven, Connecticut). "Nicotine Effects on Signal Transduction: Possible Mechanisms Underlying Addiction"

Andrey Ryabinin (Assistant Professor, Department of Behavioral Neuroscience, Oregon Health and Science University, Portland). "The Urocortin Neuropeptide System and Its Relation to Alcohol Consumption"

Joe Tsien (Assistant Professor, Department of Molecular Biology, Princeton University, Princeton, New Jersey). "Inducible Protein Knockout and Ensemble Recording For the Analysis of Memory Process in Mice"

Summer 2004

Mike Edwards (Postdoc, Genetics Department, University of Wisconsin, Madison). "Characterization of Age-Related Effects on the Transcriptional Response to Oxidative Damage in Mouse Cardiac and Skeletal Muscle"

Mouse Day. Mouse day is devoted to the exchange of information among researchers who work with mice on the University of Colorado campuses.

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

Research and Administrative Staff

Research

Lindly Alston
Raven Astrom
Melissa Barba-Espinoza
Melissa J. Beckner
Mary Beeson
Adrienne Blackwood
Stephanie Bogott
Susan Boorman
Heather Bosler
Josh Bricker
Joshua Brooks
Robert Brown
Kathryn Burleson
Clint Carlson
Phyllis Carosone-Link
Matthew Cirbo
Hilda Rowena Clark
Leza Clymer
Rachael Cole
Mark Conner
Kimberly Corley
June Crenshaw
Vanessa Crittenden
Robert Curtis
Hilary Davis
Patricia Davis
Antonio DiLeo
Jennifer Drapeau
Barbara Elliott
Julie Ernisse
Lauren Farnham
Jmil Ferguson
Alex Flynn
Mary Ellen Flynn
Virginia Fonte
Elizabeth Glasser
Drew Goldberg
Elizabeth Gooding
Lena Gordon
Andrew Gross
Terry Grupp
Melissa Harth
Heather Henderson
Brian Hiester
Sena Hitt-Lausten
Dina Huber
Jacqueline Hulslander
Eli Iacob
George Jayne
Anne Johnson
Elizabeth Johnson-Wold
Jeff Jones
Peter Jones
Jennifer Ziemba Keith
Ashleigh Keller
Jason Keller
Nathan King
Colin Larson
Eric Laudenslager
Amy Ledbetter
Elizabeth Legg
Jacques Machol
Christine Martin
Gregory McGinty
Natalie Meinerz
Lauren Milner
Jill Miyamoto
Donna Moore
Ryan Morrow
Christina Nelson-Goens
Erin Ochman
Lara Pallas
Bradley Pemberton
Nancy Phares-Zook
Benjamin Pressley
Sally Ann Rhea
Taylor Roy
Amy Rudolph
Cathy Ruf
Daniel Ryan
Scott Sabella
Jerome Salazar
Isabel Schlaepfer
Jaquelyn Schon
Robert Schroder
Sean Shelby
Elizabeth Siewert
Ingrid Simecek
Isaac Sisneros
Margaret Spring
Justin Springett
Gretchen Stein
Pat Tedesco
Kerry Thomson
Patricia Townsend
Jennifer Tripodi
Stephanie Tseeng
Rebecca Vanderbilt
William Van Morter
Natascia Ventura
Laurel Wade
Larisa Wilder
Corrine Wright
John Yerg
Jean Yu
Joanna Sue Zeiger

Student Hourly

Chelsie Ankler
Norm Armstrong
Sierra Atkinson
Alex Benison
Gail Bleakney
Karley Bloom
Ann Buechler
Blake Buhlig
Yoo Jung Choi
Avni Doshi
Sydni Edwards
Renee Ferguson
Kathy Fitzpatrick
Anthony Giordano
Benjamin Gurney
Jonathon Hayes
Zac Herin
Julie Kachinski
Jessica Kaplan
Alison Kell
Alexander Knuckles
Rachel Kobza
Barbara Krei
Carrie Liston
Estaban Loetz
Ashley Lowe
Michael Luckow
Tristan McClure-Begley
Alison Mickiewicz
Richard Moore
Sarah Moyle
Jennifer Mueller
Carie Muhlhauser
Sarah Nakata
Stacy Niemeyer
Jerilyn Phipenny
Kimberly Pierce
Pidchaya Prindavong
Brian Rabern
Billie Riley
Katherine Shaw
Dawn Shields
Tricia Torgensen
Chelsea Trinka
Ari Van Schilfgaarde
Brice Young

Administrative

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

Publications

July 1, 2003—June 30, 2004

Abiola, O. et al., including Johnson, T.E., Complex Trait Consortium. (2003). The nature and identification of quantitative trait loci: A community's view. *Nature Reviews Genetics, 4,* 911-916.

Alarcón, M., Plomin, R., Corley, R.P., and DeFries, J.C. (2003). Multivariate parent-offspring analyses of specific cognitive abilities. In S.A. Petrill, R. Plomin, J.C. DeFries, and J.K. Hewitt (Eds.), *Nature, nurture, and the transition to early adolescence* (pp. 28-48). New York: Oxford University Press.

Barr, C.S., Newman, T.K., Becker, M.L., Parker, C.C., Champoux, M., Lesch, K.P., Goldman, D., Suomi, S.J., and Higley, J.D. (2003). The utility of the non-human primate; model for studying gene by environment interactions in behavioral research. *Genes, Brain and Behavior, 2,* 336-340.

Barr, C.S., Newman, T.K., Shannon, C., Parker, C., Dvoskin, R.L., Becker, M.L., Schwandt, M., Champoux, M., Lesch, K.P., Goldman, D., Suomi, S.J., and Higley, J.D. (2004). Rearing condition and rh5-HTTLPR interact to influence limbic-hypothalamic-pituitary-adrenal axis response to stress in infant macaques. *Biological Psychiatry*, *55*, 733-738.

Bennett, B., Carosone-Link, P., Rikke, B., and Johnson, T.E. (2004). Genetic mapping for ethanol-related behaviors in the LXS panel of recombinant inbred strains from ILS and ISS. *Complex Trait Consortium Abstracts*, Bar Harbor, Maine. (Abstract)

Bennett, B., and Johnson, T.E. (2003). A new panel of recombinant inbred strains from ILS and ISS. *Alcoholism: Clinical and Experimental Research, 27(suppl. 5),* #262, 49A. (Abstract)

Bennett, B., Williams, R.W., Lu, L., Gu, J., Carosone-Link, P., Rikke, B., and Johnson, T.E. (2004). Genetic mapping for ethanol-related behaviors in the LXS panel of recombinant inbred strains from ILS and ISS. *Alcoholism: Clinical and Experimental Research, 28(suppl. 5),* #486, 87A. (Abstract)

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