Institute for Behavioral Genetics University of Colorado at Boulder

Annual Report July 1, 2002–June 30, 2003

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



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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 US and, arguably, in the world." In its summary findings, the Program Review Panel stated that the "... Institute for Behavioral Genetics is an independent academic enterprise that is peerless in its field and a superb asset to the University of Colorado and to the Boulder Campus." (Program Review Final Report, May 2002)

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

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

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

From the Director

As the pages of this report document, the institute had another year of outstanding accomplishments during 2002–03.

During the past year IBG faculty published 71 journal articles, 1 book, 10 book chapters, and 49 abstracts. In addition, 53 research grants and 3 training grants provided support for IBG research and training activities. The total IBG budget during 2002–03 was \$11,703,929 (including general fund support, grants and gifts), and the institute had a total of \$57,318,435 in research grant awards in place, which represents a 13.2 percent increase in grant funding over the previous fiscal year.

Contributing to those accomplishments were six newly appointed faculty fellows who I would like to congratulate and welcome to the institute.

Dr. Soo Rhee's election coincided with her appointment as assistant professor in the behavior genetics program in psychology at CU-Boulder. Soo is trained in both clinical psychology and behavior genetics. She is the recipient of a five year Career Development Award to develop her work on the Causes of Comorbidity in Substance Use Disorders, ADHD, and Conduct Disorder, using new quantitative methods in behavior genetics. She is involved in several collaborative projects with other IBG faculty. Her paper on "Genetic and environmental influences on antisocial behavior: a meta-analysis of twin and adoption studies" was published in the May 2002 issue of the *Psychological Bulletin*, one of the most prestigious journals in psychology. Another rapidly ascending scientist is Dr. Kent Hutchison, an associate professor of clinical psychology at CU-Boulder. Since he came to Boulder four years ago, he has established a vigorous research program on addiction, including important collaborative research with several IBG faculty on the genetics of craving and addiction. A recently funded R01 was on that topic and, specifically, on the role of dopamine system genes in the development of craving.

In pharmacogenetics and animal models, Richard Radcliffe is an assistant professor of pharmaceutical sciences at the University of Colorado Health Sciences Center. He is a highly valued collaborator, an investigator in the Alcohol Research Center, and his recent funding includes an R01 grant to study "Gene expression analysis of drug-induced alterations in sensitivity to alcohol." His animal models now include the zebrafish as well as rodents.

In molecular genetics, we would like to welcome two new fellows. The first is Jim Sikela, associate professor of pharmacology at the University of Colorado School of Medicine. Jim has been an innovator and leader in the development of molecular genetics technologies and their application to psychiatric and behavioral traits. He has collaborated with other IBG faculty fellows on a number of these projects, including in the Alcohol Research Center, and has played an important role in mentoring graduate students in molecular behavior genetics.

Ken Krauter is a professor of molecular, cellular, and developmental biology at CU-Boulder. A major research focus is the use of molecular genetic analysis



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



Twin Workshop Faculty: Back row, left to right, Meike Bartels, Jonathan Flint, Jeffrey Lessem, Andrew Morris, Ben Neale, Lon Cardon, Stacey Cherny, Pak Sham. Front row, left to right, Andrew Heath, Shaun Purcell, Caroline van Baal, Goncalo Abecasis, Hermine Maes, Michael Neale, Bas Heijmans, David Evans, Nick Martin, Dorret Boomsma, John Hewitt

to identify genes involved in complex traits such as behavioral disorders. He is an important collaborator in and director of molecular genetic research for our P60 Center on Antisocial Drug Dependence (PI: Tom Crowley, see below.) He is the first IBG faculty fellow rostered in MCD biology.

Last, but not least, Tom Crowley is professor of psychiatry and director of the Division of Substance Dependence at the University of Colorado School of Medicine. He has been a leader of collaborative behavior genetic research on substance dependence in clinical populations, especially in adolescence, for some years. He is the director of the Center for the Genetics of Antisocial Drug Dependence and a longstanding colleague of IBG faculty. He is currently the recipient of a NIDA funded MERIT award.

The appointment of these new faculty fellows will help keep the institute vigorous and at the forefront of interdisciplinary behavior genetics research, facilitating new collaborations, affirming current associations, and opening up exciting new opportunities for graduate and postdoctoral training.

Among honors and awards to IBG faculty during 2002–03, Mike Breed, professor of ecology and evolutionary biology and a Faculty Fellow of IBG, was elected as a Fellow of the American Academy for the Advancement of Science. His election cited his pioneering research on nest-mate recognition mechanisms in social insects, illuminating the understanding of kin

selection as a potential force in evolution. In November 2002, Tom Johnson was presented with the Kleemeier Award from the Gerontological Society of America at its annual meeting in Boston, and in February 2003, Al Collins was presented with the Langley Award from the Society for Research on Nicotine and Tobacco at its annual meeting held in New Orleans. Brad Rikke, an IBG research associate, received a four year Ellison Scholar Award for his work on genetics of aging in mice. Congratulations to the recipients of these awards.

As ever, it is a real pleasure to be associated with the work and the people of IBG. I once again want to thank all of the faculty, staff, and students of the institute for another year of superb professional and scientific performance and for the collegiality that is one of the distinguishing characteristics of the institute and an essential ingredient of our success. A special thanks goes to the assistant director, Dr. Toni Smolen, and to Ms. Debbie Aguiar and Mr. Sean Shelby for their work in preparing this report.

> John K. Hewitt Director

Faculty Fellows

Michael D. Breed

Professor, Department of Ecology and Evolutionary Biology; PhD, University of Kansas, Lawrence, 1977. Professor Breed's research emphasis is the genetics of social recognition systems in animals. His current interests include behavioral and genetic studies of the recognition cues used by honeybees to discriminate nestmates from nonnest-



mates. He is presently engaged in investigating the role of cuticular compounds in recognition, and the patterns of inheritance of chemical cuticular signatures.

Gregory Carey

Associate Professor, Department of Psychology; PhD, University of Minnesota, 1978. Dr. Carey's research interests are in the areas of genetics and human psychopathology. Within these areas, his work concentrates on the anxiety disorders and on the development of externalizing behavior (antisocial tendencies, drug abuse, and alcohol abuse) during ado-



lescence. A second major interest is the use of quantitative models to represent mechanisms of assortative mating, development, cultural transmission, and sibling interactions.

Allan C. Collins

Professor of Psychology and Pharmacology, Department of Psychology; PhD, University of Wisconsin, 1969; NIAAA Research Scientist Award, 1978–83; NIDA Level V Research Scientist Award, 1993–2003. Professor Collins is a biochemical pharmacologist whose primary research specialization is neurochemistry. His current research interests



include neurochemical correlates of nicotine use, tolerance development, and withdrawal; neurochemical bases of alcohol tolerance; biochemical bases of behavior; and 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, University of Colorado School of Medicine; 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 adoles-



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



genetics. His current research interests include twin and adoption studies of human cognitive abilities; the genetics of learning disabilities; and the use of DNA markers to map quantitative trait loci (QTLs) that influence behavioral characters.

Richard A. Deitrich

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



Colorado Alcohol Research Center, 1977–02; NIAAA Merit Award, 1996–2004. Professor Deitrich is a pharmacologist whose current research concerns the molecular basis of the actions of alcohol. His research uses genetically selected lines of mice and rats to discover mechanisms of central nervous system depression, tolerance, and dependence. These data are used to identify specific genes responsible for these actions in animals, and eventually to identify similar genes in humans at risk for development of alcoholism.

V. Gene Erwin

Professor of Pharmacology, School of Pharmacy; PhD, University of Colorado, 1965; Co-Scientific Director of the University of Colorado Alcohol Research Center 1977–92; NIAAA Research Career Award, 1984–94. Professor Erwin's research has been in biochemical neuropharmacology. Studies have focused on using pharma-



cogenetics as a tool for understanding the neuropharmacology and neurochemistry of alcohol and cocaine. Recent studies have focused on genetic correlations and quantitative trait locus analyses for alcohol- and cocaine-related behaviors and for brain neurotensin and dopamine receptors.

John K. Hewitt

Director of IBG and Professor of Psychology, CU-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

Assistant Professor, Department of Psychology; PhD, Oklahoma State University, 1995. Dr. Hutchison is a clinical psychologist whose research examines mechanisms that underlie substance abuse and dependence (e.g., craving and drug reinforcement), individual difference variables that may moderate these mechanisms, and



behavioral and pharmacological treatments that may moderate these mechanisms with the intention of reducing substance use. His studies employ research techniques that include: Ecological Momentary Assessment using palm pilot computers to collect daily data from participants in the field; novel medications that are useful for teasing apart the pharmacology of substance abuse as well as treating substance abuse; and novel phenotypic and physiological markers. His lab also has an active interest in how stress may moderate the pharmacological and behavioral effects of alcohol and drugs.

Thomas E. Johnson

Professor of Behavioral Genetics, Department of Psychology; 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 web site ibgwww.colorado.edu/tj-lab.

Kenneth Krauter

Professor, Department of Molecular, Cellular, and Developmental Biology; 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, CU-Boulder.

Carol B. Lynch

Professor, Department of Ecology and Evolutionary Biology; PhD, University of Iowa, 1971. Professor Lynch's research interests are the genetic basis of evolutionary adaptation and brain mechanisms underlying adaptive behaviors. Her current research uses a model system, which has been the study of cold adaptation in mice, with



emphasis on nest building. This involves the use of replicated genetic lines of mice that have been selectively bred for over 60 generations for differences in 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; 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 nor-



mal and subnormal development. Heritability of these component processes is being evaluated through twin analyses. Additional projects focus on the use of computer speech feedback in the remediation of reading disabilities.

Bruce F. Pennington

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



studies include developmental dyslexia, attention deficit hyperactivity disorder, and several mental retardation syndromes: early treated phenylketonuria, fragile X syndrome, Down's syndrome, and infantile autism. The long-term goal of this work is to understand how different genetic influences alter brain development to produce the distinct profiles of cognitive strengths and weaknesses found in each of these disorders.

Dennis R. Petersen

Professor of Pharmacology and Pharmacogenetics, School of Pharmacy; PhD, University of Wyoming, 1974; NIAAA Research Scientist Development Award, 1987–92. Professor Petersen's research concerns biochemical pharmacology and toxicology of alcohols and aldehydes. This research focuses on enzyme systems in liver,



kidney, and brain that are involved in the biotransformation of endogenous and exogenous aldehydes. Of particular interest is the interaction of acute or chronic alcohol consumption with these enzymatic pathways. His recent research efforts have emphasized the use of genetics in studying the molecular and biochemical mechanisms underlying the hepatotoxic potential of various drugs and chemicals.

Pennington Laboratory: Front row (left to right): Rachel Tunick, Suzanne Miller, Nancy Raitano, Erin Phinney. Back row (left to right): Christa Hutaff, Richard Blada, Dr. Margaret Riddle, Dr. Bruce F. Pennington, Debbie Porter.

Richard A. Radcliffe

Assistant Professor of Pharmacology, Department of Pharmaceutical Sciences; PhD, University of Colorado Health Sciences Center, 1996. Dr. Radcliffe's research focuses on the genetic and molecular basis of drug and alcohol abuse. Current projects include gene expression microarray analyses of CNS systems involved in behav-



ioral responses to methamphetamine and alcohol, QTL mapping of alcohol-related traits, mutagenesis approaches applied to the study of acute alcohol tolerance, and studies of the nonlinear dynamics of the fear conditioning response.

Soo Rhee

Assistant Professor of Psychology, Department of Psychology, 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

Associate 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 genemapping 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 alcoholism and drug abuse. His laboratory is also involved in the identification of genes important to hominoid evolution, including those that are specific to the human lineage.

Andrew Smolen

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





Tabakoff Laboratory

Toni N. Smolen

Research Associate, Assistant Director, IBG; PhD, University of Colorado, 1981. Dr. Smolen's research interests are in the areas of pharmacogenetics and neuropharmacology. Her current projects use genetically inbred and selected lines of mice in studies of biochemical and neurochemical mechanisms that underlie the development of drug



tolerance and dependence, the role of the adenosine neuromodulatory system in the mediation of the effects of acute and chronic alcohol administration, and drug metabolism in young and aging mice.

Michael Stallings

Assistant Professor, IBG and Department of Psychology; PhD, University of Southern California, 1993. Dr. Stallings' 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.

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, the University of Colorado Health Sciences Center. Professor Tabakoff's research concerns physiological, pharmacological, and biochemical correlates of alcohol and opiate/cannabinoid abuse. Current studies focus on behavioral genetic factors mediating tolerance development; the involvement of brain glutamate receptors in addiction; and the interaction of addictive drugs with adenylyl cyclase signaling in the brain.

Jeanne M. Wehner

Professor of Psychology; PhD, University of Minnesota Medical School, 1976; NIAAA Research Scientist Development Award, 1991–96; 1997– 2002. Professor Wehner is a biochemist whose primary research interests are pharmacogenetics and neurobiology. Current projects include biochemical and genetic studies of learning



and memory, the role of nicotinic receptors in modulation of learning and the role of protein kinase C in alcohol's actions.

Erik Willcutt

Assistant Professor of Clinical Psychology; PhD, University of Denver, 1998. Professor Willcutt's current research focuses on the causes and consequences of attention deficit hyperactivity disorder, learning disabilities, and their comorbidity. He uses genetic linkage and association techniques in studies of families and twins to identify genes that

increase susceptibility to these difficulties.

Visiting Faculty

Juko Ando

Visiting Faculty Scholar, Professor, Faculty of Letters, Keio University, Tokyo, Japan. Dr. Ando has been a member of BGA and is currently conducting the Keio Twin Project in Japan. He is exploring genetic and environmental structure of personality, cognition, and academic achievement.



James R. Wilson

Professor Emeritus, Department of Psychology; PhD, University of California, Berkeley, 1968. Professor Wilson's primary field of specialization is behavioral biology. His research interests have included the endocrinological and genetic bases of maternal behavior, sexual behavior, activity differences, and learning differences in mice; and genet-



ic studies of cognitive functions in humans. Recent work 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.

Postdoctoral Fellows and Research Associates

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

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

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.

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

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 neuro-transmitters 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.

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

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

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

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

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

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

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.

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, U.K., 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 on aging in *C. elegans*.

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



Above: Professional Research Assistant Virginia Fonte from the Link Laboratory. Right: Senior Research Associate Dr. Brad Rikke.



Drs. Jeffrey Lessem and Susan Young from the Hewitt Laboratory.



Research Support: 2002-03 Fiscal Year

Source of Funding	Number of	Fiscal Year	Total Grant
Federal Anencies	Awdius	Dullars	Dullais
National Institute of Asing	6	¢ 916 522	¢ 5 792 962
National Institute of Aging	0	\$ 810,333	\$ 3,782,802
National Institute on Alcohol Abuse	13	2,340,056	15,344,736
and Alcoholism			
National Institute of Child	6	2,583,504	13,528,853
Health and Human Development			
National Institute on Drug Abuse	10	1,685,290	9,790,687
National Institute of Mental Health	7	1,373,530	6,662,163
National Eye Institute	2	333,185	2,352,300
National Institute on Deafness and	1	278,883	1,396,834
Other Communication Disorders			
National Institute of Neurological Disorders and Stroke	1	6,250	100,000
Other			
Abbott Laboratories	1	22,750	85,000
Alzheimer's Association	1	81,920	250,000
Colorado Tobacco Research Program	2	332,250	882,000
The Ellison Medical Foundation	2	154,958	1,073,000
Polis-Schutz Research Gift	1	11,667	70,000
TOTAL	53	\$ 10,020,776	\$ 57,318,435

Expenditures



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

> Sponsored Research University of Colorado at Boulder Fiscal Year 2002–03, p. 25

Research Activities

2002-03 Fiscal Year

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

Aging

The Ellison Medical Foundation Senior Scholar Award– "Detection of Gerontogenes in Mice" (\$873,000; \$109,125), 1/1/99–4/30/03: These studies in mice aim to detect gerontogenes specifying life expectancy, rate of aging, and other life history traits using QTL mapping and mutagenic strategies.

Principal Investigator: Thomas E. Johnson

NIA (AG-012423)–"Transgenic *C. elegans* as Amyloid Disease Model" (\$944,720; \$60,100), 9/1/99-3/31/03: The formation of insoluble, fibrillar protein deposits, designated β amyloid, is central to the pathology of Alzheimer's disease. The major goal of this project is to investigate the biological factors involved in this formation and the toxicity of β amyloid, using *C. elegans* as a model system.

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

NIA (AG-16219)–"Molecular Genetics of Aging in *C. ele*gans" (\$1,347,387; \$341,289), 8/1/99–7/31/03: The focus of this work is to extend and deepen our understanding of the mechanisms underlying the increased life expectancy of long-lived (Age) mutants in the nematode *Caenorhabditis elegans*.

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

NIA (AG-17949)–"Biometrical Analysis of Personality in Adulthood" (\$277,872; \$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; \$81,920), 8/1/01-7/31/04: The major goals of this project are to use co-immunoprecipitation and mass spectrometry to identify intracellular proteins that interact with the human A β peptide in a transgenic *C. elegans* model.

Principal Investigator: Christopher D. Link

NIA (AG-08761)–"Oldest Old Mortality–Demographic Models and Analysis" (\$10,635,276; \$2,221,839), 1/1/99– 12/31/03: The continuation of this program of demographic research on the oldest-old (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 demographic research on the genetic and nondeterminants of longevity, including research on the interaction between fertility and mortality and research on why age-specific mortality decelerates with age.

"IBG Subcomponent" (\$674,012; \$263,094), 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

The Ellison Medical Foundation New Scholar Award (AG-NS-0169-02)–"QTLs Specifying the Retardation of Reproductive Senescence by Dietary Restriction" (\$200,000; \$45,833), 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; \$61,118), 5/1/03-3/31/07: The goal of this project is to understand the cellular and molecular basis of β -amyloid peptide (A β) toxicity using genetic and molecular genetic analysis of transgenic *C. elegans* animals expressing the human A β -peptide.

Principal Investigator: Christopher D. Link

NIA (AG-021037)–"Comparative Modeling of Neurodegenerative Diseases" (\$1,150,374; \$23,694), 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

Alcohol

NIAAA (AA-03527)-"Genetic Approaches to the Neuropharmacology of Ethanol" (\$8,900,388; \$1,105,958), 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" (\$1,640,960; \$282,645): 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; \$67,181): 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; \$75,463): This subproject is conducting studies 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; \$311,230), 3/1/00–2/28/04: These studies will complete the construction of a large number of recombinant inbred strains from the inbred Long Sleep (ILS) and the inbred Short Sleep (ISS) strains of mice and will map, genetically, eight traits involved in the actions of alcohol.

Principal Investigator: Thomas E. Johnson

NIAAA (AA-08940)—"Mapping of Genes Predisposing to Alcohol Sensitivity" (\$1,339,918; \$21,046), 8/1/96– 7/31/02: These studies will position quantitative trait loci (QTL) on the genetic map using a multi-point localization strategy.

Principal Investigator: Thomas E. Johnson

NIAAA (AA-008940)–"Mapping of Genes Predisposing to Alcohol Sensitivity" (\$2,803,556; \$69,288), 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-12301)–"Identification of Genes Regulating Alcohol Consumption" (\$662,550; \$220,837), 7/1/01– 3/31/04: The major goal of this study is to fine map alcohol avoidance behavior in congenic recombinant strains of mice carrying portions of the DBA Alcp1 QTL for alcohol avoidance on a C57BL/6 background.

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

Biotechnology

Abbott Laboratories–"Nicotinic Acetylcholine Receptor Collaboration" (\$85,000; \$22,750), 6/30/98–9/20/02: This collaborative project is testing novel nicotinic compounds for function at natural nicotinic receptors.

Principal Investigator: Michael Marks

The Colorado Adoption Project and Longitudinal Studies

NICHD (HD-10333)–"Determinants of Behavioral Development in Children" (\$1,455,520; \$327,905), 6/1/98–5/31/03: This award, a continuation of a previous grant from NICHD, provides funds to begin culmination of the Colorado Adoption Project. Adopted and control children are being interviewed at 13, 14, and 15 years of age; then, when they are 16 years old, these children are administered the same test battery that was completed by their parents more than a decade and a half earlier.

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

NICHD (HD-36773)–"Nature and Nurture in Social Demography: An Adoption Study" (\$1,609,705; \$268,792), 6/1/98–5/31/03: This project addresses familial influences on educational attainment, family formation choices of young adults, and how the quality of early family relationships shapes adult child-parent relationships.

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

NIMH (MH-43899)–"Transition Into Early Adolescence: A Twin/Adoption Study" (\$996,960; \$201,561), 3/1/00–11/30/03: This grant continues support for testing of adopted and nonadopted children in the Colorado Adoption Project, and twins in the Colorado Twin Study at ages 9 through 12, on a multidimensional battery of psychological measures.

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

NIMH (MH-63207)–"Behavior Genetic Analyses of Executive Functions" (\$1,133,060; \$252,731), 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" (\$20,936,289; \$2,306,535), 2/1/99–1/31/04: The primary purpose of this grant (J. Richard Udry, 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; \$113,716), 7/1/02– 1/31/04: 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; \$29,684), 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 proposed 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

Drug Abuse Vulnerability

NIDA (DA-11015)–"Antisocial Drug Dependence: Genetics and Treatment" (\$7,399,816; \$1,596,140), 8/1/97–6/30/03: This grant supports a Drug Abuse Research Center (Thomas J. Crowley, Principal Investigator). This center was established to study genetic influences on, and treatment of, antisocial drug dependence. The center is a joint program of the Addiction Research and Treatment Service of the University of Colorado Health Sciences Center, the Institute for Behavioral Genetics, and the Department of Molecular, Cellular, and Developmental Biology. It includes six research components and Administrative, Assessment, and Molecular Genetics Cores:

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

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

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

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

"A Longitudinal Adoption Study of Adolescent Substance Experimentation" (\$624,409; \$110,813): This component is designed to assess genetic and environmental influences on experimentation with tobacco, alcohol, marijuana, and other drugs using a longitudinal adoption design. It builds on more than 20 years of data collected by the Colorado Adoption Project (CAP) and focuses on the transmission of substance use and antecedent behaviors such as conduct disorder symptoms, other behavioral problems, and academic achievement difficulties.

Principal Investigator: Robin P. Corley Co-Investigators: John C. DeFries, Gregory Carey

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

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

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

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

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

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

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

"IBG Subcomponent" (\$471,861; \$39,332): 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-11949)–"NYS Family Study: Problem Alcohol Use and Problem Behavior" (\$6,070,829; \$1,384,204), 9/30/00–8/31/05: The proposed research (Delbert S. Elliott, Principal Investigator) will estimate the heritability of cue-elicited craving; will determine whether the polymorphism influences cue-elicited craving using a within-family design that controls for population effects; will examine how the polymorphism interacts with the environment over a two year period marked by a transition from initial tobacco use to dependence; and test whether an association between the polymorphism and the transition to dependence is mediated by the effect of the polymorphism on the development of cue-elicited craving.

"IBG Subcomponent" (\$1,393,102; \$287,236): This project is a major intergenerational and life course study of problem alcohol use and related problem behaviors, including the victimization and perpetration of violent and other criminal offenses, illicit substance use, high risk sexual behavior, and mental health problems.

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

NIDA (DA-14642)–"Progression of Craving and Addiction: Genetic Factors" (\$1,466,216; \$197,771), 9/30/01–6/30/06 (Kent Hutchison, Principal Investigator). Our preliminary research has suggested that the DRD4 VNTR polymorphism influences cue-elicited craving for tobacco and alcohol and that this effect is specifically related to dopamine neurotransmission. This research will estimate the heritability of cue-elicited craving to determine whether the polymorphism influences cue-elicited craving using a withinfamily design that controls for population effects.

"IBG Subcomponent" (\$464,553; \$90,079): This project investigates the heritability of cue-elicited craving for tobacco and whether the DRD4 VNTR polymorphism influences craving during nicotine consumption.

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

Learning Disabilities

NICHD (HD-27802)–"Differential Diagnosis in Learning Disabilities" (\$6,661,612; \$1,314,403), 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; \$179,557): 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; \$293,052): 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; \$242,812): 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; \$184,074): 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; \$134,265): 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; \$280,896): This unit is responsible for coordinating the four research projects as well as maintaining communication among them, ascertaining and scheduling subjects, obtaining questionnaire data, managing a master file of combined data sets, and administering the center budget and other fiscal matters.

Principal Investigator: John C. DeFries Co-Investigator: Richard K. Olson NICHD (HD-38526)–"A Longitudinal Twin Study of Early Reading Development" (\$2,372,158; \$529,004), 3/1/99–2/28/05: This research will assess the etiology of individual differences in prereading and early reading development, and their covariation with individual differences in attention/hyperactivity.

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

NIMH (MH-62120)–"DSM-IV ADHD in an Ethnically Diverse Community Sample" (\$1,692,334; 367,576), 8/1/00–7/31/05: The goal of this project is to assess ethnic group differences in the manifestation of DSM-IV ADHD. A large community sample of children will be ascertained in the Denver metropolitan area to test the internal and external validity of DSM-IV ADHD in an ethnically diverse population that includes a large proportion of African American and Hispanic children.

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

NIMH (MH-62116)–"Behavior Genetics of Attentional and Co-Occurring Problems" (\$147,383; \$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-63941)–"Validity of DSM-IV ADHD Subtypes in a Community Sample" (\$1,679,145; \$340,396), 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; \$278,883), 2/15/02–1/31/07: This project will initiate the first longitudinal twin study of reading disability and its relation with ADHD and other psychopathology.

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

Nicotine

NIDA (DA-003194)–"Genetics of Nicotine Tolerance: Role of Receptors" (\$1,417,325; \$273,221), 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 NIDA (DA-12242)–"Alpha-Conotoxin MII: A Selective Nicotinic Receptor Probe" (\$1,310,348; \$269,708), 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

NIAAA (AA-11156)–"Ethanol, Nicotine, and Brain Nicotinic Receptors" (\$1,106,231; \$277,250), 9/1/00– 8/31/04: The goal of this project is to study alcohol and nicotine interactions, focusing on ethanol effects on brain nicotinic receptors.

Principal Investigator: Allan C. Collins

NIDA (DA-12661)–"Analysis of Nicotinic Cholinergic Systems in Mutant Mice" (\$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

Colorado Tobacco Research Program (2R-033)–"Nicotinic Receptor Mediation of Anxiety and Cognition" (\$771,750; \$257,250), 7/1/00–06/30/05: The goal of the study is to support research that will help us understand the biology of nicotine addiction.

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

NINDS (NS-042196)–"Cognitive Dysfunction After TBI: Role of α 7 nAChRs" (\$775,000; 225,000), 4/1/02–3/31/06: The purpose of this study is to understand the neurochemical alterations that occur following damage to the CNS in order to develop therapeutic strategies to prevent and/or remediate the detrimental effects of trauma.

Principal Investigator: James Pauly

"IBG Subcontract: Nicotinic Receptor Regulation of Cerebellar Development" (\$100,000; \$6,250): This study evaluates the effects of chronic nicotine administration on cognitive deficits induced by chronic brain injury.

Principal Investigator: Michael Marks

NIAAA (AA-13018)–"Role of Nicotinic Receptors in Effects of Alcohol" (\$2,371,673; \$458,582), 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 Colorado Tobacco Research Program (2I-034)–"Candidate Genes for Tobacco Use and Nicotine Dependence" (\$110,250; \$75,000), 7/1/02–12/31/03: 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; \$47,333), 5/1/03–6/30/07: This is a program project that 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

Statistical Models

NEI (EY-12562)–"Variance Components Models for Mapping QTLs" (\$1,620,719; \$281,011), 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-19918)–"Workshop on Methodology of Twin and Family Studies" (\$462,656; \$97,326), 9/1/98–8/31/03: The major goal of this project is to hold a series of international workshops on the methodology of twin studies at the Institute for Behavioral Genetics in Boulder, Colorado.

Principal Investigator: John K. Hewitt

Research Career Awards and Fellowships

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

Awarded to: Allan C. Collins

NIAAA (K02-AA-00195)–"Identifying Genes Predisposing to Alcoholism" (\$510,575; \$102,115), 9/1/99–8/31/04: This award allows the principal investigator to pursue his research on the genetic basis of alcohol action.

Awarded to: Thomas E. Johnson

NIAAA (K02-AA-00141)–"Ethanol's Actions in Gamma-PKC Null Mutants" (\$491,918; \$8,303), 8/1/97-7/31/02: This award allows the principal investigator to further her investigations into the role of γ -PKC in the development of alcohol dependence.

Awarded to: Jeanne M. Wehner

NIDA (K01-DA-13956)–"Causes of Comorbidity: Substance Use Disorder, ADHD & CD" (\$498,497; \$103,648), 9/1/01–8/31/06: This award allows the PI to examine the causes of comorbidity among substance use disorders (SUD), attention-deficit/hyperactivity disorder (ADHD), and conduct disorder (CD).

Awarded to: Soo Rhee

NIMH (K01-MH-01865)–"Executive Function: Links to Drug Use and Psychopathology" (\$550,625; \$107,800), 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

NIDA (F32-DA-14152)–"Genetic Studies of Nicotine Tolerance-Withdrawal" (\$75,028; \$33,497), 5/1/01–4/30/03: This postdoctoral fellowship award is to examine genetic influences on effects of chronic nicotine in mice, including withdrawal and changes in nicotinic receptor function.

Awarded to: Sarah E. McCallum

NIAAA (F31-AA-13350)–"Plieotropy for Alcohol-Related Phenotypes" (\$47,886; \$23,942), 9/1/01–8/31/03. This predoctoral fellowship will provide a better understanding of the genetic and neurological systems underlying alcohol abuse.

Awarded to: Jeremy C. Owens

NIAAA (F32-AA-13465)–"Nicotinic Receptor Polymorphisms and Ethanol Sensitivity" (\$84,740; \$39,670), 5/7/02–5/6/04. This project uses classical genetics, null-mutation technology, neurochemistry, and behavioral studies to assess the possible role of a genetic polymorphism in the nicotinic acetylcholine receptor in mechanisms of nicotine and alcohol abuse.

Awarded to: Christopher M. Butt

IBG Highlights Longitudinal Twin Study

The Longitudinal Twin Study (LTS) is grounded in its history and the work of the present and former IBG principal investigators, John DeFries, John Hewitt, Robert Plomin, and David Fulker, along with numerous internal and external collaborators and co-investigators. The project was launched more than 20 years ago when development funds from the University of Colorado were used to explore the possibility of working with the state Department of Health to identify and contact parents of twins. Successful cooperation with that agency led in 1983 to a 3-year award from NICHD to use the twin method to investigate the reliability of measures of infant cognition. This first LTS project set the tone for the ensuing years of the study as IBG researchers collaborated extensively with notable experts in this field, Marshall Haith, PhD, and Joseph Fagan, PhD.

Two years later, the MacArthur Foundation provided its first seven years of support to LTS for testing children in their homes and the laboratory at ages 14, 20, 24, and 36 months. Later grants allowed for continued testing of the sample through age 7. The MacArthur project was remarkable for both the breadth and depth of its measures. Renowned researchers, including Robert Emde, MD, Jerome Kagan, PhD, J. Steven Reznick, PhD, and Carolyn Zahn-Waxler, PhD, collaborated in the development of assessments conducted both in the families' homes and at our laboratories measuring cognition, personality, and social functioning. During this period, IBG research associates played critical roles in ensuring the project's success: Joanne Robinson, PhD, was the project coordinator and Robin Corley, PhD, became the data manager, a position that has continued to the present. The research design and many of the results from the first MacArthur grant have been published as a book: Infancy to Early Childhood: Genetic and Environmental Influences on Developmental Change, Emde, R., & Hewitt, J.K. (Eds.), Oxford University Press, 2001.

From its earliest days, some LTS assessments were designed to replicate key elements of IBG's other major longitudinal study, the Colorado Adoption Project (CAP). Beginning at age 4, complete CAP protocols were used in addition to the ongoing MacArthur measures. From ages 9–16, CAP and LTS assessments have been identical. These assessments are currently



IBG/CU-Boulder Family Studies Staff: Back row: Annie, Amy, Drew, Rob, Beth, Kerry Margaret, Patricia, Blake, and Sally Ann. Middle row: Rebecca, Scott, Matt, Carrie, Alex, Jen, and Corrine. Front row: Dan, Heather, Leza.

under the direction of Sally Wadsworth, PhD. The merging of these projects has provided researchers at IBG with a unique opportunity to cross-validate the assumptions of the twin study and the adoption study while harnessing the power of each. There is no better approach to the investigation of the genetic and environmental etiology of individual differences than the longitudinal adoption design combined with the longitudinal study of adopted and nonadopted pairs of siblings and pairs of identical and fraternal twins. Separately, each design has its strengths, but also its weaknesses. Together the strengths reinforce each other and the weaknesses are minimized.

The older twins in the LTS are now participants in an NIMH funded study of executive functioning, a relatively new and rapidly growing field of research. Executive function refers to a collection of varying cognitive abilities including planning ahead and problem solving, shifting between actions easily, initiating goal-directed behavior, and regulating attention in order to complete tasks. It is believed that executive functioning is central to an individual's ability to concentrate and is tied to intelligence and self control. The study of executive function is another way to look at how individuals perceive and act in the world. By studying executive functioning we may be able to understand more about complex human behaviors, as well as find correlations between levels of functioning and certain traits or disorders.

During the session in which the executive functioning assessments are administered, the twins also participate in a NIDA funded study of "Heritable Early Indicators of Risk for Drug Dependence." In this project, the twins were initially interviewed at age 12 and are reinterviewed at age 17. Among other important results, the findings from this study have played a significant role in contributing to our understanding of the links among different aspects of problem behavior such as conduct disorder, attention deficit hyperactivity disorder, substance experimentation, and novelty seeking by refining the concept of a latent behavioral disinhibition trait (Young, S.E., Stallings, M.C., Corley, R.P., Krauter, K.S., & Hewitt, J.K. (2000). Genetic and environmental influences on behavioral disinhibition. *American Journal of Medical Genetics*, 96, 684–695).

Today researchers such as Akira Miyake, PhD, of the executive function study or Susan Young, PhD, and Soo Rhee, PhD, of the study of substance abuse turn to early measures such as the videotaped assessment of inhibition developed by Dr. Kagan to explore early antecedents of present behavior of current societal concern. In the research programs now underway, we routinely collect and analyze DNA for use in candidate gene studies such as exploring the role of the variations in the dopamine transporter genes in relation to externalizing behavior problems (Young, S.E., Smolen, A., Corley, R.P., Krauter, K., DeFries, J.C., Crowley, T.J., & Hewitt, J.K. (2002). Dopamine transporter polymorphism associated with externalizing behavior problems in children. American Journal of Human Genetics, 114, 144–149). Thus, as the project continues to move forward, we appreciate the foresight of the initial investigators who developed the LTS that has proven to be of great benefit to contemporary investigations.

> Sally Ann Rhea Project Coordinator

Additional information about the Longitudinal Twin Study, including a list of published research articles, is available at ibgwww.colorado.edu/lts.

Genetic and Other Individual Differences in Substance Abuse: Treatment and Prevention

The long-term objective of our research is to develop more effective treatment and prevention efforts that target behavioral disorders with significant health consequences, such as tobacco dependence, alcohol dependence, and obesity. Not coincidentally, these behavioral problems are the leading causes of the mortality, morbidity, and socioeconomic costs associated with cancer, cardiovascular disease, liver disease, and diabetes. The treatment and prevention efforts currently available are only modestly effective. To develop more effective efforts, we need a better understanding of the mechanisms that influence these behavioral problems. Thus, a necessary first step and the immediate objective of our research is to advance our understanding of the genetic, biological, and behavioral determinants of health behavior broadly defined.

The majority of our work has been focused on addictive behavior, specifically alcohol and tobacco dependence. Recent reviews of the literature suggest that repeated administration of alcohol and drugs produces long-term neuronal changes in the brain structures that are involved in appetitive motivation. This process, also known as incentive sensitization, results in the development of craving for and loss of control over alcohol and tobacco use. To date, my research has focused on the development of a comprehensive experimental paradigm that is designed to examine the behavioral sequellae of these neuronal changes and the genetic factors that influence the progressive development of these changes. This paradigm allows for the systematic manipulation of specific biological and behavioral parameters that are thought to be related to addiction, and also allows for the systematic analysis of genetic factors that may explain individual differences in these mechanisms. A more refined understanding of these mechanisms and the role of genetic factors will aid in the identification of individuals who are at risk with respect to a specific mechanism (e.g., alcohol cueinduced activation of the orbitofrontal cortex) and will guide efforts to match those individuals with treatments that address their particular vulnerability. Thus, the findings from these studies are expected to expand the knowledge base and set the stage for the development of more effective biological and behavioral interventions for addictive behavior.

One of the major findings of a recently completed project was that a variable number of tandem repeats (VNTR) polymorphism in the dopamine DRD4 gene influences the expression of craving after a priming dose of alcohol. In addition, olanzapine (a medication that blocks D4 dopamine receptors) generally attenuates craving, and this effect appears to be more pronounced among individuals with this genetic vulnerability (Hutchison et al., 2003). Based on this preliminary evidence, we are currently conducting a treatment study that combines psychosocial treatment with a low dose of olanzapine among a group of treatment-seeking alcoholics.

One of the primary limitations of my research to date has been the lack of a reliable measure of activation of regions of the brain that putatively control appetitive motivation. To address this limitation, we have begun to incorporate functional neuroimaging into our research. A necessary first step was to export our experimental paradigm to an imaging environment. After some experimentation, we developed a protocol to administer trace amounts of alcohol (enough to elicit craving). The specific objectives of this research are to refine our measurement of cue-elicited craving with an assessment of activation of brain structures that putatively underlie appetitive motivation (e.g., orbitofrontal cortex, nucleus accumbens, amygdala), to examine whether subjective craving is related to activation of these structures, to determine whether a genetic factor (e.g., the DRD4 VNTR) moderates this activation, and to determine whether the activation is pharmacologically related to dopamine activity at dopamine receptors. We hope to receive funding to conduct this study in the near future.

> Kent Hutchison Faculty Fellow Institute for Behavioral Genetics

See lab photos on page 40

Animal Production

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

Ongoing selection studies include various lines of mice that differ in sensitivity to alcohol (projects supported by NIAAA grants to Dr. V. Gene Erwin and the University of Colorado Alcohol Research Center), and the development of congenic lines by intergressing various QTLs on LS or SS inbred backgrounds (supported by NIAAA grants to Dr. Thomas E. Johnson).

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

- A/Ibg, BALB/CBy Ibg, C57BL/6Ibg, DBA/2Ibg, C3H/2Ibg, & 129 Svev/Taconics inbred strains, C58/J
- Heterogeneous Stock (HS)
- Open-field Activity lines
- Long-Sleep (LS) and Short-Sleep (SS) selected lines
- ILS and ISS inbred strains
- LSXSS recombinant inbred strains
- Nesting behavior lines
- PKC null mutants
- ISS X ILS recombinant inbred strains
- High Acute Functional Tolerance (HAFT 1) &
- Low Acute Functional Tolerance (LAFT 1)

- Congenic ILS.Lore Short & ISS.Lore Long Bilineal Selection
- B6.D2 Congenic for voluntary ethanol consumption
- D2.H2 Nicotinic Congenics
- Nicotinic Knockouts

Faculty Director:

Allan C. Collins

Lab Supervisor:

Jerry Salazar

Staff:

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

Professional Research Associates:

Matt Battaglia Rowena Clark Vanessa Crittenden Christine Martin Cathy Ruf

Student Assistants:

Yoo Jung Choi Anthony Giordano John Hays Heather Henderson



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

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 heterogeneous 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.



IBG Molecular Biology Core Facility: Graduate student Brett Haberstick assists visiting student Krishna Tobon with her molecular genetic studies on the monoamine oxidase A promoter polymorphism.

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, **Ouantitative 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 also to the appropriate department for application information. For application forms for admission into the IBG training program, or for further information, write to: Director, Behavioral Genetics Training Program, Institute for Behavioral Genetics, University of Colorado at Boulder, 447 UCB, Boulder, CO 80309-0447. If you prefer to call, the telephone number is 303-492-7362.

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*.

Robert Buchwald (PhD program, ecology and evolutionary biology). Genetic diversity and evolution of nestmate recognition pheromones in bees.

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

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

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

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

Christie Hartman (PhD program, psychology). Genetic and environmental contributions to externalizing behavior, cognitive ability, and the relationship between the two.

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

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

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

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

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

Visiting Students

Visiting research students in the Collins' lab from the Department of Biology and Biochemistry at the University of Bath, Bath UK:

Robert (Rob) W. B. Brown, April–October 2002 Alexander (Alex) Flynn, March 3–Sept. 19, 2003

These students are in an undergraduate Master's degree program in Biochemistry at the University of Bath, during which time they also earn the equivalent of a Bachelor's degree. To enter this program, students must have outstanding qualifications. The program involves increased and more difficult course work and requires two placements of not less than 22 weeks each during the second and third years of the course. When they graduate they can go directly to the PhD degree program. IBG is the second placement for both Robb and Alex. Both of them did their first placement at Novartis Pharma AG in Switzerland.



Rob Brown presents a poster detailing the research he conducted under the supervision of Dr. Paul Whiteaker at IBG.

Krishna Tobon, undergraduate student, William Paterson University. Krishna was involved in studies of the potential association of a monoamine oxidase A promoter polymorphism with development of conduct disorder in adolescents. (Krishna is pictured on page 26.)

Courses Taught

Fall 2002

Gregory Carey

Michael D. Breed	EPOB 5310, UCB EPOB 2650, UCB	Ecology and Conservation Honors Environmental Biology	
Gregory Carey	PSYC 3102/5102, UCB	Behavioral Genetics	
Richard A. Deitrich	PHCL 7605, UCHSC	Ethics in Research	
Kent Hutchison	PSYC 3313, UCB	Psychopathology	
Bruce F. Pennington	PSYC 4525, DU	Developmental Neuropsychology	
Richard Radcliffe	TXCL 7326, UCHSC	Physiology I	
James Sikela	DSBS 6600, UCHSC	Dental Pharmacology	
Michael C. Stallings	PSYC 5112, UCB	Concepts in Behavioral Genetics	
Boris Tabakoff	DSBS 6600, UCHSC PHCL 7600, UCHSC PHCL 7605, UCHSC	Dental Pharmacology Frontiers in Pharmacology Ethics in Research	
Jeanne M. Wehner	PSYC 7102, UCB	Seminar in Behavioral Genetics	
Spring 2003			
Michael D. Breed	EPOB 3240, UCB	Animal Behavior	
Gregory Carey	PSYC 5741, UCB	General Statistics	
Allan C. Collins	PSYC 4132/5132, UCB	Behavioral Neuropharmacology	
John C. DeFries	PSYC 5122, UCB	Quantitative Genetics	
John K. Hewitt	PSYC 7102, UCB	Seminar in Behavioral Genetics	
Kent Hutchison	PSYC 5423, UCB	Research Problems in Clinical Psychology	
Richard Olson	PSYC 4521, UCB PSYC 4001, UCB	Critical Thinking: Genes and Environment Honors Seminar	
Richard Radcliffe	TXCL 7327, UCHSC	Physiology II	
Soo Rhee	PSYC 3102, UCB	Behavioral Genetics	
Michael Stallings	PSYC 3102, UCB PSYC 5112, UCB	Behavioral Genetics Concepts in Behavioral Genetics	
Boris Tabakoff	PHCL 6000, UCHSC PHCL 7620, UCHSC	Medical Pharmacology Graduate Pharmacology	
Erik Willcutt	PSYC 3313, UCB PSYC 5453, UCB	Psychopathology Developmental Psychopathology	
Summer 2003			
Michael D. Breed	EPOB 4630, UCB EPOB 4350/5350, UCB	Field Techniques in Environmental Science Field Studies/Field Biology	

PSYC 3102, UCB

Behavioral Genetics

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Colloquia and Informal Talks

Summer 2002

Irwin Waldman (Professor, Department of Psychology, Emory University). Dopamine Genes and Children's Disruptive Behavior Disorders.

Bill Gregory (PhD, Visiting IBG Research Associate, University of Edinburgh, Scotland). Bioinformatic Analyses of Gene Families in Parasitic Nematodes.

Fall 2002

Christopher Link (Research Associate, Institute for Behavioral Genetics, University of Colorado at Boulder). Transgenic Modeling of Neurodegenerative Diseases.

Richard Radcliffe (Assistant Professor, School of Pharmacy, University of Colorado Health Sciences Center and Faculty Fellow, Institute for Behavioral Genetics, University of Colorado at Boulder). Applications of Gene Expression Microarrays in the Study of Quantitative Behavioral Traits.

Spring 2003

Andrea Beckel-Mitchener (Research Scientist, Beckman Institute, University of Illinois, Urbana-Champaign). From Genes to Behavior: Molecular Contributors to Fragile X Mental Retardation Syndrome.

Beth Bennett (Research Associate, Institute for Behavioral Genetics, University of Colorado at Boulder). The LXS RI Panel: An Incredible Mapping Resource.

Marissa Ehringer (Research Associate, Institute for Behavioral Genetics, University of Colorado at Boulder). The Study of Candidate Genes in Mice and Humans: Using the Genomics Resources.

Jerry Stitzel (Assistant Research Scientist, Department of Psychiatry, University of Michigan Medical School). Molecular Genetic Approaches Towards Understanding the Behavioral and Physiological Effects of Nicotine.





Research and Administrative Staff

Research

Lindly Alston Sara Bailey Melissa Barba-Espinoza Matthew Battaglia Melissa Beckner Mary Beeson Todd Bizzigotti Adrienne Blackwood Stephanie Bogott Susan Boorman Leslia Bova Robert Brown Phyllis Carosone-Link Hilda Rowena Clark Leza Clymer Rachael Cole Mark Conner Kimberly Corley June Crenshaw Vanessa Crittenden **Robert Curtis** Patricia Davis Brendan DePue Antonio DiLeo Linda Drullinger Barbara Elliott Julie Ernisse Margaret Fatovic Danelle Ferguson Alex Flynn Mary Ellen Flynn Virginia Fonte Kari Gilmore Elizabeth Glasser Elizabeth Gooding Lena Gordon Kari Gottschling Andrew Gross Terry Grupp Jessica Hall Sena Hitt-Laustsen Dina Huber Jacqueline Hulslander Scott Hutton George Jayne Anne Johnson Elizabeth Johnson-Wold Peter Jones Nicole Kandel Billy Keith

Jason Keller Nathan King Colin Larson Eric Laudenslager Amy Ledbetter Elizabeth Legg Caren Lowe Christine Martin Natalie Meinerz Lauren Milner Jill Miyamoto Ryan Morrow Christina Nelson-Goens Nicole Neubauer Lara Pallas Cyrus Peterson Nancy Phares-Zook Kathryn Player Jonathan Potter **Benjamin Pressley** Sally-Ann Rhea Noel Rieder Julia Rifkin Taylor Roy Amy Rudolph Cathy Ruf Daniel Ryan Scott Sabella Jerome Salazar **Elizabeth Siewert** Isaac Sisneros Abigail Smith Margaret Spring Justin Springett Tara Stahla Gretchen Stein Andrew Taft Pat Tedesco Kerry Thomson Patricia Townsend Ingrid Ullring William Van Morter Natascia Ventura Angela Villella Satori Waddle Laurel Wade Larisa Wilder Corrine Wright Jean Yu Jennifer Ziemba

Student Hourly

Sierra Atkinson Gail Bleakney Karley Bloom Joshua Brooks Kelsy Lee Cain Jerod Cox Kevin Cox Avni Doshi Jennifer Drapeau Margaret Enion Renee Ferguson Jaclyn Francese Vishwas Ganesan Anthony Giordano Scott Gorman Sybil Greenberg Julie Kachinski Jennifer Kanaley Jessica Kaplan Christopher Leeds Erin Marshall Tristan McClure-Begley Jessica Michael Alison Mickiewicz Richard Moore Brigid Moriarty Carie Muhlhauser Sarah Nakata Isaac Newland Erin Nix Zach Noteman Erin Ochman **Kimberly Pierce** Theodore Pokrywka Pidchaya Prindavong Brian Rabern Krystle Sarkissian Renee Schmitz Amit Singh Tricia Torgensen Chelsea Trinka Ari Van Schilfgaarde Mark Windland

Administrative

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

Publications

July 1, 2002–June 30, 2003

Adams, J.B., Heath, A.J., Young, S.E., Corley, R.P., Hewitt, J.K., & Stallings, M.C. (2003). Relationships between personality and preferred substance and motivations for use among adolescent substance abusers. *American Journal of Drug and Alcohol Abuse*, 29, 691-712.

Anchordoquy, H.C., McGeary, C., Liu, L., Krauter, K.S., & Smolen, A. (2003). Genotyping of three candidate genes after whole-genome preamplification of DNA collected from buccal cells. *Behavior Genetics*, *33*, 73-78.

Anton, R.F., Lieber, C., & Tabakoff, B. for the CDTect Study Group (2002). Carbohydrate-deficient transferrin and γ -glutamyltransferase for the detection and monitoring of alcoholic use: Results from a multisite study. *Alcoholism: Clinical and Experimental Research*, 26,1215-1222.

Balogh, S.A., Bowers, B.J., Logue, S.F., Ernisse, J., LaBarca, C., Lester, H.A., & Wehner, J.M. (2003). α4containing neuronal nicotinic receptors modulate appetitive learning. *Society for Research on Nicotine and Tobacco*. (Abstract)

Balogh, S.A., Owens, J.C., Butt, C.M., Wehner, J.M., & Collins, A.C. (2002). Animal models as a tool for studying mechanisms of co-abuse of alcohol and tobac-co. *Alcoholism: Clinical and Experimental Research*, *26*, 1911-1914.

Balogh, S.A., Owens, J.C., McClure-Begley, T.D., Paylor, R., Beaudet, A., Collins, A.C., & Wehner, J.M. (2003). α7 nicotinic receptor subunit null mutant mice exhibit altered responses to alcohol. *Society for Research on Nicotine and Tobacco*. (Abstract)

Balogh, S.A., Picciotto, M., Paylor, R., Booker, T.K., Beaudet, A., Heinemann, S., Collins, A.C., & Wehner, J.M. (2002). Contextual fear conditioning in neuronal nicotinic receptor null mutant mice: Effects of nicotine and ethanol. Program No. 9.11, *Society for Neuroscience* (online). (Abstract)

Balogh, S.A., Radcliffe, R.A., Logue, S.F., & Wehner, J.M. (2002). Contextual fear conditioning in C57BL/6J and DBA/2J mice: Context discrimination and the effects of retention interval. *Behavioral Neuroscience*, *116*, 947-957.

Balogh, S.A., & Wehner, J.M. (2003). Inbred mouse strain differences in the establishment of long-term fear memory. *Behavioural Brain Research*, *140*, 97-106.

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Bishop, E.G., Cherny, S.S., Corley, R., DeFries, J.C., & Hewitt, J.K. (2003). Developmental genetic analysis of general cognitive ability from 1 to 12 years in a sample of adoptees, biological siblings, and twins. *Intelligence*, *31*, 31-49.

Boada, R., Willcutt, E.G., Tunick, R.A., Chhabildas, N.A., Olson, R.K., DeFries, J.C., & Pennington, B.F. (2002). A twin study of the etiology of high reading ability. *Reading and Writing: An Interdisciplinary Journal, 15,* 683-707.

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Davis, C.J., Fisher, S.E., Francks, C., MacPhie, I.L., Gayán, J., Smith, S.D., Cardon, L.R., Pennington, B.F., Olson, R.K., Monaco, A.P., & DeFries, J.C. (2002). Bivariate linkage analyses for reading difficulties and rapid naming. *Behavior Genetics*, *32*, 462. (Abstract)

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Top: Hutchison laboratory researcher Erica Sandman prepares fellow researcher Patrick Finan for a startle trial, which measures facial muscular reactivity to static sounds, before and after smoking.

Bottom: Patrick Finan demonstrates how research participants are tested for cue-elicited craving. Participants in these studies are asked to light and hold a cigarette, or hold and smell a glass of beer, for a short period of time prior to smoking or drinking. Following the drug cue, they are asked to complete a questionnaire to determine the strength of their craving.

See Research Highlights page 24.

Many thanks to: Debbie Aguiar, Dawn Caillouet, Kathy Huckfeldt, and Sean Shelby for their assistance in the preparation of this Annual Report.