

*to your health*



**abmrf**

THE FOUNDATION FOR  
ALCOHOL RESEARCH

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[www.abmrf.org](http://www.abmrf.org)

**abmrf**

THE FOUNDATION FOR ALCOHOL RESEARCH

Annual Report 2006

*salud*

spanish

*santé*

french

*sanitas bona*

latin

*sláinte*

irish

no matter how you say it, the goal is clear:

abmrf is committed to *nurturing significant research* in the area of health and alcohol.

*to your health!*

# our vision

To be a premier private foundation that fosters and communicates research to understand the effects of alcohol on health and behavior

# our mission

To achieve a better understanding of the effects of alcohol on the health and behavior of individuals,

To provide the scientific basis for prevention and treatment of alcohol misuse and alcoholism,

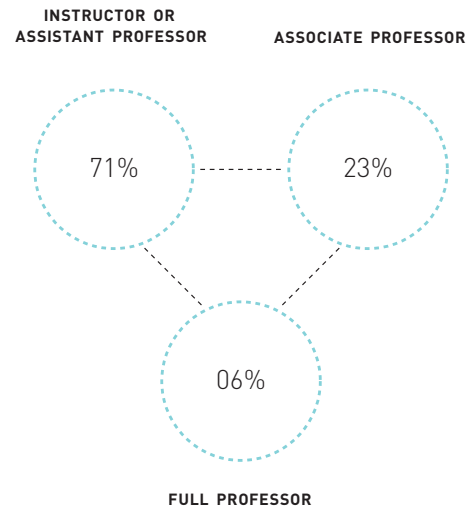
To fund innovative, high quality research,

To support promising new investigators,

To communicate information effectively with the research community and other interested parties.

## The Year IN REVIEW

### Academic Rank of 2006 Grantees



### The Grant Program

The mission and vision of ABMRF centers on its grant program. Twice during the year, promising investigators, most in the early stages of their careers submit grant proposals for consideration by the Foundation's Advisory Councils. With a dedication to nurturing innovative, high-quality research in alcohol and health, specifically in the important areas of biomedical and sociobehavioral science, the Medical Advisory Council and the Behavioral and Social Advisory Council identify and select the most deserving projects to fund, setting in motion an established pattern of enhancing a career or creating a synergistic effect for related research in the field. In the concluding months of 2006, ABMRF successfully embarked on its 25th year as a premier, private foundation established to foster and achieve a better understanding of the effects of alcohol on health and behavior through its system of funding research.

In 2006, the Foundation supported a number of innovative projects with exciting research goals that included providing insights for the development of drugs to treat alcohol abuse disorders, understanding how genetic variations affect drinking behavior, and creating more effective interventions to reduce high-risk drinking behavior in college athletes. From a total of 128 applications submitted during the year, the Behavioral and Social Advisory Council approved 17 projects for funding, 8 of which were for new or revised applications. The Medical Advisory Council approved 7 new or revised projects, for a combined total of 15 approved applications. Considering the academic rank of the 2006 grantees, 71 percent were at the level of instructor or assistant professor, 23 percent were associate professors, and 6 percent were full professors who were well established in other fields and brought their expertise to research questions concerned with alcohol.

A listing of the grant projects supported in 2006, as well as more detailed project summaries and references to publications resulting from Foundation funding, are featured within this Annual Report. Each of these sections reflects both the scope and quality of the important work generated by ABMRF support.

### Conferences and Meetings

The 34th International Medical Advisory Group (IMAG) Conference was hosted in Copenhagen, Denmark, at the Skt. Petri Hotel by the Brewers of Europe, with scientific program planning provided by the European Research Advisory Board (ERAB), an organization started in 2003 and based on many of the principles as ABMRF. Many of the scientific presentations featured work by ERAB grantees. The two-day IMAG program featured five major sessions in the areas of Alcohol, Vascular Disease and Lifestyle; Neuroscience–Alcohol and Nicotine Interactions; Alcohol, Cancer and Epidemiology; Genetics; and Young People and Drinking.

ABMRF is proud of our continuing commitment to the Research Society on Alcoholism (RSA). The Foundation provided funds for the 2006 RSA Annual Meeting, held in Baltimore, Maryland, from June 23-28. In addition to our customary contribution in support of travel awards for Canadian and U.S. graduate students, to recognize that the conference was taking place in our home town, ABMRF provided an additional contribution in support of the Opening Reception. To mark the beginning of our celebration of our first 25 years of funding alcohol research, a large poster was displayed at the reception and throughout the meetings listing the names of almost 450 current and former grantees, many of whom are RSA members, to recognize their contributions to the field. The RSA meeting was attended by over 1,400 delegates. Our travel awards helped to fund the travel for a handful of the 100 graduate students and post-doctoral fellows who attended the Baltimore meeting.

The Foundation also provided modest support to the International Society for Biomedical Research on Alcoholism (ISBRA) for the ISBRA 2006 World Congress on Alcohol Research that was held at the Sofitel Wentworth Hotel in Sydney, Australia, from September 10-13. The relationship with ISBRA is strong; ABMRF has supported the organization since the First Congress was held in 1982, and many of our leaders and "alumni" independently belong to ISBRA.

### Communications

ABMRF's website enjoyed some advances in 2006, as an intranet service was initiated for Board and Council member use. The intranet feature allows ABMRF to share updated outgoing information and facilitates an exchange of information from those we serve.

In addition to these communications, a weekly ABMRF Research Alert service continues to provide a timely account of major press reports and research on alcohol studies to a growing list of subscribers. The communications department monitors national and international news and sends pertinent reports by email. Original research articles are often obtained to provide more complete background and perspective on the news stories. The alerts include a brief description of the research, the article reference and a link to the abstract or full-text article if available. Research Alerts make special mention whenever an ABMRF-funded research project is featured.

## President's REPORT



**Mack C. Mitchell, Jr., M.D.**  
President, ABMRF

The concluding months of 2006 marked an important milestone for ABMRF: The start of our 25th year. As ABMRF begins its celebration of 25 years of funding research on the effects of alcoholic beverages on health and behavior, those of us who work with the Foundation have taken the opportunity to re-examine our vision and purpose. ABMRF was fortunate to have been founded by a visionary group of leaders in the brewing industry and academic medicine. They reasoned that a partnership between the brewing industry and academic medicine would offer the opportunity for leaders in both fields to work collaboratively toward understanding the effects of alcoholic beverages on health and behavior. They were deeply committed to developing the scientific basis for understanding what effects the consumption of moderate amounts of alcohol would have on health and exploring why the majority of people consume alcoholic beverages in moderation, while a few drink excessively. This partnership offered a platform for sharing ideas in a collegial forum and for the support of promising investigators in the field of alcohol research.

As we reflect on our beginnings and on the role that ABMRF plays in supporting alcohol research today, it is clear that we have succeeded in promoting collaboration between industry and academia. We have accomplished that goal while preserving the integrity of the grant review process by maintaining strict separation between the source of our support and decisions regarding which grant proposals are most meritorious and innovative. Although much of

the support for research in the early years of ABMRF was given to scientists with established records of excellence, more recently we have focused on investigators who are relatively new to the field of alcohol research, but show promise in becoming major contributors and future leaders in the field. Throughout the history of ABMRF, we have encouraged open communication of all research findings through publication in peer-reviewed scientific journals. The process of peer review of publications has proven to be a mechanism for assuring quality and independence in science. We also support meetings that promote open exchange and discussion of the findings from research. All of these efforts are reflected in the mission of the ABMRF and serve as a guide to all of our planning and decision making.

Over the last 25 years, the ABMRF has contributed nearly \$39,000,000 in support of research and conferences exploring the effects of alcoholic beverages on health and behavior. We have supported more than 450 individual scientists many of whom are now leaders in the field. Although the individual awards are modest in size, for many investigators they come at a crucial time in their careers when they are establishing their independence and often embarking on novel and creative paths that will help us all to understand better how alcohol affects our health and behavior. By having a senior group of scientists as members of our Advisory Councils we are in a unique position to identify promising young scientists at an early stage in their careers. Many of these young scientists have told us how important the awards from ABMRF are, crediting the grant with enabling them to become independent investigators. Over time, we have seen the legacy continue as many of those who were grantees in the past have become highly respected leaders in the field with many serving as members of our Advisory Councils. The tradition of giving back time and wisdom to identify the most talented investigators who are most likely to conduct innovative research is an important part of the culture of science and academic medicine. It is one of the values that we endorse heartily. As we consider the next 25 years,

we are interested in exploring other ways that the ABMRF and its council members can help to mentor these young scientists also.

Since its inception in 1982, ABMRF has supported research concerned with all aspects of the effects of alcohol consumption. The research portfolio includes both behavioral and biomedical research in relatively equal amounts. Furthermore, ABMRF has supported studies to understand how the moderate consumption of alcoholic beverages affects our health so that we will address the questions of the majority of those who drink alcoholic beverages. Much of this work has shown clearly that those who drink in moderation enjoy better health than those who drink excessively or than those who abstain completely from drinking. Of the research projects we fund, we continue to address problems related to excessive consumption of alcohol, particularly insight into why some people seem to be more vulnerable than others. In recent years, our grantees have been particularly concerned with the effects of alcohol consumption in certain populations such as underage youth, who may be uniquely vulnerable to particular effects of alcohol. The explanation for why moderate amounts of alcohol are beneficial to health while too much is clearly harmful remains poorly understood but provides a potentially fruitful area for future studies.

ABMRF has been fortunate to attract many of the leaders in the alcohol research community to serve on its Advisory Councils and Board of Trustees. The Foundation has benefited tremendously from the collective wisdom of these individuals who have given countless hours of their time to support its activities. The combined accomplishments of the grantees, council members and Board members are very impressive. Forty-eight percent of both the Distinguished Researcher and Young Investigator Awards given by the Research Society of Alcoholism went to investigators who were supported by ABMRF or who served on its advisory councils. Of the four lifetime achievement awards given by RSA, one was given to Dr. Thomas B. Turner, the founder and first President of ABMRF, and the other was given to a

former grantee. In addition, one third of the Seixas Awards for service went to individuals with an ABMRF connection, including Dr. Al Pawlowski who was vice president of ABMRF until his retirement in 2001. These awards illustrate one of the principles that Dr. Turner followed during the initial establishment of the ABMRF. He believed strongly that the long-term success of ABMRF depended on the people who were involved with the Foundation.

As we embark on our 25th year and review our history of supporting research, we must realize that despite our past success, many challenges remain for the future. To continue the work that we have begun will require new sources of funds in addition to the continued support of those members of the brewing industry who have generously contributed in the past. The cost of research continues to rise beyond the usual increases due to inflation. If we are to encourage young investigators to pursue careers in alcohol research, ABMRF and other organizations will need to provide a steady source of support to help these studies begin. At the November meeting, the Board of Trustees endorsed a campaign to secure additional funds to ensure that its mission will be fulfilled in the future. These additional funds will not only restore the erosion of our funding by inflation, but will also provide opportunities for scientists to develop new directions in research, particularly through interdisciplinary studies, and ensure continued strong leadership in the field. As a measure of its commitment, the Board approved a new position of Director of Development for the Foundation. With the assistance of members of the Board and the newly created Development Committee, this person will direct our campaign over the next few years as we seek to enhance our support for research on alcoholic beverages and the impact that we have had on the alcohol research community. With this new level of commitment, our future promises to be exciting and rewarding. We look forward to honoring our mission with renewed purpose as we celebrate our important 25th anniversary throughout 2007.

## Chairman's REPORT



**Bruce M. Ambler**  
Chairman, Board of Trustees

On behalf of the Board of the ABMRF, it is a privilege to invite readers to share this exciting record of the important accomplishments of our very talented grantees. Their research projects and conference activities are all made possible by the generous commitment of our donors.

I have a tradition as chairman of ABMRF whereby we begin every Board meeting by reading over our Mission and Vision statements. Much work went into writing them during a strategic planning retreat in the late 1990s and they are as real today as in the past. It is striking that all aspects of the mission, from funding high quality research by promising new investigators to communicating information effectively with the research community, fundamentally require two things. One is good people, and certainly there have been very good people involved with ABMRF for a long, long while. The second part is the money to support the activities.

The organization is at a very important crossroads in terms of continuing to support research at the same levels that we have in the past. While the commitment from the brewing industry has remained firm, the loss of an important donor in 2001 and the natural effects of inflation have eroded our ability to support research at the same levels that we were able to do back in the early nineties. In attempting to keep grant levels consistent, we cut our administrative overhead significantly. ABMRF staff is to be commended for operating the organization so effectively under great financial

restraint. There is widespread consensus among the Board that the organization has become as lean as possible and it is time to raise additional revenue to assure a future that is as strong as our past.

In early 2006 the Foundation engaged a consulting firm to assist with preliminary fundraising planning and later in the year we devoted one of our Board meetings to strategic planning. The overall direction from the Board was to create a development position and create a very strong fundraising plan with the framework being to raise additional annual revenue for the research grant program and to increase our endowment to a level that will assure we have dependable annual income to fund our operations. We are closing the year with a development committee working toward the involvement of the entire Board and are conducting a nationwide search for a development director who will be joining us to make these plans a reality in 2007.

We are very grateful to our U.S. and Canadian donors who provide vital support for the Foundation's programs. They have been very supportive of ongoing discussions that acknowledge that ABMRF has been accomplishing quite a bit in spite of our limited resources and they understand we need to improve our financial situation so we can more effectively carry out our mission. On behalf of the Board of Trustees, I would like to extend our thanks for this commitment that enables us to carry out the vision of ABMRF to be a premier, private foundation that fosters and communicates research to understand the effects of alcohol on health and behavior.

## Contributors TO THE FOUNDATION

*We are grateful to our U.S. and Canadian donors who provide vital support for the Foundation's programs.*

### CANADA

Brewers Association of Canada

### *Individual Members*

Fort Garry Brewing Company Limited  
Great Western Brewing Company  
Labatt Breweries of Canada  
Lakeport Brewing Corporation  
Magnotta Brewery  
Molson Canada  
Moosehead Breweries Limited  
Nelson Brewing Company Limited  
Northern Breweries Limited  
Pump House Brewery  
Sleeman Breweries Limited  
Storm Brewing in Newfoundland Limited  
Tree Brewing/Fireweed Brewing Corporation  
Wellington County Brewery Inc.  
Yukon Brewing Company

### UNITED STATES

Anchor Brewing Company  
Anheuser-Busch Companies Inc.  
Boulevard Brewing Company  
Cerveceria India Inc.  
Coors Brewing Company  
Deschutes Brewery Inc.  
McKenzie River Partners  
Sierra Nevada Brewing Company  
Spoetzl Brewery Inc.  
Summit Brewing Company

### *Wholesalers*

National Beer Wholesalers Association

## Personnel TRANSITIONS



01 Dr. David A. Brenner / 02 Dr. Ivan Diamond / 03 Dr. Raymond F. Anton / 04 Mr. Craig Purser / 05 Dr. Tamara J. Phillips

### BOARD OF TRUSTEES

#### *Public Members*

##### **Dr. David A. Brenner**

Samuel Bard Professor and Chairman of the Department of Medicine at Columbia University College of Physicians and Surgeons in New York, Dr. Brenner was appointed to the Board of Trustees in 2006. He is a distinguished physician-scientist who began his academic career at UC San Diego and has previously served as a member of the ABMRF Medical Advisory Council.

##### **Dr. Ivan Diamond**

Dr. Diamond began a new term on the Board of Trustees, having previously served in this capacity. He is vice president of neuroscience at CV Therapeutics and founding director of the Ernest Gallo Clinic and Research Center at the University of California at San Francisco.

##### **Dr. Raymond F. Anton**

Distinguished University Professor of Psychiatry and Behavioral Science at the Medical University of South Carolina, Dr. Anton became vice chairman of the Board. The director of the Center for Drug and Alcohol Programs at the Medical University of South Carolina, he is an international authority on medications for treating alcoholism.

##### **Dr. Richard Jessor**

Professor, Department of Psychology and director of the Institute of Behavioral Science at the University of Colorado, Dr. Jessor ended his term as a public member of the Board in 2006.

#### *Industry Members*

##### **Mr. Craig Purser**

Mr. Purser joined the Board of Trustees in 2006, after being appointed president of the National Beer Wholesalers Association (NBWA) in Alexandria, Virginia during the previous year. Prior to multiple posts with the NBWA, Mr. Purser worked for the public affairs firm Fleishman-Hillard on behalf of Anheuser-Busch and its distributors.

##### **Dr. David K. Rehr**

Dr. Rehr completed his term on the Board of Trustees after leaving his position as president of the National Beer Wholesalers Association.

### THE ADVISORY COUNCIL

#### *Behavioral and Social Advisory Council*

Three new members and a new chairperson were added to the Behavioral and Social Advisory Council in 2005; therefore no changes are reported for 2006.

#### *Medical Advisory Council*

##### **Dr. Tamara J. Phillips**

The Medical Advisory Council gained one new member, Dr. Phillips, professor and vice-chair of Behavioral Neuroscience at Oregon Health & Science University, who holds the position of Research Career Scientist at the Veterans Administration Medical Center in Portland, Oregon. Dr. Phillips has particular research interest in behavioral genetics, gene mapping for traits relevant to drug and alcohol addiction, and pharmacology.

##### **Dr. Francois M. Booyse and Dr. Neil L. Harrison**

Dr. Booyse and Dr. Harrison completed their terms as members of the Medical Advisory Council. Dr. Booyse is a professor in the departments of Medicine and Cell Biology and director of Cardiovascular Disease Research and Molecular Cardiology at the University of Alabama at Birmingham. Dr. Harrison, director of the CV Starr Laboratory of Molecular Neuropharmacology at Cornell Medical College serves as professor of multiple pharmacologic disciplines at Cornell and at Memorial Sloan Kettering Cancer Center.

### MANAGEMENT AND STAFF

##### **Ms. Wendy Graves**

The Foundation restructured some of the communications operations, concentrating activities in the Baltimore headquarters in preparation for the fundraising campaign planned to start in 2007. Ms. Graves, who began as Communications Coordinator in 1997 and was later promoted to Communications Director, will remain in Pittsburgh to pursue other opportunities. The entire ABMRF community wishes her the best.

## Financial HIGHLIGHTS

### Overview of Foundation Finances

A comprehensive independent auditor's report is available upon request.

#### Revenue and Support

	<b>2006</b>	<b>2005</b>
Industry Contributions	\$ 1,954,636	\$ 1,901,841
Investment Income	348,902	134,358
<b>Total Revenue and Support</b>	<b>\$ 2,303,538</b>	<b>\$ 2,036,199</b>

#### Grants and Programs

Grants and Related Expenses	1,509,651	1,531,173
Conferences	159,141	212,496
Communications	60,141	56,475
<b>Subtotal Grants and Programs</b>	<b>\$ 1,728,933</b>	<b>\$ 1,800,144</b>

#### Other Expenditures

Administration	372,920	381,010
Depreciation	2,528	2,335
Fundraising	19,796	0
<b>Subtotal Other Expenditures</b>	<b>\$ 395,244</b>	<b>\$ 383,345</b>

<b>Total Grants, Programs, and Other Expenditures</b>	<b>\$ 2,124,177</b>	<b>\$ 2,183,489</b>
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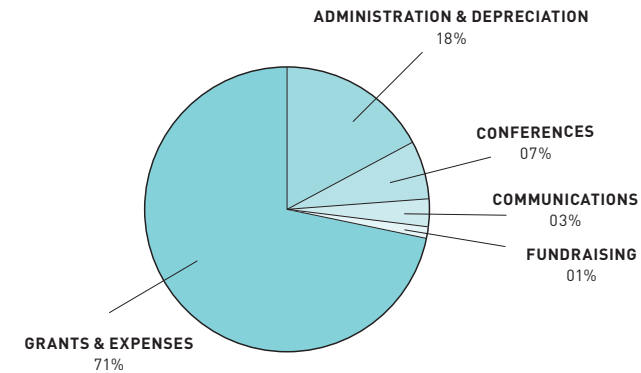
#### Assets

Change in Net Assets	179,361	(147,290)
Unrestricted Net Assets at Beginning of Year	2,563,416	2,710,706
<b>Unrestricted Net Assets at End of Year</b>	<b>\$ 2,742,777</b>	<b>\$ 2,563,416</b>

## Funding ALLOCATIONS

The research grant program makes up most of the ABMRF annual budget, with conference support, communications and publishing activities, and administration accounting for the remainder. This year, ABMRF was able to fund 15 new grant projects and 17 continuation grants from a total of 128 applications submitted. The vast majority of these grants were awarded to principal investigators who are working at the level of assistant professor or research associate and so are at the beginning of their careers in alcohol research.

#### 2006 Foundation Expenditures



### Conference Support

ABMRF participated in the 34th International Medical Advisory Conference in Copenhagen, Denmark hosted by the Brewers of Europe, with scientific program planning provided by the European Research Advisory Board (ERAB). The IMAG Conference is an important international meeting of scientific, industry and government representatives who gather to discuss significant topics in alcohol research. This year's conference featured many speakers who had been ERAB grant recipients.

The Foundation also supports the Research Society on Alcoholism (RSA) Annual Meeting, which is the largest North American alcohol research conference, by providing financial support for Student Merit and Junior Investigator Awards. These awards enable the newest members of RSA to attend this important event. The 2006 RSA Annual Meeting was held in Baltimore, Maryland where the ABMRF was granted permission to display a poster symbolizing its upcoming 25th anniversary. The poster, at 36 by 42 inches, listed the names of all Foundation grantees over the last 25 years, including many leaders in the field of alcohol research.

IMAG Conference Expenses	\$131,141
RSA Annual Scientific Meeting	20,000
Other Conferences / Workshops	5,000

<b>Total Conference Support</b>	<b>\$159,141</b>
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	<b>2006</b>	<b>1982-2006</b>
Research Grants	\$1,449,284	\$33,780,440
Conferences	159,141	4,802,107
<b>Total Grants and Conferences</b>	<b>\$1,608,425</b>	<b>\$38,582,547</b>

abmrf is

the largest independent nonprofit foundation in North America that solely supports *research on alcohol*.

abmrf has supported scientists embarking on *innovative research* on topics including youth, work-related issues, biomedical and health effects, traffic safety, moderate use, and prevention of alcohol misuse.

## Grants AWARDED 2006



01 Lori Keyser-Marcus, PhD / 02 Susan E. Luczak, PhD / 03 Albert Perrino, MD / 04 Jennifer Schwartz, PhD

### *Behavioral and Social Advisory Council Grantees*

#### **Kelly Cue Davis, Ph.D.**

*University of Washington*

"The effects of alcohol consumption, partner drinking, and violence on heterosexual HIV risk." Approved for \$50,000 for the second of two years.

#### **Ronald Seth Friedman, Ph.D.**

*University of Missouri at Columbia*

"Automatic effects of alcohol outcome expectancies on consumptive and non-consumptive behavior." Approved for \$61,600 for the second of two years.

#### **Elana B. Gordis, Ph.D.**

*University of Southern California*

"Role of ANS activation and PTSD in links between maltreatment and adolescent alcohol expectancies and use." Approved for \$40,300 for the second of two years.

#### **Peter N. S. Hoaken, Ph.D**

*The University of Western Ontario*

"An investigation into executive function and social perceptual processing as factors underlying the alcohol-aggression relationship." Approved for \$56,000 (Cdn) for the second of two years.

#### **Lori Keyser-Marcus, Ph.D.**

*Virginia Commonwealth University*

"Detecting problem drinking in new mothers: concordance between interviewer and computer-delivered screening methods." Approved for \$45,000 for the first of two years.

#### **Joseph W. LaBrie, Ph.D.**

*Loyola Marymount University*

"Group social norms motivational intervention with interactive real-time feedback." Approved for \$49,600 for the second of two years.

#### **Susan E. Luczak, Ph.D.**

*University of Southern California*

"Real-time assessment of alcohol involvement across *ALDH2* genotypes." Approved for \$45,000 for the first of two years.

#### **Cecile A. Marczynski, Ph.D.**

*University of Kentucky*

"Acute effects of alcohol on behavioral control and simulated driving in frequent and infrequent binge drinkers." Approved for \$50,000 for the second of two years.

#### **Ksenija Marinkovic, Ph.D.**

*Massachusetts General Hospital*

"Neural dynamics of alcohol effects on conflict monitoring and cognitive control." Approved for \$50,000 for the second of two years.

#### **Matthew P. Martens, Ph.D.**

*State University of New York at Albany*

"The effects of personalized drinking feedback programs among intercollegiate athletes." Approved for \$45,900 for the first of two years.

#### **Daniel H. Mathalon, M.D., Ph.D.**

*Yale University School of Medicine*

"Automatic processing of alcohol cues in chronic alcoholism." Approved for \$50,000 for the second of two years.

#### **Dan J. Neal, Ph.D.**

*Kent State University*

"Self-regulation, alcohol use and alcohol-related consequences: an electronic diary study." Approved for \$46,100 for the first of two years.

#### **Albert Perrino, M.D.**

*Yale University School of Medicine*

"Heightened pain processing in individuals at risk for alcoholism." Approved for \$40,000 for the first of two years.

#### **Edward Perry, M.D.**

*Yale University School of Medicine*

"Interactive psychopharmacologic effects of alcohol and nicotine in humans." Approved for \$45,000 for the first of two years.

#### **Jennifer Schwartz, Ph.D.**

*Washington State University*

"Identifying and explaining trends in drunk driving among women and men." Approved for \$49,500 for the second of two years.

#### **Samantha Wells, Ph.D.**

*Centre for Addiction and Mental Health*

"The development and validation of a multidimensional inventory to measure beliefs and attitudes toward alcohol-related aggression." Approved for \$37,900 (Cdn) for the first of two years.

### *Medical Advisory Council Grantees*

#### **Michael W. Bradbury, Ph.D.**

*Lake Erie College of Osteopathic Medicine*

"Locating ethanol responsive elements in the aspartate aminotransferase promoter." Approved for \$49,000 for the second of two years.

#### **Evgeny A. Budygin, Ph.D.**

*Wake Forest University School of Medicine*

"Chronic ethanol exposure and presynaptic dopamine regulation." Approved for \$50,000 for the second of two years.

#### **Brian Christie, Ph.D.**

*University of British Columbia*

"Effects of prenatal ethanol administration of hippocampal neurogenesis and synaptic plasticity: Role of NMDA receptor subunit topology." Approved for \$50,000 for the second of two years.

#### **Cynthia Czajkowski, Ph.D.**

*University of Wisconsin at Madison*

"Mapping the ethanol binding site on alpha4-beta-delta GABA-A receptors." Approved for \$50,000 for the first of two years.

#### **Lynette C. Daws, Ph.D.**

*University of Texas Health Science Center at San Antonio,*

"Alcohol inhibits serotonin clearance in a serotonin transporter independent manner: are organic cation transporters the missing link?" Approved for \$50,000 for the first of two years.

## Grants AWARDED 2006

### *Medical Advisory Council Grantees continued*



01 Olayinka Dina, DVM, PhD / 02 Dwayne W. Godwin, PhD / 03 Makio Iwashima, PhD / 04 Frank L. Margolis, PhD

#### **Olayinka Dina, D.V.M., Ph.D.**

*University of California San Francisco*

Catecholamine mechanisms in alcohol-induced neuropathy." Approved for \$50,000 for the first of two years.

#### **Dwayne W. Godwin, Ph.D.**

*Wake Forest University School of Medicine*

"Molecular physiology of alcohol withdrawal seizures." Approved for \$50,000 for the second of two years.

#### **Mary O. Gray, M.D.**

*University of California San Francisco*

"Moderate alcohol consumption and cardiac metabolism." Approved for \$50,000 for the second of two years.

#### **F. Woodward Hopf, Ph.D.**

*Ernest Gallo Clinic and Research Center*

" $I_{SKCa2+}$  activation and the dorsal striatum: a potential novel treatment for alcohol seeking." Approved for \$50,000 for the first of two years.

#### **Makio Iwashima, Ph.D.**

*Medical College of Georgia*

"Alcohol induced regulatory T cell expansion." Approved for \$50,000 for the first of two years.

#### **Tod E. Kippin, Ph.D.**

*University of California at Santa Barbara*

"Alcohol and adult neural stem cell function." Approved for \$50,000 for the second of two years.

#### **Xingguang Luo, M.D., Ph.D.**

*Yale University School of Medicine*

"Fine-mapping risk alleles for alcohol dependence at the *CHRM2* locus." Approved for \$50,000 for the second of two years.

#### **Frank L. Margolis, Ph.D.**

*University of Maryland School of Medicine*

"Neuronal loss and replacement after ethanol and abstinence." Approved for \$50,000 for the first of two years.

#### **M. Foster Olive, Ph.D.,**

*Medical University of South Carolina*

"Ethanol and central opioid peptide release." Approved for \$50,000 for the second of two years.

#### **Andrzej Pietrzykowski, M.D., Ph.D.**

*University of Massachusetts Medical School*

"miRNA regulation of alcohol actions in mammalian brain." Approved for \$50,000 for the first of two years.

today's junior scientists are  
*tomorrow's leaders* in the field.

## Research HIGHLIGHTS

*Awarded in 2006*

### **Cynthia Czajkowski Ph.D.**

*University of Wisconsin at Madison*

“Mapping the Ethanol Binding Site on alpha4-beta-delta GABA-A Receptors”

Recent evidence has shown that gamma-aminobutyric acid type A receptors (GABARs) containing the delta subunit, instead of gamma, display a high sensitivity to ethanol and likely play a key role in mediating the behavioral effects of alcohol. The overall goal of the experiments is to identify the ethanol binding site in delta-containing GABARs. Several research groups have conflicting results when investigating the ethanol sensitivity of delta-containing GABARs, and ethanol sensitivity may be dependent on the subunit isoforms present. While it is generally believed that delta simply replaces the gamma subunit in delta-containing GABARs, the exact stoichiometry, or quantitative relationship, has not been determined. Thus, if delta-containing receptors are the ethanol target in the brain, it is critical to determine the stoichiometry of these receptors. The research will clarify and further characterize delta-containing receptors by determining their subunit stoichiometry, using alpha4-beta2-delta receptors as a model.

The responsiveness of these two receptors to low doses of ethanol will be established. The ethanol-binding site will then be mapped using two approaches. The drug, Ro15-4513, which is currently used clinically to antagonize the behavioral effects of excessive alcohol consumption, binds with high affinity to delta-containing GABARs and alcohol competitively displaces Ro15-4513 binding, indicating that they bind to the same site. Ro15-4513 contains an azido group that can be used to photolabel the delta-containing receptors. The study will identify the subunit that is photolabeled and the region/residues labeled will be mapped. The second approach will involve mutation of candidate ethanol binding site residues to cysteine followed by derivitization of the introduced cysteines with an ethanol ana-

log that has been chemically modified to react with cysteines. The completion of the experiments will increase the understanding of the mechanisms underlying the biomedical effects of alcohol and will provide insight for the development of drugs to treat alcohol abuse disorders.

### **Lynette C. Daws, Ph.D.**

*University of Texas Health Science Center at San Antonio*

“Alcohol Inhibits Serotonin Clearance in a Serotonin Transporter Independent Manner: Are Organic Cation Transporters the Missing Link?”

The study addresses a rapidly growing area of research, that of polymorphisms, or genetic variations, in the serotonin transporter gene and predisposition to alcoholism. Specifically, using a mouse model, this project will investigate the influence of genetic alterations in expression of the serotonin transporter on serotonin clearance from extracellular fluid in brain. We have recently published exciting new data that show ethanol more potentially inhibits serotonin clearance in hippocampus of mice that lack the serotonin transporter. These results reveal the existence of another transporter for serotonin, which is a site of action for ethanol, and which appears to be upregulated in serotonin transporter knockout mice. This work provides evidence that the organic cation transporters may well be the “missing link” and may in fact be an important site of action for ethanol. Such findings will be instrumental in leading to the design of better treatment strategies for alcoholism and also in developing preventative strategies for relapse.

### **Olayinka Dina, D.V.M., Ph.D.**

*University of California San Francisco*

“Catecholamine Mechanisms in Alcohol-induced Neuropathy”

Small-fiber peripheral neuropathy is a common and disabling painful complication of chronic ethanol ingestion. In contrast to the acute analgesic action of ethanol in the central nervous system, pain experienced by individuals

who consume alcohol is thought to result from effects of alcohol on the peripheral nervous system by inducing a painful small-fiber peripheral neuropathy. Although symptomatic therapy may provide some relief, in the majority of patients, treatment is at best only partially effective. Development of successful therapies has been hampered by lack of understanding of the underlying mechanisms.

In previous work, a model was established, consisting of enhanced nociception, or perception of pain, in rats chronically consuming amounts of alcohol equivalent to that consumed by patients with painful peripheral neuropathy. The studies demonstrated mechanical and thermal hyperalgesia, hyperexcitability of sensory nerve fibers, and a critical contribution of the epsilon isoform of protein kinase C (PKCε) to the enhanced pain perception. Similar to what is observed clinically, alcohol withdrawal exacerbated the condition.

One of the major physiological effects of alcohol ingestion is stimulation of the sympathoadrenal axis, an effect that is exacerbated by alcohol withdrawal. The effects of alcohol withdrawal in humans are mainly those of a hyperadrenergic state and denervation of the adrenal medulla, in the rat, leads to marked attenuation in alcohol withdrawal symptoms. Since alcohol can potentiate other neurotoxic insults and monoamine oxidase metabolites of catecholamines are neurotoxic, this project will test the hypothesis that sympathoadrenal-dependent neurotoxicity contributes not only to alcohol-induced painful peripheral neuropathy, but also to its enhancement following withdrawal from alcohol.

An ultimate goal of the research is to provide a rational basis for the design of novel strategies to prevent or treat painful neuropathy in patients who chronically ingest alcohol, which may aid their attempts to moderate this behavior as well as its consequence on their health.

### **F. Woodward Hopf, Ph.D.**

*Ernest Gallo Clinic and Research Center*

“I<sub>SKCa2+</sub> Activation and the Dorsal Striatum: A Potential Novel Treatment for Alcohol Seeking”

Human alcoholics attempting to maintain abstinence often undergo major periods of craving, relapse, and continued consumption. Thus, it is critical to identify the persisting neuro-adaptations that enhance susceptibility to relapse-inducing stimuli. The dorsal striatum (DS), and the lateral DS in particular, plays a critical role in regulation of habits and compulsions. This habitual responding could contribute significantly to the expression of addictive behaviors and facilitate relapse, especially after long-term drug self-administration. Relative to some other brain areas, the lateral DS is particularly depressed in terms of action potential firing, and this is likely due to strong activity of a particular type of potassium channel, the small-conductance calcium-activated potassium channel (SK). Experiments by this group have found that a nearby region of the striatum, the nucleus accumbens core (Core), also had a strong SK, reducing the ability of these neurons to fire. In addition, SK function was significantly reduced in the Core in brain slices prepared from animals that had chronically self-administered ethanol (40-45 days) followed by 3 weeks of abstinence. With less SK control of firing, these neurons became more excitable. Since the Core is also important for motivated behavior, the loss of SK and increased excitability may allow drug-related stimuli a greater control over drug-seeking. To this end, infusion of an activator of SK into the Core significantly reduced the relapse for ethanol normally observed after the 3 weeks of abstinence. Infusion of the SK activator did not alter general locomotion or another motivated behavior (responding for sucrose in animals trained to lever press for sucrose). Preliminary experiments examining protein expression with Western blot methods suggest that SK protein levels may be reduced in the Core as well as the lateral DS. The present project will examine the impact of injection of SK activators into the lateral DS, which

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would depress firing of lateral DS neurons and could reduce ethanol relapse by decreasing the ability of habitual drives to control behavior. These studies may significantly advance the development of a potential novel therapeutic intervention for the treatment of relapse in alcoholics.

### **Makio Iwashima, Ph.D.**

*Medical College of Georgia*

“Alcohol Induced Regulatory T Cell Expansion”

Alcohol has long been known to cause suppressive effect on immune responses. Chronic consumption of alcohol is often associated with a higher frequency of infection with agents such as hepatitis C virus. However, the precise molecular mechanism for how alcohol suppresses immune response is currently not clearly identified.

One of the enzymes that is affected by alcohol is called phospholipase D (PLD). PLD is an enzyme that exists in many cells and works by coupling a type of lipid in cells with water. In the presence of alcohol, PLD prefers to work with alcohol instead of water and starts coupling alcohol and the lipid. As a result, cells no longer can produce the lipid-water coupled molecule, called phosphatidic acid (PA).

Our data shows that PA is an essential molecule for survival of a group of immune cells that attack pathogens. In the presence of a relatively high concentration of alcohol, these cells stop growing and eventually die. However, another group of immune cells that play regulatory roles during immune responses and suppress attacking cells do not require PA for survival. As a result, immune cells that expand in the presence of alcohol consist predominantly of cells with the regulatory functions.

Based on this data, it is hypothesized that alcohol suppresses the immune system by inducing the preferential expansion of regulatory cells over attacking cells. This study will determine the mechanism of how alcohol blocks growth

of attacking cells. Successful completion of this study will provide the critical information for prevention and treatment of alcohol-associated immune-suppression and infectious diseases. Moreover, it may reveal potential use of alcohol for the treatment of disease causes by excessive immune responses such as autoimmune diseases and allergy.

### **Lori Keyser-Marcus, Ph.D.**

*Virginia Commonwealth University*

“Detecting Problem Drinking in New Mothers: Concordance between Interviewer and Computer-delivered Screening Methods.”

Maternal alcohol use is an area of great concern, with the potential for serious physical, psychological and cognitive consequences to child development. Research has shown that early identification and intervention are associated with positive outcomes for both mother and child. To date, however, the majority of research has focused on screening for prenatal drinking. In contrast, postpartum drinking has received much less attention. This is of particular concern, as many women who successfully abstain from alcohol during pregnancy resume drinking during the postpartum period. One of the reasons postpartum drinking has been understudied is that mothers of young children often do not access medical care for themselves after they deliver. They are much more diligent, however, about maintaining their child’s healthcare appointments. This pattern suggests that pediatric offices may be an ideal setting in which to screen and potentially intervene on maternal drinking. Unfortunately, hectic clinic schedules often leave pediatric staff with little time to do more than address the primary reason for the visit.

One promising alternative for identifying maternal alcohol problems is the use of computerized screening measures. The present study seeks to directly compare computer-based with more traditional face-to-face interviews for detecting maternal risk drinking. Both methods will be

examined in an urban, university-based pediatric clinic setting, using standardized screening measures. Specifically, the research project will: 1) determine the prevalence of at-risk alcohol consumption in this overlooked population of women; 2) assess test-retest reliability for both face-to-face and computer-delivered alcohol screening methods; and 3) compare rates of alcohol problem detection using the interview and computerized assessment methods.

It is hypothesized that both interviewer and computer-administered screening methods will demonstrate high test-retest reliability. In addition, we hypothesize that the computer-administered method will yield higher rates of alcohol problem detection than face-to-face interviews. In summary, the research will provide benchmark data on alcohol prevalence in this overlooked population of women. It will also directly compare computer and interviewer-based methods for assessment and determine their relative reliabilities for assessing alcohol risk.

### **Susan E. Luczak, Ph.D.**

*University of Southern California*

“Real-time Assessment of Alcohol Involvement across ALDH2 Genotypes”

To date, the gene most strongly associated with alcohol dependence is the aldehyde dehydrogenase 2 (*ALDH2*) gene. A mechanistic pathway has been hypothesized for the process by which possession of an *ALDH2\*2* allele leads to lower rates of alcohol consumption and problems. The current study proposes to test this hypothesized pathway using ecologically valid assessment of the real-time drinking behavior of individuals who possess one *ALDH2\*2* allele and compared with those who possess no *ALDH2\*2* alleles.

This project has two key objectives: 1) to demonstrate feasibility of using the Alco-Sensor IV with memory and a Personal Data Assistant (PDA) to collect real-time data on alcohol use and responses, and 2) to obtain effect sizes to

determine the necessary sample size for a larger study that will be submitted for additional funding.

It is hypothesized that individuals with an *ALDH2\*2* allele will drink to reach similar subjective levels of response to alcohol compared with those without this protective allele, but will have lower rates of consumption, breath alcohol concentrations (BrACs), and negative consequences during a typical drinking session compared with individuals without an *ALDH2\*2* allele. Study feasibility will be assessed using a number of objectives (e.g., percentage of assessments missed) and subjective (e.g., perceived effects of self-monitoring on behavior) measures. Multilevel (hierarchical) regressions will be used to simultaneously estimate within-person (e.g., responses to alcohol, BrACs) and between-person (e.g., *ALDH2* genotype) data. These two- and three-level models will compare patterns of alcohol use, BrACs, subjective responses, and negative consequences across genotypes to determine effect sizes. Results of this study will improve understanding of how genetic variations affect drinking behavior, reactions to alcohol, and the development of alcohol-related problems.

### **Frank L. Margolis, Ph.D.**

*University of Maryland School of Medicine*

“Neuronal Loss and Replacement after Ethanol and Abstinence”

Human alcoholics are reported to suffer from a deficit in their sense of smell. Interestingly, this deficit is significantly alleviated on abstinence. This phenomenon could be due to a direct effect of alcohol on the brain or to effects on the olfactory sensory neurons in the nose that are responsible for detecting odors. To address this question we are studying the effects of alcohol on the olfactory pathway in mice. We find that administration of alcohol to mice results in the loss of olfactory sensory neurons and that these neurons are replaced upon abstinence. Consistent with this observation, measurements of the sense of smell

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in these mice also shows an initial loss followed by recovery with abstinence. This is a very exciting observation since it is known that the olfactory sensory neurons have the ability to be replaced from immature progenitor neurons in olfactory tissue after other kinds of damage. This suggests that alcohol can regulate the loss of mature neurons and their replacement from immature cells in an adult animal. Thus, our preliminary data shows that this is a useful model to explore the mechanisms of neuronal death and rebirth in response to alcohol abuse.

### **Matthew P. Martens, Ph.D.**

*State University of New York at Albany*

“The Effects of Personalized Drinking Feedback Programs among Intercollegiate Athletes”

This project will test the effectiveness of brief, personalized drinking feedback (PDF) among intercollegiate athletes. Prior research has established that intercollegiate athletes are more likely to engage in heavy drinking and experience negative alcohol-related problems than non-athletes. Few studies, however, have examined the effectiveness of intervention programs with this high-risk group, and those that have encountered a number of methodological limitations that make the effectiveness of the interventions difficult to evaluate. Research has shown that PDF interventions are effective in reducing alcohol use among college students, both as a stand-alone intervention and as a facet of multi-component programs. PDF interventions have not, however, been tested in a targeted sample of intercollegiate athletes, and the effects of different types of PDF content have never been systematically tested. It is possible that personalized feedback focusing on the impact of heavy alcohol use on one’s athletic performance would be particularly powerful for college athletes. Therefore, approximately 300 intercollegiate athletes will be enrolled into one of three conditions: a standard PDF intervention (PDF-standard), a PDF intervention that includes standard feedback plus sport-related feedback

(PDF-sport), and a control condition that includes educational information only. It is anticipated that both PDF interventions will be superior to the control condition, and that the PDF-sport condition will be superior to the PDF standard condition. Data will be collected at baseline, 30-day, and 6-month follow-ups, and mixed-model analyses will be used to assess both within-group and between-group effects.

### **Dan J. Neal, Ph.D.**

*Kent State University*

“Self-regulation, Alcohol Use and Alcohol-related Consequences: An Electronic Diary Study”

This project will investigate the relationship between self-regulation, or the ability to control one’s drinking behavior, and alcohol. There is much literature to suggest that individuals who have low self-regulation tend to drink more heavily and have more negative problems when they drink. Little is understood about the nature of self regulation and how it relates to heavy drinking. The study will test a feedback model of self-regulation as a framework for explaining heavy alcohol use and alcohol-related consequences in a college student sample. The study has two components. Participants will first complete several self-report measures in the laboratory. Second, following extensive training in the protocol, participants will self-monitor their thoughts, emotions, and behaviors using an Electronic Diary (ED). The ED protocol includes a morning assessment and random prompts throughout the day that will assess components of self-regulation, including current mood, recent self-regulatory demands, alcohol-related cognitions, and drinking motives. The ED protocol will also require participants to initiate an assessment immediately before and after alcohol use episodes. Research goals including testing of hypothesized self-regulatory mechanisms on drinking behavior and consequences, including main effects for self-regulation resources, the potential moderating influences of alcohol-use attitudes on the association

between self-regulation, drinking, and consequences, and elevated negative affect following unintended heavy use and consequences. Hypothesis testing will be conducted within a multilevel modeling framework (i.e., linear mixed models, generalized linear mixed models, or generalized estimating equations) that is consistent with the nature of each dependent variable. The study will quantify the effects of self-regulation in alcohol use and alcohol-related consequences, using a high-risk demographic group. The relative importance of cognitive and affective predictors of use and consequences will be evaluated at both the event and global levels. These results, based on Electronic Diary assessment in a natural environment, will inform the development of innovative new interventions that focus on individuals’ specific deficits in self-regulatory processes.

### **Albert Perrino, M.D.**

*Yale University School of Medicine*

“Heightened Pain Processing in Individuals at Risk for Alcoholism”

Evidence suggests that glutamate systems contribute to the neurobiological underpinnings of alcohol dependence as well as to the vulnerability for developing alcohol dependence. The ionotropic N-methyl D-aspartate (NMDA) glutamate receptor has received particular attention in alcohol research as ethanol has high affinity for this receptor acting as an antagonist. From experimental protocols using the NMDA antagonist ketamine as a neurobiologic probe, this group and others have demonstrated altered responses in mood and affect, both in alcohol dependent patients and those at high risk to develop alcoholism.

The glutamatergic system, and foremost the NMDA receptor, is also recognized as the center pin of the spinal cord’s regulation of pain. The guiding hypothesis of this research project is that if there are inherited abnormalities in excitatory glutamatergic neurotransmission characteristic of individuals who are at high risk for developing alcoholism,

then these are manifested as heightened pain processing that can be evaluated in a laboratory paradigm. We propose an innovative study to evaluate the differences in the central nervous system (CNS) responses to pain stimuli in individuals at high risk of developing alcoholism compared to those not at high risk. We plan to show that at-risk individuals develop heightened spinal cord excitability in response to pain stimuli. Secondly, by using ketamine as a pharmacologic probe, we will test the hypothesis that the heightened pain response is attributable to enhanced dorsal horn neuron glutamatergic activity.

The data obtained from this study will be the first to provide insights into the contributions of altered CNS glutamatergic responses at the sub-cortical level and explore the relationship of spinal cord responsiveness to brain responses including perceptions of pain and mood. As such, this study will provide a novel understanding of the underlying neurobiology which results in excessive drinking.

### **Edward Perry, M.D.**

*Yale University School of Medicine*

“Interactive Psychopharmacologic Effects of Alcohol and Nicotine in Humans”

Studies have demonstrated high correlations between alcohol consumption and tobacco use. It has also been shown that nicotine reverses alcohol-induced cognitive deficits in some but not all animal models. However, there is limited data on the interactive effects of acute nicotine and alcohol exposure on cognitive measures in humans. The purpose of this study is to characterize the interactive effects of acute intravenous alcohol and nicotine administration in male and female smokers who do not abuse alcohol. The primary hypothesis is that nicotine will attenuate the disruptive effects of alcohol on cognitive domains including memory and concentration. The secondary, exploratory hypothesis is that nicotine will attenuate the

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disruptive effects of alcohol on impulse control (risky decision-making). It is also hypothesized that nicotine will decrease the effects of alcohol on mood, and that alcohol will increase nicotine craving and withdrawal. If nicotine is found to attenuate the disruptive effects of alcohol on cognition and impulse control, this may translate into improved performance on real-world tasks (e.g., driving) and explain in part why social drinkers smoke more when they drink.

### **Andrzej Pietrzykowski, M.D.**

*Ph.D., University of Massachusetts Medical School*  
“miRNA Regulation of Alcohol Actions in Mammalian Brain”

The discovery of the RNA interference (RNAi) process has been heralded as a major scientific breakthrough. The importance of RNAi was recently highlighted by awarding the 2006 Nobel Prize in Medicine or Physiology to its discoverers. RNAi is a natural process in which short, non-coding RNAs (microRNA, miRNA) are key elements regulating diverse cellular processes. We have recently discovered that in mammals alcohol regulates expression of voltage- and calcium-sensitive potassium channel of high conductance (BK)—one of the most important targets of alcohol in the brain as determined on both, molecular and behavioral levels. Moreover, we determined that alcohol regulation of the BK channel mRNA expression utilizes RNAi through a specific miRNA species (miR-9). We observed that alcohol increases expression of miR-9, which leads to selective destruction of BK channel mRNAs encoding alcohol-sensitive isoforms of BK channel. Concomitantly, BK channel messages encoding alcohol-insensitive isoforms are resistant to alcohol actions. These results are the very first example of the role of miRNA in neuronal adaptation to alcohol.

The major aim of these studies is to determine the role of miR-9 in alcohol effects on gene expression in the CNS in the early stages of the development of drug addiction.

Using cellular, molecular and biochemical approaches, experiments will test the hypothesis that *in vivo*, single alcohol exposure increases expression of miR-9 in brain regions important in drug addiction. Additional aims will focus on miR-9-controlled downregulation of specific BK channel mRNA variants and consequences of that regulation. Results of this study will provide new insights into the cellular and molecular actions of alcohol, and can be a first step towards new treatments of alcohol abuse by targeting miRNA.

### **Samantha Wells, Ph.D.**

*Centre for Addiction and Mental Health, Canada*  
“The Development and Validation of a Multidimensional Inventory to Measure Beliefs and Attitudes toward Alcohol-related Aggression”

Alcohol-related aggression is a common social problem among young males. The main aim of the proposed research is to develop, refine, and evaluate the validity of a set of questions to measure young men’s attitudes and beliefs toward male-to-male alcohol-related aggression. Using a preliminary questionnaire that was developed based on a theoretical model of attitudes and beliefs related to male aggression when drinking, this study involves two phases. In Phase 1, focus groups will be used to ensure coverage of all domains related to young men’s attitudes and beliefs about male aggression when drinking; a pilot test will be conducted to improve and refine questionnaire items; and a revised questionnaire will be reviewed by experts for clarity and relevance to the proposed dimensions. In Phase 2, using a diverse sample of young men, the study will evaluate the validity of the hypothesized dimensions of the questionnaire and test the theoretical model predicting male-to-male aggression when drinking. Findings from this research will be used to develop prevention programs designed to reduce aggression between men in drinking situations.

many former grantees report that the *abmrf grant* helped establish their independent research career.

## Publications AND PRESENTATIONS

### *2006 Published Studies and Presentations*

ABMRF grantees are assembling an impressive collection of publications that detail research advances made possible by Foundation grants. To date over 1,750 papers have been published since our first research grants were awarded in 1982. Behind each of the following publications and presentations is a compelling story of long hours and dedication as our grantees contribute important pieces to the growing body of knowledge that enables a better understanding of the effects of alcohol on health and behavior.

Several of the publications listed have been reported in the press over the past year or singled out in publications within the scientific community. For example, we are very pleased to share that dual publications in the *Proceedings of the National Academy of Sciences (PNAS)* by Dr. Martin Wallner, a junior faculty member at the University of California Los Angeles, were singled out in a guest commentary for that issue by Dr. Steven Paul, the former scientific director of the National Institute of Mental Health. Dr. Paul wrote, "In this issue of *PNAS*...Wallner et al. provide exciting new evidence for a highly specific interaction of alcohol with a subtype of GABA<sub>A</sub> receptor that may mediate (at least in part) some of this drug's most important behavioral effects" (*PNAS* 103:8301, 2006). Dr. Paul goes on to discuss implications of the work of Wallner and his colleagues and raises the question of whether specific drugs might be developed that could mediate the addictive properties of alcohol. Readers will be interested to know that the *Proceedings of the National Academy of Sciences* in which Dr. Wallner's work was published has been rated as the second most-cited journal in all fields of science in the past ten years, by Thompson Scientific, formerly known as the Institute for Scientific Information.

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since nineteen *eighty-two*

the Foundation has funded more than  
*450* investigators, who have published  
over *1,750* peer-reviewed articles.

### *A Showcase for the ERAB Grant Program*

Copenhagen was the setting for the 34th International Medical Advisory Conference hosted by the Brewers of Europe October 15-19, with scientific program planning provided by the European Research Advisory Board (ERAB). Many of the scientific presentations featured work by ERAB grantees, signifying that the grantmaking organization founded in Brussels in 2003 has come of age. ERAB, while funded by the Brewers of Europe, operates independently with administrative oversight provided by a Board of Directors that includes ABMRF's President, Dr. Mack Mitchell.

Structured similarly to ABMRF's biomedical and psychosocial Advisory Councils, ERAB has an Advisory Board chaired by Professor Philippe de Witte of the Université Catholique de Louvain that oversees a grant program offering several types of awards. ERAB Research Grants provide funding on any aspect of biomedical or psychosocial research on beer or alcohol for researchers from established European research institutions or universities and are available in amounts up to EUR 120,000. ERAB Travel Awards facilitate conference participation by young researchers based at academic institutions in European Union member countries. ERAB Research Exchange Awards fund visits by European Union-based young researchers to alcohol-related laboratories or research groups anywhere in the world to help the junior researchers gain expertise or exchange information.

The two-day IMAG program featured five sessions:

- *Alcohol, Vascular Disease and Lifestyle*
- *Neuroscience-Alcohol and Nicotine Interactions*
- *Alcohol, Cancer, and Epidemiology*
- *Genetics*
- *Young People and Drinking*

### *Alcohol, Vascular Disease and Lifestyle*

The session on Alcohol, Vascular Disease and Lifestyle featured six papers and was chaired by Professor Wolfgang Koenig of the University of Ulm Medical Center and Professor Victor Preedy of King's College London. The session opened with a talk by Dr. Michel de Lorgeril, an ERAB Research Grant recipient from the Université Joseph Fourier in France and was entitled, "Alcohol, Good or Bad in Ageing? An Overview." The talk cited a number of studies examining whether alcohol modifies the risk of cardiovascular diseases, cancers, and dementia, which are the main causes of death when aging.

Professor Preedy's talk mentioned the work of several former ABMRF grantees including Drs. Charles Hennekens, Umed Ajani, and Paul Ridker. Dr. Armin Imhof, an ERAB Research Grant recipient from the University of Ulm in Germany, presented a paper entitled, "Alcohol, Inflammation and Atherosclerosis," that offered insights into evidence of an anti-inflammatory action of moderate alcohol consumption. Professor Filippo Crea, an ERAB Research Grant recipient from the Catholic University of the Sacred Heart in Rome, presented "Mechanisms of the Protective Effects of Alcohol Consumption on Cardiovascular Risk and on Myocardial Preconditioning," concluding that cardiovascular risk reduction associated with moderate alcohol consumption appears to be mediated by beneficial effects on atherogenesis, on arterial thrombotic events, and on the response to myocardial necrosis. Dr. Joline Beulens from TNO Nutrition and Food Research in The Netherlands and a recipient of an ERAB Research Exchange Award, presented a paper entitled, "Alcohol Consumption and Risk of Coronary Heart Disease and Stroke in Hypertensive Men," offering conclusions that alcohol consumption is associated with decreased risk of coronary heart disease among hypertensive men, a similar association as found in non-hypertensive men in the general population. Professor Giovanni de Gaetano of the Catholic University in Campobasso, Italy, presented an overview paper

entitled, "Effects of Alcohol on Cardiovascular Risk and Total Mortality," confirming the hazards of excess drinking and the existence of potential windows of light-moderate alcohol intake which may confer a net beneficial effect of drinking, in terms of survival for men and women. The session concluded with a speaker familiar to those audience members who attended the 2002 IMAG in Brussels, Professor Jonathan Powell of the Medical Research Council Collaborative Centre for Human Nutrition Research in Cambridge, who provided an overview of "Moderate Alcohol Ingestion and Bone Quality: Old Associations but New Mechanisms." Dr. Powell discussed research showing that excessive alcohol consumption is associated with abnormal bone loss, whereas moderate alcohol intake is associated with suppression of the loss of bone substance, or resorption. He offered insights into the role of orthosilicic acid in the process, a nutrient in beer that is also involved in bone formation.

### *Neuroscience – Alcohol and Nicotine Interactions*

The session on Neuroscience – Alcohol and Nicotine Interactions was chaired by Professor Philippe de Witte of the Université Catholique de Louvain and Professor Giovanni Addolorato at the Catholic University of Rome. It featured four presentations with the first being by Professor Giancarlo Colombo, an ERAB Research Grant recipient from the CNR Institute of Neuroscience in Cagliari, Italy. He presented a paper entitled, "Animal Models for Studying Alcohol Effects on the Brain," highlighting his work with Sardinian lines of alcohol-preferring and alcohol non-preferring rats as a model to examine excessive alcohol consumption. Professor Philippe de Witte, session co-chair and recipient of an ERAB Research Grant, presented a paper entitled, "Alcohol and Nicotine Interactions: Molecular Studies," exploring at a molecular level the intriguing finding that 80% of alcoholics smoke cigarettes. Dr. Przemyslaw Bienkowski, a recipient of an ERAB Research Exchange Award from the Institute of Psychiatry and Neurology in Warsaw, presented a paper entitled, "Alcohol and Nicotine Interactions: Behavioural Studies," offering findings that chronic nicotine administration leads to long-lasting increase in alcohol administration and that acquiring cigarette smoking early may facilitate heavy drinking and development of alcohol abuse or dependence. Dr. Bo Söderpalm of Sweden's Göteborg University offered a talk entitled, "Experimental and Clinical Implications of the Relationships between Alcohol and Nicotine," presenting findings in animal studies that nicotine exposure during the third trimester or later in life enhances ethanol consumption and the effects may derive from nicotine-development of behavioral disinhibition and may involve certain peripheral nicotinic acetylcholine receptors. Both Drs. Bienkowski and Söderpalm cited the work of former ABMRF grantee, Dr. Pamela Madden.

*Alcohol, Cancer and Epidemiology*

Professor Piet van den Brandt of Maastricht University and Dr. Silvano Gallus of the Instituto di Ricerche Farmacologiche Mario Negri in Milan, chaired the session on Alcohol, Cancer and Epidemiology. Prof. van den Brandt offered an overview of the topic with his talk entitled, "Alcohol and Cancer Risk," that discussed an increased risk of several cancers that is seen in consumption levels above 2-3 drinks per day. Dr. Silvano Gallus, a recipient of an ERAB Research Grant, offered a paper entitled, "Role of Different Types of Alcohol on the Risk of Cancer," that offered new insight into cancer risk of different types of alcoholic beverages from an Italian perspective, noting that most knowledge to date came from data collected in northern Europe and North America. Dr. Martje Weijenberg, a recipient of an ERAB Research Grant and her doctoral student Brenda Bongaerts, from the University of Maastricht, presented a paper entitled, "Alcohol Consumption and Risk of Genetic Alterations in Genes Involved in Colorectal Cancer in the Netherlands Cohort Study on Diet and Cancer," that offered findings that alcohol intakes above 30 grams/day increases the risk of colorectal cancer and that the risk seems independent of the presence or absence of genetic aberrations.

*Genetics*

Professor Oliver James of the University of Newcastle upon Tyne chaired the session on Genetics. Professor Chris Day, a Newcastle colleague, presented work funded by an ERAB Research Grant in his paper entitled, "Susceptibility to Alcoholic Liver Disease," that offered exciting insights into development of state-of-the art techniques that have significant potential to offer new prevention and therapeutic strategies. The work by Professor Howard Thomas, a recipient of an ERAB Research Grant from the Department of Medicine, Imperial College, St. Mary's Hospital in London, comprised the other half of this session with "Identification of a Candidate Gene Influencing Alcohol Intake, Using a Mouse Line with Alcohol Preference Induced by ENU Mutation." ENU, or ethylnitrosourcea, is an agent that is used in the laboratory to induce gene mutations that enable the study of various dominant and recessive traits.

*Young People and Drinking*

The session on Young People and Drinking, featuring four presenters, was chaired by Mr. Robert Madelin, Director-General for the Health and Consumer Protection Directorate of the European Union. Dr. Marie Choquet from Inserm in Paris opened the session with a talk, "Binge Drinking in Europe," that offered important insights into differences between the Northern countries, the Mediterranean countries, and eastern European countries. Dr. Marianne Van den Bree, a recipient of an ERAB Research Grant from Cardiff University in the UK, presented a talk entitled, "Genetic and Environmental Influences on Risk Factors of Adolescent Alcohol Use and Problem Use," noting that in order to develop effective prevention and intervention initiatives, the risk factors contributing to adolescent alcohol involvement must be clearly understood. Professor Mary McMurrin, a recipient of an ERAB Research Grant from the University of Nottingham in the U.K., offered a talk entitled, "Alcohol Aggression Outcome Expectancies," that included among the findings that increased beliefs that alcohol leads to violence, may lead to an increase in alcohol-related aggression. The final talk of the conference was presented by Ms. Bridgette Maree Bewick, an ERAB Research Grant recipient from the U.K.'s University of Leeds. It was entitled, "The Effectiveness of Web-Based Interventions Designed to Decrease Alcohol Consumption—A Systematic Review," and offered preliminary evidence that web-based interventions have potential to prevent alcohol abuse, but much further research is needed to design effective web-based programs.

*IMAG Conference Locations*

1st	Montebello, Québec, Canada	1972
2nd	Hamilton, Bermuda	1973
3rd	London, United Kingdom	1974
4th	Victoria, British Columbia, Canada	1975
5th	Rossllyn, Virginia, USA	1976
6th	London, United Kingdom	1977
7th	Toronto, Ontario, Canada	1978
8th	Melbourne, Australia	1979
9th	Washington, DC, USA	1980
10th	Stratford-Upon-Avon, United Kingdom	1981
11th	Halifax, Nova Scotia, Canada	1982
12th	Sydney, Australia	1983
13th	Cambridge, Massachusetts, USA	1984
14th	Turnberry, Scotland, United Kingdom	1985
15th	Ottawa, Ontario, Canada	1986
16th	Melbourne, Australia	1987
17th	Charleston, South Carolina, USA	1988
18th	Eastbourne, Sussex, United Kingdom	1989
19th	Jasper, Alberta, Canada	1990
20th	Gold Coast, Australia	1991
21st	La Jolla, California, USA	1992
22nd	London, United Kingdom	1993
23rd	Québec City, Québec, Canada	1994
24th	Sydney, Australia	1995
25th	Tucson, Arizona, USA	1996
26th	Bath, United Kingdom	1997
27th	Vancouver, British Columbia, Canada	1998
28th	Melbourne, Australia	1999
29th	San Francisco, California, USA	2000
30th	Brussels, Belgium	2002
31st	Niagara-on-the-Lake, Ontario, Canada	2003
32nd	Canberra, Australia	2004
33rd	Chicago, Illinois, USA	2005
34th	Copenhagen, Denmark	2006

the strength of any organization is in its leadership. abmrf benefits from a *tremendous commitment* on the part of a very talented group of individuals—a group representing a strong partnership between industry and science. while relationships among the participants flourish, a clear separation between the funding source and the research decision is maintained.

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## Research GRANT PROGRAM

ABMRF accepts applications for grants to conduct research on important aspects of alcohol consumption and its effects. Overall, the following areas are more directly related to the mission of the Foundation, and therefore, are of greater interest:

- *Factors influencing transitions in drinking patterns and behavior,*
- *Effects of moderate use of alcohol on health and well-being,*
- *Mechanisms underlying the behavioral and biomedical effects of alcohol,*
- *Biobehavioral/interdisciplinary research on the etiology of alcohol misuse.*

The Foundation does not encourage applications on treatment of the complications of advanced alcoholism. However, research involving treatment intended to elucidate the pathogenesis of alcohol-related problems will be considered. Non-research activities such as education projects, public awareness efforts and referral services are not eligible for support.

The Foundation does not support training of pre- and post-doctoral fellows, graduate students and medical students, interns and residents. It does not fund thesis or dissertation research.

Highest funding priority is given to young investigators, new to or trained in the field, to start a new line of independent research. The next level of priority is to investigators outside alcohol research bringing an innovative idea to the field. Lowest priority is given to established investigators in the alcohol research field unless the application offers an extraordinary new idea.

Grants are made to academic and research institutions in Canada and the United States, not to individuals. Applicants are usually notified within two weeks following the Advisory Council meetings, which are held in April and November.

Applications for research grants should be forwarded to the headquarters of the Foundation. Deadlines for submitting applications are February 1st and September 1st. Depending on the nature of the proposed research, applications submitted to the ABMRF are reviewed by the Medical Advisory Council or the Behavioral and Social Advisory Council. Both Councils meet twice each year, in the spring and fall.

### *Funding Rate*

In 2006, the Medical Advisory Council and the Behavioral and Social Advisory Council reviewed a total of 86 new grant applications and recommended funding for 15, for a combined funding rate of 17%. During 2006, 17 applications for continuation funding were also approved by the Councils for second year support for applications that were approved during the previous year.

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has been able to fund *innovative, high  
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in Canada and the United States.

*to your health!*