

REPORT 2008



EDITORIAL

As Chairman of the Board of Directors it gives me great pleasure to commend this report to you. You will find here not only our achievements in 2008 but also a review of the published results of the research ERAB funded in its first two years. I am delighted with the recognition which this tangible element of our success has brought us both in the scientific community and among the European Union institutions.



Raymond Georis
Chairman, ERAB Board of Directors

A handwritten signature in black ink, appearing to read 'R. Georis'.

ERAB continues to be a success story which The Brewers of Europe and its members can be very proud of! ERAB has achieved a great deal in its first five years. The quality of the applications it receives are of an increasingly high level and it is supported by a growing number of internationally renowned peer reviewers. The number of publications being published in top scientific journals is growing and the review of just the first two years publications in this report clearly shows the quality of the science which ERAB is funding. One of the teams ERAB has funded has been particularly successful this year with a paper published in the Lancet and the most prestigious ESBRA award for its key researcher.



Philippe De Witte
Chairman, ERAB Advisory Board

A handwritten signature in black ink, appearing to read 'P. De Witte'.

INTRODUCTION

The European Research Advisory Board (ERAB) was established as an independent Charity in Brussels in 2003 to fund European biomedical and psychosocial research into the effects of beer and other alcohol beverages. In May 2008 ERAB was five years old.

NEWS

The recipient of an ERAB grant starting in 2007, Lorenzo Leggio, was honoured this year with the ESBRA Nordmann Award 2008. He is working at the Catholic University of Rome, Italy and Brown University Medical School, Centre for Alcohol and Addiction Studies, Providence, RI, USA. The abstract for his paper entitled "Understanding and treating alcohol craving and dependence via GABA_B system: Recent pharmacological and neurological findings" can be viewed on the ESBRA website www.esbra.com/esbra08/abstracts.htm. ERAB would like to congratulate Dr. Leggio on this award.

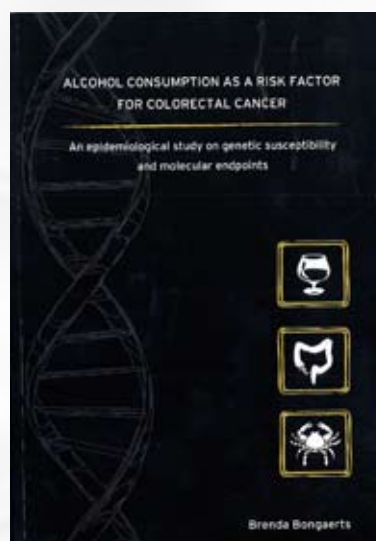


Dr. Leggio receiving his award from Prof. Helmut Seitz, ESBRA President (left), and Prof. Roger Nordmann (right)

Dr. Leggio and colleagues, including Professor Giovanni Addolorato who is a member of the ERAB Advisory Board, have recently published ERAB funded research in the *Lancet*, a very highly rated, peer reviewed journal¹. This is the first publication in the *Lancet* published by an ERAB grantee.

¹ Addolorato G, Leggio L, Ferrulli A, Cardone S, Vonghia L, Mirijello A, Abenavoli L, D'Agelo C, Caputo F, Zambon A, Haber PS, Gasbarrini G (2007) Effectiveness and safety of baclofen for maintenance of alcohol abstinence in alcohol-dependent patients with liver cirrhosis: randomised, double-blind controlled study. *The Lancet*, 370:1915-1922.

ERAB is also delighted to congratulate the first of its researchers to gain a doctorate from research funded in part by ERAB. Dr. Bongaerts was appointed as molecular epidemiologist to work on the successful application of Dr. Weijenberg and colleagues in Maastricht University. Her thesis was entitled "Alcohol consumption as a risk factor for colorectal cancer" and she was examined for her doctorate on October 16th 2008.



Dr. Bongaerts receiving her certificate from Prof. P.A. van den Brandt.

THANKS

Dr. David Long has worked for the British Beer & Pub Association since 1981 and will retire from the Association in 2009. David organised the Medical Advisory Group of the British Beer & Pub Association and has participated in IMAG conferences since 1985. He saw the need for a European member of the International Medical Advisory Group many years ago and lobbied The Brewers of Europe tirelessly until the ERAB was founded. He has been a member of the Board of Directors since its foundation in 2003 and has been responsible for securing almost a quarter of the total ERAB subscription income. Without this support initially ERAB would not have had sufficient resources to start. Now that it has proven success there are plans to approach all members of The Brewers of Europe with a view to consolidating the subscription base. ERAB is indebted to Dr. Long who will step down from the Board of Directors when he retires next May.



Thanks are also due to the Grants Committee of the British Beer & Pub Association and the Institute of Brewing & Distilling the UK brewing Charity who granted the annual subscription paid by the British Beer and Pub Association. The Grants Committee was funded in 2001, with capital from the sale of the Association's London headquarters and allocates funding to brewing research projects in the UK. Their continued support for the ERAB is much appreciated.

KEY PERFORMANCE INDICATORS 2003 - 2008

Total subscriptions	€ 2,789,000
Total grant spend	€ 2,195,427
Applications	154
Full grants funded	37
Two year grants	29
Biomedical grants	26
Psychosocial grants	11
Travel Awards	25
Exchange Awards	7

Funding research in many different parts of EU - 10 countries to date

CONTRIBUTORS

Without the continued support of the European Brewing Sector ERAB would not be able to continue to fund independent research into the biomedical and socio-behavioural aspects of alcohol consumption. ERAB is grateful to its contributors.

The following associations and companies supported the ERAB in 2008:

- **APCV - Associação Portuguesa dos Produtores de Cerveja, Portugal;**
- **Associazione degli Industriali della Birra e del Malto, Italy;**
- **Brasseurs de France, France;**
- **Bryggeriforeningen, Denmark;**
- **Belgian Brewers, Belgium;**
- **Centraal Brouwerij Kantoor - CBK, Netherlands;**
- **Cerveceros de España, Spain;**
- **Deutscher Brauer-Bund e.V., Germany;**
- **Grants Committee of the British Beer & Pub Association and the Institute of Brewing & Distilling;**
- **Greek Brewers' Association, Greece;**
- **Irish Brewers' Association, Ireland;**
- **Panimoliitto, Finland;**
- **Sveriges Bryggerier AB, Sweden;**
- **The Brewers of Europe.**
- **Verband der Brauereien Österreichs, Austria;**
- **Carlsberg**
- **Heineken**
- **InBev**
- **SABMiller**
- **Scottish & Newcastle**

SPONSORSHIP

ERAB is proud of its continuing commitment to the European Society for Biomedical Research on Alcohol (ESBRA) biennial Congress. In 2005 ERAB sponsored travel awards for the leading young presenters at the conference in Canterbury, UK. In 2007 we funded a keynote speaker for the conference in Berlin, Germany as well as travel awards. This is an important targeted means of communication about ERAB.

THE ERAB WEBSITE

The ERAB website includes biographies of the members of both Boards, information about how to apply for a grant including the deadlines, details of grants already funded and proforma report forms for grantees to download. An intranet allows the Advisory Board to download the extensive paperwork for their meetings.

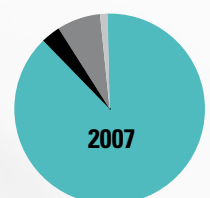
The website receives a growing number of visits each year – almost 48,000 in 2007. This activity peaks in the Spring when grant applications are due and shows that it is being consulted by the research community.

www.erab.org

FINANCE

An average of five full (€120,000) grants is funded each year together with 4 or 5 travel awards and one or two exchange awards. The research grant expenditure accounts for the majority of the annual budget.

	2004	2005	2006	2007
	€	€	€	€
Revenue and Support				
Industry contributions	434,500	445,000	425,000	535,00
Investment income	2,365	7,972	1,926	6,098
Expenditure				
Grants and Awards				
Grants	390,390	496,600	421,846	426,398
Awards	-	2,500	11,656	12,219
Sub Total	390,390	499,100	433,502	438,617
Other Expenditures				
Communications	9,195	9,334	5,310	17,017
Meetings and Conferences	59,023	33,838	19,222	32,371
Other	5,743	7,077	5,370	5,562
Total Expenditure	464,351	549,349	463,404	493,567
Assets carried over	354,470	256,742	220,264	267,795



- Grants and Awards
- Communications
- Meetings and Conferences
- Other

BOARDS

The ERAB has two boards – a Board of Directors and an Advisory Board.

ERAB is grateful to the members of both Boards who generously give their time and expertise without reward.

CHANGES TO THE BOARD IN 2008

This year Mr. Kieran Simpson of Scottish & Newcastle UK resigned from the Board of Directors and ERAB would like to thank him for his support since ERAB's foundation. In his place we would like to welcome Mr Rutger Goethart who was appointed to the Board at its meeting in October 2008.

We are also delighted to welcome Ms. Vanessa Witkowski of the Research Institute Bruegel who joined the Board of Directors in October 2008 as a public member.

BOARD OF DIRECTORS

The ERAB's independence is guaranteed by a Board of Directors made up of a majority of public members. Their role is to administer the funds.

PUBLIC MEMBERS

Mr Raymond Georis
(Founder Member, Chairman).

Professor Daniel Bessa
University of Porto Business School, Portugal.

Mr Jean Martin
European Confederation of the Food & Drink Industry, Belgium.

Professor Mack Mitchell
ABMRF The Foundation for Alcohol Research, USA.

Mrs Heidrun Piwernetz
Representation of Bavaria to the European Union, Belgium.

Dr. Erik Skovenborg
Medical Doctor, Denmark.

Vanessa Witkowski
Research Institute Bruegel, Belgium.

Professor Philippe De Witte
Université Catholique de Louvain-la-Neuve, Belgium.
Chairman of the ERAB Advisory Board.

ADVISORY BOARD

The members of the Advisory Board have a proven international independent scientific reputation. Their role is to examine the applications, suggest peer reviewers and recommend to the Board of Directors which applications should be funded.

Professor Philippe De Witte
Department of Biology, Université Catholique de Louvain-la-Neuve, Belgium. *Chairman.*

Professor Giovanni Addolorato
Department of Internal Medicine,
Università Cattolica del Sacro Cuore,
Rome, Italy.

REPRESENTATIVES OF BREWERS AND TRADE ASSOCIATION OFFICIALS

Mr Alberto da Ponte
President of The Brewers of Europe.

Mr Rutger Goethart
Heineken.

Dr. David Long
The British Beer & Pub Association.

Mr Jacobo Olalla Marañón
Cerveceros de España.

Mr Knud Hedeager Nielsen
Carlsberg.

HONORARY MEMBERS (ACCORDING TO ARTICLE 6 OF THE BY-LAWS)

Professor Oliver F W James
former Pro Vice Chancellor, Faculty of Medical Sciences, University of Newcastle upon Tyne, UK. *(Founder Member).*

Mr Piero Perron
Heineken. *(Founder Member).*

Professor Richard Smallwood
former Commonwealth Chief Medical Officer (1999-2003),
Australia.

Professor Christopher P. Day
Centre for Liver Research, University of Newcastle upon Tyne, UK.

Professor Wolfgang Koenig
Department of Medicine, University of Ulm, Germany.

Dr. Kari Poikolainen
Finnish Foundation for Alcohol Studies, Helsinki, Finland.

Dr. Martje P. Weijenberg
Department of Epidemiology, Maastricht University,
The Netherlands.

INTERNATIONAL MEDICAL ADVISORY GROUP CONFERENCES

International Medical Advisory Group (IMAG) conferences have been held since 1972 and offer an opportunity for the Medical Advisors to the brewing industry worldwide to discuss topical issues and recent research advances in the alcohol field.

IMAG 2006

The 2006 IMAG was the 34th conference and was held in Copenhagen. The scientific programme was planned by ERAB and the conference was hosted by The Brewers of Europe with assistance from Carlsberg. Delegates from 22 countries on six continents attended.



IMAG 2007

The 2007 IMAG was held in Halifax, Nova Scotia. Delegates from 16 countries on six continents attended. The scientific programme was planned by the ABMRF / The Foundation for Alcohol Research and the conference was hosted by the Brewer's Association of Canada.



IMAG 2009

The 36th IMAG conference will be held in the USA in October 2009 and will be hosted by the ABMRF / The Foundation for Alcohol Research. Provisional dates are 25th - 28th October 2009

IMAG 2010

The 37th IMAG conference will be hosted by The Brewers of Europe between 17th and 21st October 2010. The programme which is being prepared by the ERAB Advisory Board is being drafted and the location for the conference venue is being explored.

ERAB GRANTS

ERAB invites applications for funding by advertising in relevant medical journals at the beginning of each year. The applications are sent for review to experts in the relevant subject from all over the world. The recommendations as to which grants are funded are based on these peer reviews which give great emphasis to the scientific merit of the application. Grants are funded up to the maximum of €120,000 over, either one, or two years. Of the 37 major grants funded so far seven were completed at the end of 2006, four were completed at the end of 2007, three complete this year, eight will complete at the end of 2009, ten will complete at the end of 2010 and 5 will complete in 2011.

While the maximum level of funding available for grants is modest this "seed-corn" funding is important as it can attract higher levels of funding from other bodies. This is indeed the case for at least one of the ERAB grantees who is now in receipt of significant further financial support from the Wellcome Trust.

GEOGRAPHICAL SPREAD

To date ERAB grants have been undertaken in 10 different EU countries. Belgium, Denmark, Finland, France, Germany, Italy, the Netherlands, Portugal, Sweden and UK.

AWARDS FOR YOUNG RESEARCHERS

As well as providing major research grants ERAB is keen to encourage young researchers to work in the field of alcohol research and offers a number of much smaller travel and exchange awards for researchers under the age of 35. The travel awards enable scientists to travel to conferences to present their data and the exchange awards allow periods of study / collaboration in centres of excellence anywhere in the world.

In addition to the above awards for young researchers the Board of Directors has also approved that small awards may be made available to help publish PhD theses from next year.

2008 GRANTS

At its ninth meeting on 9th October 2008 the ERAB Board of Directors agreed that the following eight research projects should be funded during 2009 / 2010.

Dr. Clare MACKIE	Institute of Psychiatry, London, UK
Psychosocial	The reduction of adolescent alcohol misuse: examining the potential universal effects of a targeted prevention programme
One and a half year	
Dr. Marcus Robert MUNAFÒ	University of Bristol, Bristol, UK
Psychosocial	Effects of alcohol rating of attractiveness: examining the role of alcohol in social interaction
Two year	
Prof. Dr. Med Stefan BLEICH	University Hospital Erlangen, Germany
Epidemiology	Risk factors for alcohol binge drinking in native adolescents and immigrants in Germany
Two Year	
Prof. Giovanni DE GAETANO	Università Cattolica del Sacro Cuore, Campobasso, Italy
Epidemiology	Alcohol consumption and mortality risk among patients with cardiovascular disease: a meta-analysis and a longitudinal study on patients with coronary artery disease undergoing surgical revascularization
Two Year	
Prof. Emanuele ALBANO	University "A.Avogadro" of East Piedmont, Novara, Italy
Biomedical	Characterization of the role of immune mechanisms in the progression of alcoholic liver disease
Two year	
Dr. Henk HENDRIKS	TNO Quality of Life, Zeist, The Netherlands
Biomedical	Effects of moderate alcohol consumption on gene expression in subcutaneous adipose tissue in lean and overweight postmenopausal women
One year	
Dr. Tamzin Louise RIPLEY	University of Sussex, Brighton, UK
Biomedical	Alcohol-induced changes in learning bias: a possible 'gateway' to drug addiction.
Two year	
Prof. Jaakko KAPRIO	University of Helsinki, Helsinki, Finland
Epidemiology	Alcohol and smoking in adolescence - a causal relationship or common underlying liability ? An analysis of European and Asian data on twins
One Year	

PUBLICATIONS RELATING TO ERAB FUNDED RESEARCH

The ERAB encourages its grantees to publish their research findings in peer reviewed journals. Peer review of publications has been shown to be an effective mechanism for assuring quality and independence in science. This can be a lengthy process. A review of the publications resulting from the first and second years funding including the key results appears below together with a review of the publications resulting from exchange awards taken up between 2004 and 2006.

GRANTS FUNDED IN 2003 / 2004

Dr. Silvano Gallus

Istituto di Ricerche Farmacologiche "Mario Negri", Milan - Italy

"Role of different types of alcohol on the risk of cancer: Analysis of data from case-control studies conducted in Italy, Greece and Switzerland over the last two decades".

Dr. Gallus and his team quantified the role of various aspects of alcohol consumption on the risk of several common cancers and cardiovascular diseases in Southern Europe, by analysing existing data from a large number of case-control studies carried out in Italy. Where possible the effect of different beverages was observed.

The findings included:

- Alcohol consumption during meals was inversely related to the risk of AMI (acute heart attack), whereas alcohol consumption outside meals only was unrelated to the risk. (Augustin et al., 2004¹);
- The suggestion that the protection of alcohol drinking against AMI (acute heart attack) may persist, at least in part, for several years after giving up drinking. (Negri et al., 2005²);
- Alcohol consumption did not increase the risk of cutaneous malignant melanoma (CMM). Compared to non-drinkers, beer drinkers showed a 20% reduced risk of CMM but this was not statistically significant due to the relatively low number of beer drinkers (Naldi et al., 2004³);
- Alcohol consumption showed no consistent association with risk of prostate cancer, but a significant reduced risk for benign prostatic hyperplasia (BPH). The patterns of risk were similar for all alcohol beverages (Crispo et al., 2004⁴);
- Compared to abstainers or light drinkers, drinking 3–4 drinks/day was associated with a 2-fold increased risk of oral and pharyngeal cancer, those consuming 5-7 drinks/day a 5-fold increase, those drinking 8-11 drinks/day a 12-fold increase, and those drinking ≥ 12 drinks/day a 21-fold increase. For beer drinkers compared to non beer drinkers the

increased risk of cancers of the oral cavity and pharynx was less marked (moderate drinkers had 20% more risk, and relatively heavy drinkers doubled their risk (Altieri et al., 2004⁵);

- Compared to abstainers or light drinkers, drinkers of 5-7 drinks/day had a 2-fold increased risk of laryngeal cancer, those consuming 8-11 drinks/day a 4-fold increase, and those drinking ≥ 12 drinks/day a 5-fold increased risk. No excess risk was evident for beer and spirit drinkers (Garavello et al., 2006⁶);
- Overall their findings do not confirm a greater risk of upper aero-digestive tract cancers from beer and/or spirits consumption compared to wine which has been shown in studies from other parts of the world but they do confirm that the most prevalent alcohol beverage in each population (and hence most likely the cheapest one) tends to be the one with the highest risk. (Altieri et al., 2005⁷);
- The apparent discrepancy between studies can be explained in terms of different patterns of drinking, and variable (baseline) characteristics of heavy drinkers in various populations.

Dr. Armin Imhof

Department of Internal Medicine, University of Ulm - Germany

"Alcohol, inflammation and atherosclerosis Parts 1, 2 and 3".

Dr. Imhof and colleagues studied particular mechanisms by which alcohol beverages lower cardiovascular risk. This research has added to the growing body of evidence that alcohol has an anti-inflammatory effect and that this contributes to the reduction in cardiovascular risk by reducing the inflammation in blood vessel walls which decreases the risk of constriction and blockage. This study looked at markers of inflammation in the laboratory and showed a positive effect (inhibition of monocyte migration) after consumption of low strength alcohol drinks (beer or wine or diluted ethanol) and their de-alcoholised equivalents compared to water alone and concluded that this might represent one mechanism by which alcohol beverages lower cardiovascular risk (Imhof et al., 2008⁸).

Another aspect of this research which will be published soon looked at adipolectin - a hormone secreted by adipose tissue that enhances insulin

¹ Augustin LSA, **Gallus S**, Tavani A, Bosetti C, Negri E, La Vecchia C (2004) Alcohol consumption and acute myocardial infarction: a benefit of alcohol consumed with meals? *Epidemiology*, 15(6):767-769.

² Negri E, La Vecchia C, Pelucchi C, Tavani A (2005) The risk of acute myocardial infarction after stopping drinking. *Preventive Medicine*, 40:725-728.

³ Naldi L, **Gallus S**, Tavani A, Imberti GL, La Vecchia C (2004) Risk of melanoma and vitamin A, coffee and alcohol: a case-control study from Italy. *European Journal of Cancer Prevention*, 13:503-508.

⁴ Crispo A, Talamini R, **Gallus S**, Negri E, Gallo A, Bosetti C, La Vecchia C, Dal Maso L, Montella M (2004) Alcohol and the risk of prostate cancer and benign prostatic hyperplasia. *Urology*, 64:717-722.

⁵ Altieri A, Bosetti C, **Gallus S**, Franceschi S, Dal Maso L, Talamini R, Levi F, Negri E, Rodriguez T, La Vecchia C (2004) Wine, beer and spirits and risk of oral and pharyngeal cancer: a case-control study from Italy and Switzerland. *Oral Oncology*, 40:904-909.

⁶ Garavello W, Bosetti C, **Gallus S**, Dal Maso L, Negri E, Franceschi S, La Vecchia C (2006) Type of alcoholic beverage and the risk of laryngeal cancer. *European Journal of Cancer Prevention*, 15:69-73.

⁷ Altieri A, Garavello W, Bosetti C, **Gallus S**, La Vecchia C (2005) Alcohol consumption and risk of laryngeal cancer. *Oral Oncology*, 41:956-965.

⁸ **Imhof A**, Blagieva R, Marx N, Koenig W (2008) Drinking modulates monocyte migration in healthy subjects: a randomised intervention study of water, ethanol, red wine and beer with or without alcohol. *Diabetes and Vascular Disease Research*, 5:48-53.

sensitivity and glucose tolerance as well as oxidation of fatty acids in muscle. Its blood concentration is reduced in obese people and those with type II diabetes mellitus. Increased concentrations are associated with lower risk of cardiovascular disease and these are observed in women and shown in this research following consumption of alcohol drinks. It is likely that this will be shown to be another mechanism by which alcohol drinks lower cardiovascular disease risk.

Dr. Martje Weijenberg

Departments of Epidemiology and Pathology, University of Maastricht - The Netherlands

"Alcohol consumption and risk of genetic alterations in genes involved in colorectal cancer in The Netherlands Cohort Study on diet and cancer".

Dr. Weijenberg and colleagues evaluated several aspects of the association between alcohol consumption and colorectal cancer. The findings are reported in the PhD thesis of Dr. Brenda Bongaerts "Alcohol consumption as a risk factor for colorectal cancer: An epidemiological study on genetic susceptibility and molecular endpoints". The findings included:

- Confirmation that, compared to abstaining, high consumption of alcohol of 30 g/day or more is associated with at least a 30% increased risk of colorectal cancer in both men and women (Bongaerts et al., 2008)⁹;
- The increased risk was not dependent on any particular type of beverage (Bongaerts et al., 2008)⁹;
- The increased risk appeared to be more pronounced in high alcohol drinkers with the slow variant of the alcohol metabolizing ADH1C enzyme, compared to those with the fast variant¹⁰;
- The increased risk of colorectal cancer does not depend on particular molecular pathways leading to colorectal cancer (Bongaerts et al., 2007)^{11, 12}.

Professor Philippe De Witte

Laboratory of Behavioural Biology, Université Catholique de Louvain, Louvain-la-Neuve – Belgium

"Neuropsychobiological mechanisms underlying the co-dependence alcohol-nicotine and the respective neurotoxicities occurring during their combined consumptions and their withdrawals".

Professor De Witte and his team have investigated the action of nicotine on a specific part of the brain by microdialysis in rats (Kashkin and De Witte, 2005)¹¹. In addition they studied the release of specific amino acids in the withdrawal stage following a 4 week period of nicotine and alcohol administration. This research is of relevance to the treatment of alcoholics. It will help scientists to understand alcohol withdrawal symptoms and how they are affected by co-dependency with other drugs such as nicotine.

The findings included:-

- Small doses of nicotine may have a modulating effect on symptoms during the initial stages of ethanol withdrawal Lallemand et al., 2006 and 2007)^{12, 13};
- The imbalance occurring between excitatory and inhibitory amino acids during withdrawal of alcohol after long term exposure and during acute nicotine administration may be responsible for additional problems.

Dr. Marianne van den Bree

Department of Psychological Medicine, University of Wales, Cardiff, Wales - UK

"Genetic and environmental influences on risk factors of adolescent alcohol use and problem use".

Dr. van den Bree and her colleagues have carried out the first UK-based twin study (van den Bree et al., 2007)¹⁴ to investigate the aetiology of substance use and misuse in adolescence and early adulthood (Shelton et al., 2007)¹⁵. This study has contributed to the understanding of the mechanisms by which friends alcohol consumption influences adolescent drinking behaviour. It has implications for intervention programmes and policy development.

Results of this large, population-based study include:-

- Alcohol interventions focused on the development of heavier alcohol consumption are more likely to be effective than those aimed at initiation while the opposite is the case for cigarette or marijuana use (Fowler et al., 2007)¹⁶;
- There is considerable overlap in the common environmental and genetic factors which contribute to the relationship between adolescents own alcohol consumption and that of their friends¹⁷;
- Shared environmental influences (those that make family members more alike) increase likelihood of heavy and problem consumption and increase the likelihood that they will engage with peers who consume alcohol.

⁹ Bongaerts BWC, van den Brandt PA, Goldbohm RA, de Goeij AFPM, **Weijenberg MP**. Alcohol consumption, type of alcoholic beverage and risk of colorectal cancer at specific subsites. Int J Cancer. 2008 Nov 15;123(10):2411-7.

¹⁰ Bongaerts BWC, de Goeij AFPM, Wouters KAD, van Engeland M, Gottschalk RWH, van Schooten FJ, Goldbohm RA, van den Brandt PA, **Weijenberg MP**. Alcohol consumption, alcohol dehydrogenase 1C (ADH1C) genotype and risk of colorectal cancer in the Netherlands Cohort Study on diet and cancer. Submitted for publication.

¹¹ Bongaerts BWC, de Goeij AFPM, de Vogel S, van den Brandt PA, Goldbohm RA, **Weijenberg MP**. Alcohol consumption and distinct molecular pathways to colorectal cancer. The British journal of nutrition. 2007 Mar;97(3):430-4.

¹² Bongaerts BWC, de Goeij AFPM, van den Brandt PA, **Weijenberg MP**. Alcohol and the risk of colon and rectal cancer with mutations in the K-ras gene. Alcohol. 2006 Apr;38(3):147-54.

¹³ Lallemand F, Ward RJ, **De Witte P** (2007) Nicotine increases ethanol preference but decreases locomotor activity during the initial stages of chronic ethanol withdrawal. Alcohol and Alcoholism, 42(3):207-218.

¹⁴ **van den Bree MBM**, Rice F, Fowler TA, Shelton KH, Lifford KJ, Scourfield J, Harold Gordon T, Thapar A (2007) The Cardiff study of all Wales and North West of England twins (CaStNET): a longitudinal research program of child and adolescent development. Twin Research and Human Genetic, 10(1):13-23.

¹⁵ Shelton K, Lifford K, Fowler T, Rice F, Neale M, Harold G, Thapar A, **van den Bree M** (2007) The association between conduct problems and the initiation and progression of marijuana use during adolescence: a genetic analysis across time. Behavior Genetics, 37(2):314-325.

¹⁶ Fowler T, Lifford K, Shelton K, Rice F, Thapar A, Neale MC, McBride A, **van den Bree M** (2007) Exploring the relationship between genetic and environmental influences on initiation and progression of substance use. Addiction, 101(3):413-422.

¹⁷ Fowler T, Shelton K, Lifford K, Rice F, McBride A, Nikolov I, Neale MC, Harold G, Thapar A, **van den Bree M** (2007) Genetic and environmental influences on the relationship between peer alcohol use and own alcohol use in adolescents. Addiction, 102(6):894-903.

Dr. Helen Reeves

Centre for Liver Research, University of Newcastle upon Tyne, Newcastle upon Tyne - UK

"A comprehensive identification and characterisation of genes that are differentially expressed during the development and progression of alcohol induced liver disease".

Dr. Reeves research used new gene technology to study alcoholic and non alcoholic liver disease to try to find out why only 10% of heavy drinkers get liver disease with a view to developing targeted prevention strategies, for example, counselling "high risk" individuals prior to the onset of heavy drinking. It also aims to identify treatments which can prevent liver disease progressing in patients who have already developed problems.

Specific findings included:

- A variation in a particular gene (polymorphism), the KLF6 gene, was associated with advanced non alcoholic fatty liver disease (Miele et al., 2008)¹⁸;
- Reduction of a specific gene (GSTT1) supports the conclusion that its loss is an integral part of the progression of the liver disease (Beale et al., 2007)¹⁹.

GRANTS FUNDED IN 2004 / 2005

Professor Giancarlo Colombo

Department of Neuroscience, University of Cagliari, Cagliari - Italy

"Development of a rodent model of beer consumption: investigation on the differential contribution of gustatory and pharmacological factors to beer drinking behaviour".

Professor Colombo's team has studied two sets of rats one of which prefers alcohol and one which does not to study beer drinking behaviour. Both groups of rats drink alcohol free beer in equal amounts. For the study they were given alcohol free beer made alcoholic with increasing concentrations of ethanol to see if this would make the alcohol preferring rats drink more or overcome the reluctance of non alcohol preferring rats to drink.

The findings included (Orru et al., 2007)²⁰:-

- Both groups drank more of the alcohol free beer with added alcohol but
- When the alcohol free beer was removed the alcohol preferring rats did not show increased tendency to drink alcohol and
- The non alcohol preferring rats behaviour returned to normal (aversion to alcohol) and

- Beer drinking was mostly driven by the taste and did not lead to the development of "psychological" dependence on alcohol.

Professor Mary McMullan

School of Psychology, Cardiff University, Cardiff - UK

"Alcohol aggression outcome expectancies".

Professor McMullan examined the effect on alcohol-aggression expectancies in a group of men. The study compared the results of different questionnaires about alcohol consumption and aggression before and after an interview in which the subject was asked to describe past experiences of alcohol-related aggression and alcohol related pleasure compared to a control group asked to describe a neutral event.

The findings from this research have highlighted that:-

- Alcohol-expectancies can be increased by asking individuals to recall previous drinking experiences, and suggest that when developing treatment for alcohol-related violence we need to be aware of the risk of increasing alcohol-related aggression expectancies (McMullan and McCulloch, 2008)²¹; and
- It is likely that the Alcohol-Related Aggression Questionnaire (ARAQ-AA) is a valid measure of the alcohol-aggression outcome expectancy and may be of value in studying the impact of the alcohol-aggression outcome expectancy on actual aggression and violence (McMullan, 2008)²².

Professor Filippo Crea

Institute of Cardiology, Catholic University of the Sacred Heart, Rome - Italy

"Mechanisms of the protective effects of alcohol consumption on cardiovascular risk and on myocardial preconditioning".

Professor Crea investigated potential biological mechanisms to explain the association between moderate alcohol consumption and lower cardiovascular risk. These mechanisms were investigated in healthy subjects using data from a large cohort study in the southern region of Italy and in patients with coronary artery disease.

The findings from the study of the cohort included:

- Moderate consumption of alcohol drinks did not affect blood pressure but excessive drinking was associated with raised blood pressure;
- The inflammatory marker hs-CRP was associated with heavy drinking in men but not women;
- No association of a gene difference (polymorphism in the ADH3 gene with HDL cholesterol or hs-CRP was found in this cohort.

¹⁸ Miele L, Beale G, Patman G, Nobili V, Leathart J, Grieco A, Abate M, Friedman SL, Narla G, Bugianesi E, Day CP, **Reeves HL** (2008) The Kruppel like factor 6 genotype is associated with fibrosis in non-alcoholic fatty liver disease. *Gastroenterology*, 135(1):282-291.

¹⁹ Beale GS, Miele L, Abate ML, Bugianesi E, **Reeves HL**, Day CP (2007) Differential expression of GSTT1 and GSTT2 is associated with more advanced fibrosis in patients with NAFLD. *Journal of Hepatology*, suppl. 1, 46; S264.

²⁰ Orru A, Lobina C, Maccioni P, Gessa G.L., Carai M, **Colombo G.** (2007) Repeated exposure to alcoholic beer does not induce long-lasting changes in alcohol self-administration and intake in Sardinian alcohol-preferring and Sardinian non-preferring rats. *Alcohol and Alcoholism*, 42(6):513-524.

²¹ **McMullan, M.** and McCulloch, A. (2008) Alcohol-aggression outcome expectancies and their responsiveness to event recall. *Addiction Research and Theory*, in press. (DOI: 10.1080/16066350801968724)

²² **McMullan, M.** (2008). The relationships between alcohol use, trait aggression and the alcohol-aggression outcome expectancy in male students. *Journal of Substance Use*, iFirst Article 1-9.

The findings of the studies on patients included the following:

- Moderate consumption of alcohol drinks had a remarkably positive effect on risk profile for cardiovascular diseases;
- In contrast, heavy alcohol consumption increases the risk of cardiovascular events through a variety of mechanisms including activation of inflammatory cells, hypertension and abolition of ischemic preconditioning;
- The abolition of ischemic preconditioning is likely to play a key role in explaining the higher mortality following an acute myocardial infarction observed in heavy and binge drinkers;
- Intake of moderate to high doses of alcohol drinks should be avoided in patients at high risk of acute myocardial infarction (Niccoli et al., 2008)²³.

PUBLICATIONS RESULTING FROM ERAB EXCHANGE AWARDS 2004-2006

In 2004 ERAB granted 2 Exchange Awards.

The first was to Dr. Kate Atherton, a Research Assistant at the University of Manchester, who applied to work for six months as an interne at WHO, Geneva. She was attached to a new diabetes initiative called Diabetes Action Now (DAN) where her main task was to design a research study that would measure the level of diabetes awareness. She developed a study protocol, essentially a recipe for how the research is to be conducted. She was also involved in the collation of press articles following the official launch of the DAN which also coincided with the publication of new worldwide figures for diabetes. Her analysis summarised the breaking of the story, from the initial mass of wire service reports repeated ad verbatim to the more involved and locally adapted news stories that appeared later on. This provided an appreciation of the way in which media stories are generated which was of enormous use given the awareness raising goals of DAN and also interested the Department of Communications for the WHO Director General.

The second was to Dr. Joline Beulens, a PhD-fellow of Wageningen University working with TNO Nutrition and Food Research, to spend 6 months at Harvard University School of Public Health to conduct clinical research on Coronary Heart Disease and to expand collaboration between the two research-groups. The results of this work, which investigated men

with hypertension enrolled in the Health Professionals Follow-up Study, were published in 2007 (Beulens et al., 2007)²⁴ and showed that moderate alcohol consumption was associated with reduced risk of myocardial infarct (heart attack) in men with hypertension to a similar degree to that of men without hypertension and concluded that men with hypertension who drink moderately and safely may not need to change their drinking habits.

In 2005 Dr. Przemyslaw Bienkowski of the Department of Pharmacology and Physiology of the Nervous System at the Institute of Psychiatry and Neurology in Warsaw, Poland received an award for a six month visit to Professor Giancarlo Colombo at the Department of Neuroscience at the University of Cagliari in Italy. The aim of the visit was to gain experience, select topics for future collaboration between the two institutions and participate in ongoing experiments in the following areas:

- genetic selection of alcohol preferring sP and alcohol non-preferring sNP rats;
- alcohol self-administration, extinction and reinstatement of ethanol seeking in sP rats;
- nicotine self-administration in rodents.

The results of some of this work, which studied alcohol preferring rats, were published in 2007 (Maccioni et al., 2007)²⁵ with the conclusion that that odour and taste of alcohol beverages elicit immediate craving responses in abstinent alcoholics.

In 2006 Dr. Anja C. Huizink of the Erasmus University Medical Centre in Rotterdam received an exchange award to visit the well-established research group at the Department of Psychiatry at Washington University, St. Louis, programme in genetic epidemiology where there is a strong representation of experts who work in the area of substance abuse. The purpose of this research visit was to enhance the quality and depth of future genetic epidemiological analyses with regard to alcohol use disorders in Dutch cohort samples and to generate new links with strong potential for future collaboration between the Dutch and US groups.

During the course of the visit Dr. Huizink was involved in research to examine the link between depression, mania, and remission of nicotine dependence. The results of which were published in 2008 (Agrawal et al., 2008)²⁶ showed that there are patterns of factors across different development phases of adulthood which means that depending on the age of the individual different aspects of psychopathology may be of greater significance affecting the success of treatments for addiction.

²³ Niccoli G., Altamura L., Fabretti A., Lanza G.A., Biasucci L.M., Rebuzzi A.G., Maria Leone A, Porto I., Burzotta F, Trani C., **Crea F.** (2008) Ethanol abolishes ischemic preconditioning in humans. Journal of the American College of Cardiology, 51(3):271-275.

²⁴ **Beulens JWJ**, Rimm EB, Ascherio A et al. (2007). "Alcohol consumption and risk for coronary heart disease among men with hypertension". Annals of Internal Medicine, 146:10-19.

²⁵ Paola Maccioni, Alessandro Orrù, Agnieszka Korkosz, Gian Luigi Gessa, Mauro A.M. Carai, Giancarlo Colombo and **Przemyslaw Bienkowski** 2007. "Cue-induced reinstatement of ethanol seeking in Sardinian alcohol-preferring rats". Alcohol 41(1):31-39.

²⁶ Agrawal A, Sartor C, Pergadia, **ML, Huizink AC** and Lynskey MT (2008). "Correlates of smoking cessation in a nationally representative sample of US adults". Addiction Behaviour, 33(9):1223-6. Epub 2008 Apr 8.



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