GENE TECHNOLOGY FORUM 2002

Personalized Medicine: Myth or Reality

September 13-14, 2002 | Tartu, Estonia

Eesti Geenikeskus
Estonian Genome Foundation

CONTENT

PROGRAMME

FRIDAY, SEPTEMBER 13, 2002

8:30-9:00 Registration at the Vanemuise Concert Hall

9:00-9:10 OPENING
PROF. HELE EVERAUS
Vice-Rector of the University of Tartu, Estonia

9:10-9:20 PricewaterhouseCoopers Gene Technology Award

9:20-11:00 OPENING SESSION
PROF. DR. DETLEV GANTEN
Max Delbrück Center for Molecular Medicine, Berlin-Buch, Germany
"Molecular Medicine and Patient Care: What Can We Expect?"
PROF. MARK LATHROP
Centre National de Genotypagé, France
"Genetic and Epidemiological Approaches to Studying Human Disease"

11:00-11:20 Coffee/tea Break

11:20-13:30 SESSION I
DR. JØRGEN DIRACH
Research Counsellor, Corporate Research Affairs, Novo Nordisk A/S, Denmark
"An Overview of Drug Development"
PROF. DR. IVAR ROOTS
Institute of Clinical Pharmacology, Charité Clinics, Humboldt University of Berlin, Germany
"Pharmacogenomics-Based Individualisation of Drug Therapy"
PROF. ERWIN SCHURR
McGill University, Montreal, Canada
"Genetic Dissection of Susceptibility to Mycobacterial Diseases"

13:30-14:45 Lunch

14:45-16:15 SESSION II
PROF. MATHIAS UHLÉN
Stockholm Royal Institute of Technology, Sweden
"Affinity Reporter Proteomics for Whole Genome Analysis"
DR. DAVID G. WANG
Executive Vice President, First Genetic Trust, Inc., USA
"Informatics Systems and Genomics"

16:15-16:35 Coffee/tea Break

16:35-18:00 SESSION III
DR. MICHAEL D. CALDWELL
Director, Marshfield Medical Research Foundation, USA
"The Establishment of a National Resource for Personalized Medicine"
PROF. ANDRES METSPALU
Professor, University of Tartu, Estonia
"Estonian Genome Project: Present Actions and Future Directions"

20:00 Buffet Dinner at restaurant Atlantis

SATURDAY, SEPTEMBER 14, 2002

9:00-10:30 SESSION IV

PROF. RICHARD M. MYERS
Stanford Human Genome Center, Stanford University School of Medicine, USA
"Genetics and Genomics of Human Biology and Disease"

PROF. PAOLO BOFFETTA
Unit of Environmental Cancer Epidemiology, International Agency for Research on Cancer, France
"Gene-environment Interactions in Carcinogenesis: the Contribution of Molecular Epidemiology"

10:30-10:50 Coffee/tea Break

10:50-12:15 SESSION V

PROF. ANNE-LISE BØRRESEN-DALE
Institute for Cancer Research, The University Hospital, The Norwegian Radium Hospital, Norway
"Molecular Profiling of Breast Cancer; Relation to Clinical Course and Treatment Response"

PROF. RANDO L. ALLIKMETS
Columbia University, USA
"Genetics of Eye Disease: From Simple to Complex"

12:15-14:15 Lunch

14:15-15:45 SESSION VI

PROF. LEENA PELTONEN
Department of Human Genetics, UCLA, USA
"Disease Gene Identification Using Tools Produced by the Human Genome Project"

PROF. AARNO PALOTIE
Department of Pathology and Laboratory Medicine, UCLA, USA
"Migraine: Mapping of a Painfully Complex Trait"

15:45-16:05 Coffee/tea break

16:05-17:50 SESSION VII

DR. WALDEMAR KÜTT
European Commission, Research Directorate General - Life Sciences Directorates, Belgium
"Opportunities for Biotech SMEs in the New Framework Programme"

PROF. BRIGITTE FEUILLET-LE MINTIER
Rennes University, France
"Genetics and Protection of Individual Rights"

PROF. ALEXANDRE MAURON
Faculty of Medicine, University of Geneva, Switzerland
"The Genome and the Self: Bioethical Reflections"

Closing remarks

Organisers reserve a right to make changes in the programme as required.

PROGRAMM

REEDE, 13. SEPTEMBER, 2002

08:30-09:00 Registreerimine Vanemuise Kontserdisaalis

09:00-09:10 AVAMINE
PROF. HELE EVERAUS
Arendusprorektor, Tartu Ülikool

09:10-09:20 PricewaterhouseCoopersi Rakenduslik Geenitehnoloogia Auhind

09:20-11:00 AVASESSION
PROF. DR. DETLEV GANTEN
Max-Delbrücki nimeline Molekulaarmeditsiini Keskus, direktor, Berliin, Saksamaa
"Molekulaarmeditsiin ja tervishoid - millised võiksid olla meie ootused?"
PROF. MARK LATHROP
Riiklik Genotüpiseerimise Keskus, direktor, Evry, Prantsusmaa
"Geneetilised and epidemioloogilised võimalused haiguste uurimisel "

11:00-11:20 Kohvipaus

11:20-13:30 ESIMENE SESSION
DR. JØRGEN DIRACH
Novo Nordisk A/S, teadusnõunik, Taani
"Ravimi väljatöötamise protsessi ülevaade"
PROF. DR. IVAR ROOTS
Kliinilise Farmakoloogia Instituut, Charité Kliinik, juhataja, Humboldti Ülikool, Berliin, Saksamaa
"Farmakogenoomikal baseeruv ravimeetodite personaliseerimine"
PROF. ERWIN SCHURR
McGilli Ülikool, Montreal, Kanada
"Müobakteriaalsetele haigustele vastuvõtlikkuse geneetiline eelsoodumus"

13:30-14:45 Lõuna

14:45-16:15 TEINE SESSIOON
PROF. MATHIAS UHLÉN
Stockholmi Kuninglik Tehnoloogia Instituut, Rootsi
"Afiinsusmärgisega proteoomika kogu genoomi uurimiseks"
DR. DAVID G. WANG
First Genetic Trust Inc. asepresident, Ameerika Ühendriigid
"Informaatikasüsteemid ja genoomika"

16:15-16:35 Kohvipaus

16:35-18:00 KOLMAS SESSIOON
DR. MICHAEL D. CALDWELL
Marshfieldi Meditsiiniuuringute Fond, direktor, Ameerika Ühendriigid
"Rahvusliku andmebaasi loomine personaalse meditsiini kasutuselevõtmiseks"
PROF. ANDRES METSPALU
Biotehnoloogia õppetool, Tartu Ülikool, Eesti Vabariik
"Eesti Geenivaramu projekt - milline on hetkeseis ja kuhu me liigume?"

20:00 Buffet õhtusöök restoranis Atlantis

LAUPÄEV, 14. SEPTEMBER, 2002

09:00-10:30 NELJAS SESSIOON
PROF. RICHARD M. MYERS
Stanfordi Inimese Genoomi Keskus, direktor, Stanfordi Ülikool, Ameerika Ühendriigid
"Inimese bioloogia ja haigusete geneetika ning genoomika"
PROF. PAOLO BOFFETTA
Rahvusvaheline Vähiuuringute Agentuur, Lyon, Prantsusmaa
"Geenide ja keskkonna koostoime kartsinogeneesis - molekulaarse epidemioloogia panus"

10:30-10:50 Kohvipaus

10:50-12:15 VIIES SESSIOON
PROF. ANNE-LISE B¸RRESEN-DALE
Vähiuuringute Instituut, Norra Ülikooli Radium Kliinik, Oslo, Norra
"Rinnavähi klassifitseerimine molekulaarsetel alustel, seos kliinilise kulu ja ravile reageerimise vahel"
PROF. RANDO L. ALLIKMETS
Columbia Ülikool, Ameerika Ühendriigid
"Silmahaiguste geneetika - lihtsamalt keerulisemale"

12:15-14:15 Lõuna

14:15-15:45 KUUES SESSIOON
PROF. LEENA PELTONEN
Inimese Geneetika osakond, juhataja, Gonda Geneetiliste Uuringute Keskus, California Ülikool, Los Angeles, Ameerika Ühendriigid
"Haigusgeenide identifitseerimine kasutades Inimgenoomi Projekti käigus loodud vahendeid"
PROF. AARNO PALOTIE
Patoloogia ja laborimeditsiini osakond, Gonda Geneetiliste Uuringute Keskus, California Ülikool, Los Angeles, Ameerika Ühendriigid
"Migreen - erakordselt keerulise komplekshaiguse kaardistamine"

15:45-16:05 Kohvipaus

16:05-17:50 SEITSMES SESSIOON
DR. WALDEMAR KÜTT
Euroopa Komisjon, Brüssel, Belgia
Väikse- ja keskmise suurusega biotehnoloogia ettevõtete võimalused uues Raamprogrammis
PROF. BRIGITTE FEUILLET-LE MINTIER
Rennesi Ülikool, Prantsusmaa
"Geneetika ja indiviidi õiguste kaitsmine"
PROF. ALEXANDRE MAURON
Arstiteaduskond, Genfi Ülikool, Shveits
"Genoom ja indiviid - bioeetilised mõtisklused"

Konverentsi lõpetamine

Korraldajatel on õigus teha vajadusel programmis muudatusi.

PROF. DR. DETLEV GANTEN

Max Delbrück Center for Molecular Medicine, Berlin-Buch, Germany

PERSONAL DATA:
Born on March 28, 1941 in Lüneburg (Germany), Nationality: German, Passport number: 6466100474
Married to Dr. med. Ursula Ganten, 2 children: Tom-Michael, Ted-Oliver

EDUCATION AND TRAINING:

1947 - 62	Elementary School and High School: Bremerhaven and Bremen
1962 - 69	Medical School, Universities of Würzburg, Montpellier (France), Tübingen Clinical Training in Marakech, Marocco (Surgery), Tübingen (Internal Medicine and Surgery), Emden (Gynaecology)
1969 - 73	Senior Research Fellow at the Clinical Research Institute of Montreal, McGill University, Department of Experimental Medicine, Canada
1973 - 91	Department of Pharmacology, University of Heidelberg, Germany
1991-	Max Delbrück Center for Molecular Medicine (MDC) Berlin-Buch
1993-	Department of Clinical Pharmacology, Free University Berlin, University Clinic Benjamin Franklin (UKBF)

DIPLOMA
Agriculture, Elmshorn/Holstein (1959)
MD degree, University of Tübingen (1968), Licence to practice medicine (1970)
PhD, McGill University, Montreal, Canada (1973)
Full professorship at the University of Heidelberg (1975)
Specialization in Pharmacology "Facharzt" (1978) and Clinical Pharmacology (1993)

POSITIONS
Director, Max Delbrück Center for Molecular Medicine (MDC) Berlin-Buch (1992)
Chair, Department of Clinical Pharmacology, Free University Berlin, University Clinic Benjamin Franklin (UKBF) Steglitz (1994)

EDITOR
Journal of Molecular Medicine (JMM)

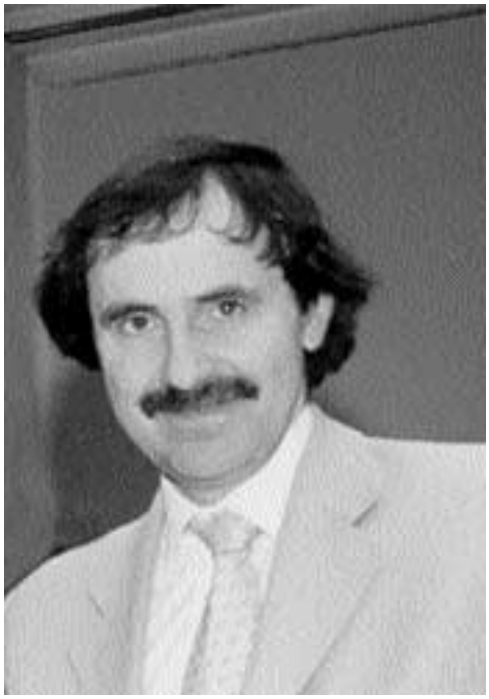
EDITORIAL BOARDS
Clinical and Experimental Hypertension, Journal of Hypertension, Hypertension, Heart and Vessels, Fundamental and Clinical Pharmacology, Journal of Clinical Investigation, Endothelium, Handbook of Experimental Pharmacology

CONTACT INFORMATION
Detlev Ganten, M.D., Ph.D.
Max Delbrück Center for Molecular Medicine (MDC)
Robert-Rössle-Str. 10
D-13122 Berlin-Buch, Germany
Tel. +49-30-9406 3278
Fax: +49-30-949 7008
e-mail: ganten@mdc-berlin.de
Internet: http://www.mdc-berlin.de

Molecular Medicine: what can we expect?

When, at the start of 2001, the first reliable complete sequences of the human genome were presented, some scientists dared to predict that the future would be shaped by this new information in the context of a new molecular form of medicine. The predictions included the availability of genetic tests which can be used for the prediction of diseases, allowing prevention on an individual basis, the treatment of cancer which will be tailor-made to suit the genetic profile of a particular tumor and tailor-made drugs to suit individual patients, with their development and selection being based on genetic testing. Even 10 years ago, anyone who had dared to make these predictions would not have been believed. Now, they are made by successful scientists and accepted by many as sensible. The next 10 years will show just how successful we will be. The future is uncertain, but it is certain, that medical care and investment in the life sciences will be more important and rewarding than ever.

The term "molecular medicine" is more than just the application of the methods of molecular biology, gene technology and genome research to the understanding of the molecular biological mechanisms governing health and disease. We regard molecular medicine as a comprehensive interdisciplinary concept, which combines all the new methodological opportunities of genome research with its use in experimental research in the laboratory, the transfer of these results to the clinics and everyday general practice, addressing new questions in bioethics as well as the practical and commercial use of the results for the diagnosis, prevention and treatment of. This also includes effective legislation to prevent any form of genetic discrimination. More rapid than ever science will shape our future and the Life Sciences have taken the lead.



PROF. MARK LATHROP

Centre National de Genotypagé, France

DEGREES

B.Sc. (Hons) Mathematics, University of Alberta, 1972.
M.A. Anthropology, University of Alberta, 1977.
Ph.D. Biomathematics, University of Washington, 1980.

ACADEMIC APPOINTMENTS

1998-	Directeur Général, Centre National de Génotypage, Evry, France
1996-	Professor of Human Genetics, University of Oxford
1994-1998	Scientific Director, Wellcome Trust Centre for Human Genetics, Oxford (Wellcome Trust Principal Fellow)
1988-1994	Directeur de recherche, INSERM, Paris, France
1986-1988	Associate, Howard Hughes Medical Institute, University of Utah, Salt Lake City, USA

PUBLICATIONS (2002)

· Heathcote K, Rajab A, Magré J, Syrris P, Besti M, Patton M, Delépine M, Lathrop GM, Capeau J, Jeffery S. Molecularanalysis of Berardinelli-Seip congenital lipodystrophy in Oman; evidence for multiple loci. Diabetes, 2002.

· Jobard F, Lef?vre C, Karaduman A, Blanchet-Bardon C, Emre S, Weissenbach J, Ozgüc M, Lathrop GM, Prud'homme JF, and Fischer J, Lipoxygenase-3 (ALOXE3) and 12(R)-lipoxygenase (ALOX12B) are mutated in nonbullous congenital ichthyosiform erythroderma (NCIE) linked to chromosome 17p13.1. Hum Mol Genet, 2002. 11(1): p.107-113.

· Lechner D, Lathrop GM, and Gut I. Large-scale genotyping by mass spectrometry : experience, advances and obstacles. Current Opinion in Chemical Biology, 2002. 6 (1): p. 31-8. (Adobe Acrobat Document, 175 KB).

· Soria JM, Almasy L, Souto JC, Bacq D, Buil A, Faure A, Martinez-Marchan E, Mateo J, Borrell M, Stone W, Lathrop GM, Fontcuberta J, and Blangero J. A Quantitative-Trait Locus in the Human Factor XII Gene Influences Both Plasma Factor XII Levels and Susceptibility to Thrombotic Disease. Am J Hum Genet, 2002. 70(3).

CONTACT INFORMATION

Gregory Mark Lathrop, Ph.D.
Directeur Général
Centre National de Génotypage
2 rue Gaston Crémieux
CP 5721
91057 Evry Cedex
France

Tel: +33 (0) 1 60 87 84 03
Fax: +33 (0) 1 60 87 84 84
e-mail: mark.lathrop@cng.fr
http://www.cng.fr/

DR. JØRGEN DIRACH

Research Counsellor, Corporate Research Affairs, Novo Nordisk A/S, Denmark

CV

Jørgen Dirach, received MD from Copenhagen University. He has worked as a clinician in hospitals and thereafter done clinical development and project management in the pharmaceutical industry for 15 years and recently joined Corporate Research Affairs at Novo Nordisk.

From 1995 to 2002 he has been instrumental in the transformation of the management of the portfolio of drug development projects in Novo Nordisk from a divisionalised structure to true portfolio management view.

He is honorary member of the Danish Society for Good Clinical Practice which he was co-founder of in 1988 and served as Chairman for 1988 to 1996. He is member of the Faculty of Pharmaceutical Physicians (UK) and the European Federation of Biotechnology (EFB) and serves as Governor on the Board of the European Association of Pharma Biotechnology. He has prepared publications and lectures on clinical research methodology, pharmacokinetics, GCP, drug development/multi project management and quality management.

CONTACT INFORMATION
Jørgen Dirach, M.D.
Research Counsellor
Novo Nordisk A/S
Corporate Research Affairs
Novo Allé 1
DK-2880 Bagsv¿rd
Denmark
Tel.: +45 4444 8888
Tel.: +45 4442 3355 direct
Tel.: +45 2829 3355 mobile
Fax: +45 4442 1286
e-mail: jdi@novonordisk.com
www.novonordisk.com

An Overview of Drug Development

Drug development is a lengthy and costly process. It can be compared to building a major bridge: It takes 10 to 11 years and costs up to USD 800 Mill.

One of the reasons for the high cost is the cost of failures; drug candidates that turn out to have toxicologic or mutagenic properties, no clinical effect or severe adverse clinical effects that inhibit the use as a medicine. For every 5000 to 10000 new active substances that are explored in the drug discovery process, 7 will enter clinical development and only one will be reaching the market.

The result of this lengthy process is a mountain of documentation on:

- The preclinical properties including safety, mutagenicity and carcinogenicity
- Documentation on drug substance, drug product and analytical methods. How is the medicine produced to ensure a pure substance, how is it analysed, how and for how long time can it be stored
- Clinical documentation on safety and efficacy in healthy volunteers, and in patients including large comparative trials with current best treatment for the disease in question.

The demand for documentation has increased resulting in the lowest output in 20 years in terms of launch of new medicines in 2000 despite a dramatic increase in cost of drug development.

Due to this vast investment, it is important for the researcher to know about the conditions for drug development.

PROF. DR. IVAR ROOTS

Institute of Clinical Pharmacology, Charité Clinics, Humboldt University of Berlin, Germany

CV

21.05.1942	born in Berlin
1949-1962	Elementary School and High School (Gymnasium) at Giessen, school leaving examination (Abitur)
1962-1968	study of human medicine at the Justus-Liebig-Universität in Giessen and the Freie Universität in Berlin. Leaving examination January 1968 in Giessen
1968-1969	internship in pediatrics, internal medicine, gynecology, and surgery at Giessen, Marburg, and Berlin
1970	registration as a physician
1972	Doctor of Medicine (pediatric clinic, head: Prof. Dr. F.H. Dost, Universität Giessen)
1970-1976	scientific assistant at the Institute of Clinical Pharmacology, Freie Universität Berlin, Klinikum Steglitz (head: Prof. Dr. H. Kewitz)
1976	assistant professor
1977	certified by the chamber of physicians as a specialist for pharmacology and toxicology
1981	habilitation for pharmacology and toxicology (Privatdozent)
1985	professor of Clinical Pharmacology
1988-1993	interim director of the Institute of Clinical Pharmacology, Klinikum Steglitz
1993	approval by the chamber of physicians as a specialist in Clinical Pharmacology
since 1993	chair of Clinical Pharmacology, director of the Institute of Clinical Pharmacology, Universitätsklinikum Charité, Humboldt-Universität zu Berlin
1998	President of the German Society of Clinical Pharmacology and Therapy
1999	speaker of the research-group association "Pharmacogenetic diagnostics: improvement of therapy and drug development" in the frame of the project "Diagnosis and therapy by the means of molecular medicine", established by the German Ministry of Education and Research
2001	Galenus von Pergamon Prize (together with others)

MAIN SCIENTIFIC INTERESTS

Pharmacogenetics: individualisation of drug therapy
Genetic susceptibility factors of cardiovascular diseases, cancer, depression, and schizophrenia
Variability of drug metabolism: genetics of cytochrome P450 enzymes, acetyltransferases, glutathione transferases, etc.
Pharmacokinetics
Clinical trials

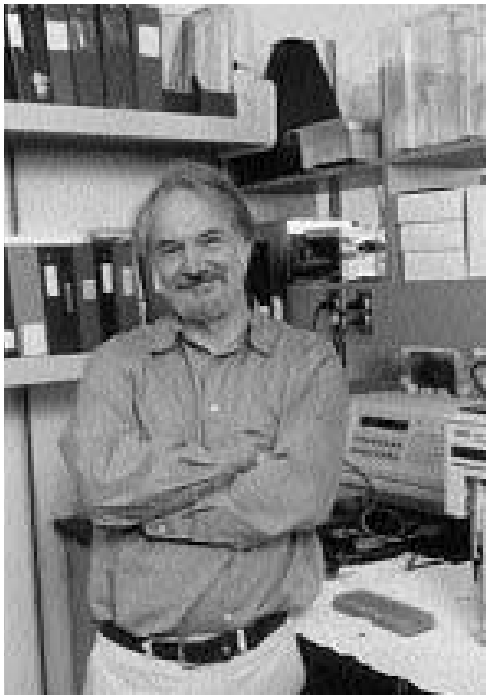
CONTACT INFORMATION

Ivar Roots, M.D., Ph.D.
Institute of Clinical Pharmacology
University Hospital Charité
Humboldt University
Schumannstr. 20/21
10017 Berlin, Germany
Tel. +49 (0)30 450 525 151
Fax. +49 (0)30 450 525 932
e-mail: ivar.roots@charite.de
http://www.charite.de/klinpharm

Pharmacogenomics-Based Individualisation of Drug Therapy

Hereditary variances in drug metabolising enzymes, drug transporters and drug targets such as drug receptors are major determinants of individual drug response. The elucidation of the hereditary basis of the variability in drug response, which is a still ongoing process, allows a more individualised and patient-tailored treatment which should improve outcome and reduce cost from adverse drug events.

There are many examples of drugs in which polymorphic expression of metabolising enzymes is responsible for therapeutic failure, exaggerated drug response or serious toxicity after taking a standard dose. Functional polymorphisms in cytochrome P450 (CYP) drug metabolising enzymes (i.e. CYP2C19, CYP2D6) are known to be able to exert dramatic influences on drug clearances. Accordingly, we have recently developed a method for the calculation of genotype-adapted drug dosages (Acta Psychiatr. Scand 2001;104:173-92). These genotype-specific dosages will lead to bioequivalent drug exposition in individuals, regardless if the patient is deficient or even displays ultra-rapid activity for the respective enzyme. The application of these pharmacogenetics-based individual drug dosages should reduce the risk of adverse drug reactions in patients deficient for drug metabolising enzymes and may on the other hand increase therapeutic efficacy. Polymorphisms in drug transporters (e.g. the MDR1 gene-product P-Glycoprotein), important in drug transport across compartments, are another major determinant of observed differences in drug disposition. There is increasing evidence that polymorphisms in drug targets such as receptors may also have an important influence on responsiveness to drug therapy and may ultimately lead to rational drug selection criteria. The development of computer-based drug prescription tools may ultimately permit to have this pharmacogenomic knowledge at hand right at the time of prescription filling and will be an important further step for individualised drug treatment.



PROF. ERWIN SCHURR

McGill University, Montreal, Canada

EDUCATIONAL BACKGROUND:
Albert-Ludwigs University, Freiburg, Germany
B.Sc. 1979 Biology/Chemistry
M.Sc. 1981 Physical Chemistry
M.Sc. 1983 Parasitology
Ph.D. 1986 Cell Biology
McGill University, Dept. Biochemistry
PDF 1986-89 Molecular Genetics

ACADEMIC APPOINTMENTS:
1990-96 Assistant Professor, Depts. of Experimental Medicine and Biochemistry, McGill University
1990 - Member, McGill Centre for the Study of Host Resistance
1993 - Medical Scientist, The Montreal General Hospital (MGH)
1996 - Associate Professor, Depts. of Experimental Medicine and Biochemistry, McGill University
1997 - Chairman, Research Advisory Committee, MGH Research Institute
1998 - Associate Professor, Dept. of Human Genetics, McGill University
1999 - Leader, Infection and Immunity Axis, McGill University Health Centre
2000 - Associate Director, McGill Centre for the Study of Host Resistance

SELECTED AWARDS:
1986-89 Postdoctoral Fellowship, Deutscher Akademischer Austauschdienst (DAAD) Sonderprogramm Moleculare Parasitologie
1990 Fraser-Monat-McPherson Award, Faculty of Medicine, McGill University
1991 ICAAC Merck Young Investigators Award of the American Society for Microbiology and the American Academy of Microbiology
1991-96 Scholar Award of the Medical Research Council of Canada
1992 Canada-USSR Exchange Award, Association of Universities and Colleges of Canada
1993 Fellowship Award, WHO/PAHO and the Canadian Society for International Health
1996-2000 Senior Researcher Award, Fonds de la Recherche en Santé du Québec
1996-2000 Dr. Phil Gold Research Award, MGH Research Institute
2000-05 Investigator Award, Canadian Institutes of Health Research

RESEARCH AREA:
Host genetics of susceptibility to infectious diseases with focus on tuberculosis and leprosy.

CONTACT INFORMATION
Erwin Schurr, Ph.D.
McGill University Health Centre Research Institute
Centre Study Host Resistance
Montreal General Hospital
1650 Cedar, Rm A61-21
Montreal, QC H3G 1A4
Canada
Tel: (514) 937-6011 ext 4513
Fax: (514) 934-4373
e-mail: erwin@igloo.epi.mcgill.ca
www.mcgill.ca

Genetic Dissection of Susceptibility to Mycobacterial Diseases

Tuberculosis (TB) is an infectious disease caused by Mycobacterium tuberculosis. This human pathogenic bacterium infects an estimated one third of the world's population resulting in over 2 million deaths each year. The rate of progression from infection to disease is highly variable. Approximately 90% of infected individuals never develop clinically overt disease. Of the 10% of M. tuberculosis infected persons who develop disease, approximately half will be diagnosed within less than 2 years of infection. These epidemiological data clearly show that not all individuals exposed to M. tuberculosis are at equal risk of developing TB.

Leprosy, an ancient and devastating infectious disease caused by Mycobacterium leprae, still affects an estimated 700,000 persons each year. Clinically, leprosy can be categorized as paucibacillary or multibacillary disease depending on the number of skin lesions and number of leprosy bacilli within the lesions. Leprosy is transmitted by contact with infected persons, however, the route(s) of transmission (skin contact or respiratory) is not known. Although leprosy can be effectively treated by chemotherapy and is not highly infectious, it has tenaciously resisted eradication and the worldwide incidence of leprosy has shown little decrease over the last 20 years. The explanation for this continued high incidence is unknown, but is likely to depend on specific associations between M. leprae and its human host.

There is good evidence that host genetic factors are important risk factors for both TB and leprosy. Ethnic variability, familial clustering, twin studies and complex segregation analyses all suggest host genetics as major contributor to TB and leprosy. Furthermore, molecular studies among rare families with hypersusceptibility to mycobacterial disease have identified specific mutations in critical immune response genes. Yet, little is known about the number and diversity of genetic variants predisposing to increased risk of TB or leprosy.

The genetic component of TB and leprosy susceptibility has been studied employing both genome-wide approaches and candidate gene analyses in either population-based or family-based case-control designs. In most studies the effect of selected candidate susceptibility genes was found to be modest. In some studies, however, a strong genetic effect of selected candidate genes on susceptibility was noticed. A possible explanation of these variable results could be provided by the specific clinical manifestations of TB or leprosy that have been investigated. In addition, it is possible that gene environment interactions are critical for revealing specific genetic effects. Consequently, genetic studies that disregard such interaction may dilute an otherwise strong genetic effect on susceptibility.

PROF. MATHIAS UHLÉN

Stockholm Royal Institute of Technology, Sweden

Mathias Uhlén is a Professor of Microbiology at the Royal Institute of Technology (KTH), Stockholm, Sweden. Dr Uhlén is member of the Royal Swedish Academy of Engineering Science (IVA) and the Royal Swedish Academy of Science (KVA). He belongs to the European Molecular Biology Organization (EMBO). Dr Uhlén has more than 300 publications in the field of biotechnology and he is part of a research group in Molecular Biotechnology consisting of approximately 50 scientists in the field of genomics, proteomics and biotechnology. Dr Uhlén serves on the advisory board for the Centre National de Genotypage (CNG), Evry, France and the German Genome Project.

CONTACT INFORMATION
Mathias Uhlén, Ph.D.
Department of Biotechnology
AlbaNova University Center
Royal Institute of Technology (KTH)
106 91 Stockholm, Sweden
Tel: +46 8 5537 8325 Secr: +46 8 5537 8326
Fax: +46 8 5537 8482
e-mail: mathias@biotech.kth.se
www.biotech.kth.se
Visiting address: Roslagstullsbacken 21

Affinity Reporter Proteomics for Whole Genome Analysis

A systematic approach to convert genomics data into biological knowledge based on protein profiling is described. The strategy relies on a high-throughput method for the recombinant production of non-homologous regions of the proteome selected by whole genome bioinformatics. Such protein fragments are individually used to generate and enrich mono-specific antibodies for systematic analysis of protein profiles (expression and localization) in different human organs using tissue arrays The affinity reagents are based on conventional antibodies and affibodies (Nord et al, Nature Biotechnology 15, 772-777, 1997) which are robust "artificial antibodies" suitable for applications such as protein "chips". Here we report the successful cloning and protein production of putative genes encoded by the human chromosome 21. More in-depth studies using tissue arrays are reported for some of the gene products. The results suggest that this affinity reporter strategy can be used to produce a proteome atlas, describing distribution and expression of proteins in normal tissues as well as in common cancers and other forms of diseased tissues.

DR. DAVID G. WANG

Executive Vice President, First Genetic Trust, Inc., USA

CV

David Wang was most recently director of applied genomics and bioinformatics at Motorola Life Scieneces and Chairman of the TSC Scientific Management Committee. Prior to his tenure at Motorola, Dr. Wang was head of human genetics at Bristol-Myers Squibb [BMS] and researcher at Whitehead Institute/MIT Center for Genome Research and head of SNP Identification, Mapping and Genotyping Project. He holds a M.D. from Beijing Medical University, and a Ph.D. in development biology from the California Institute of Technology.

The TSC is a two-year, $50 million initiative, funded by the Wellcome Trust, ten major pharmaceutical companies and two technology companies: Aventis, Bayer Group AG, Bristol-Myers Squibb Company, Glaxo Wellcome PLC, IBM, Monsanto Company, Motorola, Novartis AG, Pfizer Inc, Roche Holding Ltd., SmithKline Beecham PLC, and Zeneca Group PLC.

CONTACT INFORMATION
David G. Wang, M.D., Ph.D.
Executive Vice President
Strategy, Technology and Operations
First Genetic Trust, Inc.
Three Parkway North Center, Suite 150 North
Deerfield, IL 60015
Tel.: (847)317-9240
Fax: (847)317-9075
Cell: (847)804-2003
e-mail: dwang@firstgenetic.net
www.firstgenetic.net

Informatics Systems and Genomics

This presentation will provide insight into the progress made in recent years towards developing secure medical and genetic information management systems, large-scale data aggregation and analysis tools for genomic and pharmacogenomic research. The presentation will highlight key applications of such systems in large-scale genomic research, pharmacogenomic clinical trial, and molecular diagnostics.

DR. MICHAEL D. CALDWELL

Director, Marshfield Medical Research Foundation, USA

CV

Dr. Michael Caldwell is the Director of Medical Research at the Marshfield Clinic and Director of the Marshfield Medical Research Foundation and Director of the Marshfield Clinic's Personalized Medicine Program. The Marshfield Clinic is a large, multidisciplinary, private clinic that provides highly integrated health care for approximately 400,000 patients annually. The Marshfield Medical Research Foundation is the largest private research foundation in Wisconsin and one of the largest in the country.

Prior to joining the Marshfield Clinic, Dr. Caldwell was Professor of Surgery and Biochemistry at the University of Minnesota in Minneapolis (1990-2000); Associate Professor and Professor of Surgery at Brown University, and at the end of that tenure Acting Surgeon-in-Chief, Rhode Island Hospital (1982-1990 and 1988-1990, respectively); Lecturer at University of California, Berkeley, CA (1978-1980); LTC USAMC and Director of Surgical Metabolism, Letterman Army Institute of Research, San Francisco, CA (1976-1980). His surgical residencies were at the Medical University of South Carolina and the Hospital of the University of Pennsylvania. He completed his surgical residencies in 1982 and is Board Certified in General Surgery (1985 and 2000). He is a Fellow of the American College of Surgery. He is also board qualified in clinical nutrition and is a Fellow of the American Board of Nutrition.

He received his BS in Chemistry from the University of South Carolina in 1964, his MD from the Medical University of South Carolina in 1968, and his PhD in Physiology from Vanderbilt University in 1980.

CONTACT INFORMATION
Michael D. Caldwell, M.D., Ph.D.
Director
Marshfield Medical Research Foundation
1000 N. Oak Ave
Marshfield, WI 54449, USA
Tel.: 715-387-5107
e-mail: caldwelm@mmrf.mfldclin.edu
http://research.marshfieldclinic.org/

The Establishment of a National Resource for Personalized Medicine

During the past decade the Marshfield Clinic and its Research Foundation have developed an extraordinary combination of resources which enable a National Resource for discovery projects in Personalized Medicine.

The program brings together:
1. a highly sophisticated electronic medical record with 48 departmental lexicons which effectively stratify disease processes and responses to medications
2. a well characterized epidemiological study area
3. substantial genotyping expertise to create the resource.

Progress to date will be reported.

PROF. ANDRES METSPALU

University of Tartu, Estonia

Date and place of birth: March 11, 1951, Estonia
Citizenship: Estonian
Family status: Married, 4 sons

CV

Andres Metspalu received his M.D. at University of Tartu, Estonia in 1976 and Ph.D. at the Institute of Molecular Genetics of the Ukrainian Academy of Sciences, Kiev, in 1979. In 1981-1982 he was a fellow at Columbia University and at Yale University. Upon his return to Tartu University, Andres Metspalu started to establish a new laboratory, and received the position of the head of the laboratory in 1986. From 1986 he was appointed to the position of scientific director of Estonian Biocentre and in 1992 he was elected a position of professor at University of Tartu. Having received fellowships from FEBS, EMBO, DAAD, HUGO he worked at MPI of Molecular Genetics in berlin, EMBL in Heidelberg and University of Hamburg. 1993-1994 he was a visiting professor at Baylor College of Medicine, Houston, USA working on microarrays with Dr. Tom Caskey and in 1999 he was elected for a visiting scientist position at WHO International Agency of Research on Cancer in Lyon, France.

Andres Metspalu is a nominee of the Soviet Estonian Scientific Reward (1980) and received the Order of The Red Gross (III) from the Estonian President in 2000. He is board member of European Society of Human Genetics, member of HUGO (The Human Genome Organization), member of Tartu University Scientific and Development Committee, board member of Tartu University Centre of Technology, board member of Tartu University Institute of Molecular and Cell Biology, board member of Faculty of Biology and Geography of Tartu University, board member of Estonian Society of Human Genetics, board member of Estonian Genome Foundation, steering committee member of European Science Foundation Functional Genomics Program, member of American Society of Human Genetics.

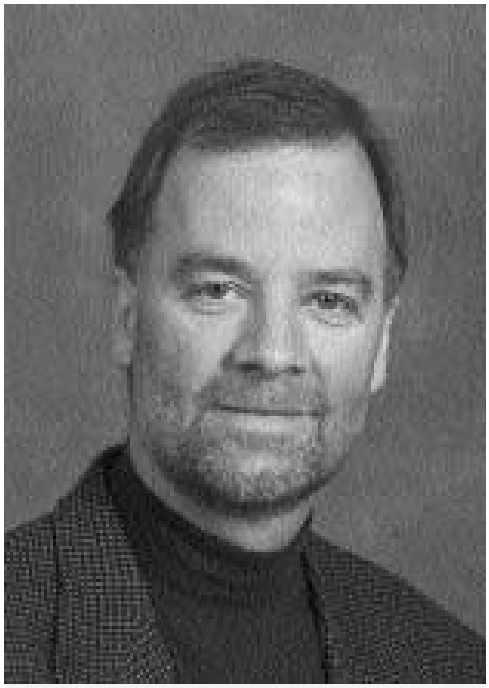
At the moment, Andres Metspalu's laboratory is 13 M.Sc. and 5 Ph.D. students. During the last 5 years, 4 Ph.D. and 12 M.Sc. thesis have been successfully prepared under his supervision.

Andres Metspalu has published more than 50 scientific articles and has held many lectures at international scientific meetings.

CONTACT INFORMATION
Andres Metspalu, M.D., Ph.D.
Head of the Department of Biotechnology
University of Tartu
Riia 23, Tartu 51010, Estonia
Tel. +37 27 375029
Fax. +37 27 420286
e-mail: andres@ebc.ee
http://www.biotech.ebc.ee/

Estonian Genome Project: Present Actions and Future Directions

The pilot phase of the Estonian Genome Project (EGP) was launched last week when new laboratory facilities together with sample storage room and coding/decoding center were opened in Tartu. The goal of the pilot project is to collect samples from 10 000 individuals (gene donors) from three counties (Tartu, Saare and West-Viru) into the EGP database during the next 6 months. According to the recent poll, about 50 000 people are willing to become gene donors from these 3 counties. Therefore, there should not be a problem to collect 10 000 samples as planned initially. I will describe how the project has been set up, how the data protection requirements were established and what are the logistical solutions. I will also describe the key issues of the EGP like working out the questionnaire, contracting general practitioners, information transfer, DNA extraction and storage. The second part of my talk will be devoted to genetics and genotyping that is the next phase of the EGP.



PROF. RICHARD M. MYERS

Stanford Human Genome Center, Stanford University School of Medicine, USA

CV

Dr. Richard Myers received his Ph.D. in Biochemistry at the University of California at Berkeley in 1982 and performed postdoctoral work at Harvard University from 1982 to 1985. He joined the faculty at the University of California at San Francisco in 1986, and moved to Stanford University School of Medicine in 1993, where he is Professor of Genetics and Director of the Stanford Human Genome Center. Dr. Myers's research focuses on understanding the roles that genes play in a wide range of human traits, including diseases and behaviors. His laboratory contributed towards the identification of genes involved in inherited diseases of the nervous system in humans and mouse, including the neurodegenerative disorder Huntington disease, Alzheimer disease, and a disease in mice that disrupts the development of the cerebellum. More recently, his lab identified a gene involved in an inherited form of epilepsy and contributed towards finding a gene responsible for the most common form of skin cancer. Because these genetic experiments required studying large amounts of the DNA in human and mouse chromosomes, he joined the early worldwide efforts to map and sequence the human genome, directing one of the first four Genome Centers established in the United States in 1990. He is continuing this work, studying the genetics of autism, atherosclerosis, hypertension, Huntington disease, progressive myoclonus epilepsy, and Parkinson disease.

POSITIONS AND EMPLOYMENT

Jan 1986-Feb 1993 Assistant and Associate Professor of Physiology and Biochemistry & Biophysics and Director of the Human Genome Center, University of California, San Francisco.

Mar 1993-Apr 1996 Associate Professor of Genetics, Director of the Stanford Human Genome Center, and Director of the Graduate Program in Genetics, Stanford University School of Medicine.

May 1996-present Professor and Chairman (beginning February 2002), Department of Genetics, and Director of the Stanford Human Genome Center, Stanford University School of Medicine.

CONTACT INFORMATION

Richard M. Myers, Ph.D.
Professor of Genetics and Director, Stanford Human Genome Center
Department of Genetics
Stanford University School of Medicine
Stanford, CA 94305-5120
Tel.: 650-725-9687
Fax: 650-725-9689
e-mail: myers@shgc.stanford.edu
http://www-shgc.stanford.edu/

"Genetics and Genomics of Human Biology and Disease"

We use genomics and genetics methods to study human biology and disease, particularly emphazing the roles that genes and their regulatory sequences play in a wide range of human traits, including diseases and behaviors. In this talk, I will discuss a variety of methods that we are using to identify cis-acting regulatory elements on a genome-wide scale, and how we search for associations between DNA sequence variants in these elements and in other functional regions of genes and several human diseases, including autism, atherosclerosis, hypertension, and Parkinson disease. I will also discuss our use of chromatin immunoprecipitation and DNA quantitation methods to study, on a genomic scale, the interactions of trans-acting regulatory factors with their sites in genes.

Because of our interest in human genetics, we have been involved in the efforts to map and sequence the human genome since the beginning of the public project in 1990. Our group at the Stanford Human Genome Center is collaborating with the Department of Energy's Joint Genome Institute at Walnut Creek, California to generate finished, contiguous sequences of human chromosomes 5, 16 and 19, which comprise more than 10% of the human genome. I will discuss our approaches for producing accurate, finished sequence, and the overall progress and status of the human genome sequence. In additional, I will present other genomic work being done at our Genome Center to sequence and study full-length cDNAs and genomic sequences from a variety of other organisms.

PROF. PAOLO BOFFETTA

Unit of Environmental Cancer Epidemiology,
International Agency for Research on Cancer, France

Paolo Boffetta (19 July 1958) was educated in Turin, Italy, and graduated in Medicine from the local University in 1985. In 1988, he obtained a Master in Public Health from Columbia University in New York, where he worked from 1986 to 1988 in the Departments of Environmental Sciences and of Health Administration; he also worked at the American Health Foundation and the American Cancer Society, and during 1989 at the Unit of Cancer Epidemiology of the University of Turin. Since 1990, he has been working as an epidemiologist at the International Agency for Research on Cancer in Lyon, France, where in 1995 he became Chief of the Unit of Environmental Cancer Epidemiology. He is also Foreign Adjunct Professor in Molecular Epidemiology at the Department of Medical Epidemiology of Karolinska Institute in Stockholm, Sweden, and at the Department of Oncology of the University of Turin, Italy.

He is the author of more than 250 scientific publications, a co-editor of 12 books and a member of the editorial board of several scientific journals. His main research interests are the causes and mechanisms of cancers of the lung, head and neck, and bladder, and of lymphoma.

SELECTED PUBLICATIONS:

Kjaerheim K, Bofffetta P, Hansen J, Cherrie J, Chang-Claude J, Eilber U, Ferro G, Guldner K, Olsen JH, Plato N, Proud L, Saracci R, Westerholm P, Andersen A. A case-control study of lung cancer nested in a cohort of European rock and slag wool production workers. Epidemiology (in press).

Boffetta P, Brennan P, Saracci R. Neoplasms. In: Detels R, McEwen J, Beaglehole R, Tanaka H, eds, Oxford Textbook of Public Health, Vol. 3, The Practice of Public Health, 4th Edition. Oxford University Press, Oxford, 2002, pp. 1155-1192.

Boffetta P, Burstyn I, Partanen T, Kromhout H, Svane O, Langard S, Järvholm B, Frentzel-Beyme R, Kauppinen T, Stücker I, Shaham J, Heederik D, Ahrens W, Bergdahl I, Cenée S, Ferro G, Heikkilä P, Hooiveld M, Johansen C, Randem B, Schill W. IARC Epidemiological Study of Cancer Mortality among European Asphalt Workers (IARC Internal Report No 01/003). IARC, Lyon, 2001.

Boffetta P, Sällsten G, Garcia-Gómez M, Pompe-Kirn V, Zaridze D, Bulbulyan M, Caballero J-D, Ceccarelli F, Kobal AB, Merler E. Mortality from cardiovascular diseases and exposure to inorganic mercury. Occup Environ Med 58: 461-466; 2001.

Ward E, Boffetta P, Andersen A, Colin D, Comba P, Deddens JA, De Santis M, Engholm G, Hagmar L, Langard S, Lundberg I, McElvenny D, Pirastu R, Sali D, Simonato L. Update of the follow-up of mortality and cancer incidence among European workers employed in the vinyl chloride industry. Epidemiology 12: 710-718; 2001.

Boffetta P, Andersen A, Hansen J, Olsen JH, Plato N, Teppo L, Westerholm P, Saracci R. Cancer incidence among European man-made vitreous fiber production workers. Scand J Work Environ Hlth 25: 222-226; 1999.

CONTACT INFORMATION

Paolo Boffetta, M.D., Ph.D.
Chief, Unit of Environmental Cancer Epidemiology
International Agency for Research on Cancer
150 cours Albert Thomas,
69372 Lyon cedex 08, France
e-mail: boffetta@iarc.fr
http://www.iarc.fr/

Gene-environment Interactions in Carcinogenesis: the Contribution of Molecular Epidemiology

The use of biomarkers in medicine, and in epidemiology in particular, is not new, but recent developments in molecular biology and genetics have increased the opportunities. Epidemiological studies based on biomarkers, which belong to the discipline defined as 'molecular epidemiology', offer new avenues to investigate associations between genetic and environmental factors, diseases, and medical interventions. The impact of high penetrance genes on the overall cancer burden is therefore limited (estimates based on known genes are in the order of 5% of total neoplasms). Low penetrance genes however represent an important group of cancer predisposing factors. Their characteristics are that: (i) they confer a modest increase in cancer risk (relative risk up to 3); (ii) they may display a high prevalence (above 1%); (iii) they may act by modifying the effect of environmental or endogenous carcinogens. Good examples of low penetrance genetic factors are the polymorphisms of genes encoding for proteins involved in the various steps of carcinogenesis, as shown in the following table.

Examples of genetic polymorphisms possibly involved in human cancer

Step	Gene	Polymorphism	Prev.	Possible target organ	RR
Exposure	DRD2	TaqIB	20	tobacco related	NA
Activation	ADH2	codon 487	30	head and neck	1.7
Detoxification	NAT2	null	45	bladder	1.4
DNA repair	XRCC1	codon 399	50	lung, other	2

Prev., prevalence (%); RR, relative risk; NA, not available

For most polymorphisms, the available evidence does not allow to conclude on whether they play a role in human cancer, and some of the positive results might results from chance, bias, or selective reporting. However, if confirmed, the role of low penetrance genetic factors might be important. For example, a polymorphism with a 20% prevalence conferring a three-fold excess risk would be responsible for 29% of cases of a given neoplasm. Critical issues in the interpretation of available data include: (i) definition and measure of polymorphism; (ii) choice of study population; (iii) interaction with environmental factors; (iv) precision of risk estimate. Future molecular epidemiological studies should be conducted according to state-of-the-art methodology for both the genetic and epidemiological components.

PROF. ANNE-LISE BØRRESEN-DALE

Institute for Cancer Research, The University Hospital, The Norwegian Radium Hospital, Norway

ACADEMIC DEGREES.

1970 M.S. Biochemistry, Technical University of Norway, Trondheim, Norway.
1978 Doctor of Science in Medical Biochemical Genetics, University of Oslo, Norway.
1987 Judged qualified as a professor in gene technology, University of Oslo, Norway.
1992 Professor in Molecular Tumorbiology, Univ. of Oslo, Norway.
2000 Professor in Molecular Oncology, Univ. of Bergen, Norway.

POSITIONS HELD

1970-72 Research assistant, Institute of Medical Genetics, University of Oslo.
1972-78 Research Fellow, Institute of Medical Genetics, University of Oslo.
1978-82 Senior Research Fellow, Institute of Medical Genetics, University of Oslo
1982-86 Senior Biochemist, head of biochemical section for prenatal diagnosis, Department of Genetics, UiO.
1987-99 Senior Scientist, Dept. of Genetics, Inst. for Cancer Research, DNR, Norway
1993-99 Head of DNA Diagnostic Service Lab, DNR, Oslo, Norway.
1999-dd Head of Department, Dept. Genetics, Inst. for Cancer Research, DNR, Norway.

HONOURS AND AWARDS.

1989 Prof. Olav Torgersens Prize and Memorial Lecture, Title: Gene technology in the fight against cancer.
1989 Honorary lecturer at the 175th anniversary of the Medical Faculty, Univ. of Oslo.
Title: Genes, inheritance and cancer; gene technology in cancer diagnosis and prevention.
1994 King Olav V's Cancer Research Prize
1998 Elected member of: "Det Kongelige Norske Videnskabers Selskab"
2001 Honorary member of The Norwegian Biochemical Society
2002 University of Oslo's Research Prize for outstanding Research

EDITORIAL BOARDS:
Pharmacogenetics (to 1999), British Journal of Cancer (to 2000), Human Mutation (corresponding editor), Biotechniques, Breast Cancer Research, Journal of the Norwegian Medical Association.

CURRENT RESEARCH PROJECTS
Molecular genetic studies of breast cancer. Identification of genotypes and gene expression profiles contributing to elevated cancer risk, radiation sensitivity, tumour aggressiveness and therapy resistance.

PUBLICATIONS: Author of 235 scientific papers in international reviewed journals, 16 chapters/reviews, 30 Nordic or popular scientific articles.

CONTACT INFORMATION
Anne-Lise Børresen-Dale, Ph.D.
Department of Genetics
Institute for Cancer Research,
DNR, Oslo, Norway
Tel.: +4722934419
Fax: +4722934440
e-mail: alb@radium.uio.no
http://www.dnr.org/

Molecular Profiling of Breast Cancer: Relation to Clinical Course and Treatment Response

The knowledge of the sequence of the human genome has created a nearly unlimited horizon of opportunities for the study, in parallel, of all human genes. Much of the challenge lies in developing new technology for these studies as well as for the statistical and mathematical approaches necessary to interrogate the massive data that are produced. In particular, the use of DNA microarray technology, in which the expression or copy number of genes can be determined genome-wide, offers great potential for improving our understanding of the causes and progression of disease, for the discovery of new molecular markers, for therapeutic intervention and for developing new prevention strategies.

Cancer diseases have in common that they arise as a result of accumulation of mutations, chromosomal instabilities, and epigenetic changes, damages that progressively impairs the cell's detailed and complex system of regulation of cell growth and cell death.

Microarray technologies, applied to the study of DNA, RNA, and protein profiles as well as to the genome-wide distribution of epigenetic changes such as DNA methylation, can be used to portray a tumor's detailed phenotype in its unique context. These methods can generate molecular signatures that can be correlated to clinical information. Eventually, advances in tumor portraiture will naturally lead to improved and individualized treatments for cancer patients.

Breast cancer is the most common malignancy and the most common cause of cancer death in women worldwide. As for most solid tumors, breast cancers are heterogeneous and consist of several pathologic subtypes with different histological appearances of the malignant cells, different clinical presentations and outcomes, and the patients show a diverse range of responses to a given treatment. Furthermore, breast tumor tissue also shows heterogeneity with respect to its microenvironment including specifically the types and numbers of infiltrating lymphocytes, adipocytes, stromal and endothelial cells. The cellular composition of tumors is a central determinant of both the biological and clinical features of an individual's disease. Current biomarkers have limited value in predicting prognosis and response to therapy, and they provide little information about the biology of the disease.

We have performed expression studies of more than 100 breast carcinomas using high-density cDNA microarrays, aiming at novel tumour classification that can predict survival and treatment response. The expression patterns observed provided a remarkably distinctive molecular portrait of each tumour, and the gene expression patterns in two tumour samples from the same individual, taken before and after treatment (16 weeks apart), were almost always more similar to each other than either was to any other sample. The tumours could be classified into novel subtypes that were distinguished by pervasive differences in their gene expression patterns. Five subtypes of tumours (two luminal epithelial derived oestrogen receptor-positive tumour subtypes, a basal epithelial-like, an ERBB2+ group, and a normal breast-like group) were identified. Survival analyses showed significantly different outcome for patients belonging to the various subtypes, including a poor prognosis for the basal-like and a significant difference in outcome for the two luminal /ER+ subtypes. Differences in TP53 mutation frequency between the subtypes indicated an important role for this gene in determining the gene expression pattern in the various tumors. Analyses of copy-number alterations using the same cDNA arrays in 40 tumours showed that at least 12% of all the variation in gene expression is directly attributable to underlying variation in gene copy number, and that 62% of the genes with high level amplification (> 4 copies) showed mRNA levels of more that 2 fold.

These findings clearly set the stage for future studies aimed at identifying specific patterns of gene activations that may predict important clinical features, such as sensitivity to specific therapies and metastatic potential. Similar variation in expression of a set of genes across a set of samples indicates similar means of regulation and function, and hence, provides a powerful way of identifying novel biologically important genes that could be used as markers and targets for therapy. The strength of this method lies in the ability to identify clusters of genes that in a unique combination will distinguish subgroups of disease and predict outcome or treatment response. Such a multi-gene approach will undoubtedly be superior to standard clinical markers currently in use.

PROF. RANDO L. ALLIKMETS

Columbia University, USA

PROFESSIONAL EXPERIENCE:
Louis V. Gerstner Scholar; Assistant Professor; Head, Laboratory of Medical Genetics; Departments of Ophthalmology and Pathology, Columbia University, New York, NY, 1999-Present
Scientist, SAIC Frederick, National Cancer Institute - Frederick Cancer Research and Development Center, Frederick, MD, 1996-1999
Visiting Fellow, Human Genetics Section, Laboratory of Genomic Diversity, National Cancer Institute, Frederick, MD, 1992-1996
Senior Scientist, Institute of Chemistry, Estonian Academy of Science, Tallinn, Estonia, 1991
Senior Scientist, Acting Chief, Laboratory of Molecular Genetics, Institute of Chemical Physics and Biophysics, Estonian Academy of Science, Tallinn, Estonia, 1988-1991
Ph.D. Guest Researcher, Department of Tumor Biology, Karolinska Institute, Stockholm, Sweden, 1990-1991
Ph.D. Guest Researcher, Laboratory of Molecular Neurobiology, Karolinska Institute, Stockholm, Sweden, 1989-1990
Scientist, Shemyakin Institute of Bio-organic Chemistry, Academy of Science, Moscow, USSR, 1988
Junior Scientist, ibid., 1986-1988
Research Associate, ibid., 1983-1986

EDUCATION:
Ph.D., Molecular Biology, Shemyakin Institute of Bio-organic Chemistry, Academy of Science, Moscow, USSR, 1988
Thesis: "New methods for construction of genomic libraries and their utilization for cloning of individual genes."
M.S., Biochemistry and Virology, Lomonossov Moscow State University, Moscow, USSR, magna cum laude, 1983

HONORS:
Fogarty Fellowship in the Laboratory of Viral Carcinogenesis, NCI, NIH 1992-1996
SAIC Science Achievement Award, 1997
SAIC 1997 Publication Prize for Biochemistry and Molecular Biology, 1998

BIBLIOGRAPHY:
Over 80 publications in peer-reviewed journals.

CONTACT INFORMATION
Rando L. Allikmets, Ph.D.
Assistant Professor
Head, Laboratory of Medical Genetics
Department of Ophthalmology
Columbia University,
Eye Research Addition, 7th Floor
630 West 168th Street
New York, NY 10032, USA
Tel: 212 305-8989
Fax: 212 305-7014
e-mail: rla22@columbia.edu
http://cpmcnet.columbia.edu/dept/eye/research/labs.html

Genetics of Eye Disease: From Simple to Complex

Diseases of the retina include a wide spectrum of photoreceptor-affecting phenotypes that have been mapped to over 130 loci on the human genome (RetNetÔ Retinal Information Network, http://www.sph.uth.tmc.edu/Retnet/home.htm) Currently, only about a half of all causal genes have been identified, although substantial progress has been made in recent years in determining the genetic basis of monogenic eye disorders. On a regular basis mutations are identified in new genes responsible for some form of retinal degeneration. The majority of these genes are involved in rare phenotypes in limited numbers of patients.

When the ATP-binding cassette (ABC) transporter gene, ABCR, was cloned and characterized in 1997 as the gene responsible for autosomal recessive Stargardt disease (Allikmets et al. 1997), it seemed as if just another missing link was added to the extensive table of genetic determinants of rare monogenic retinal dystrophies. Now, more than five years later, mutations in the ABCR gene (also called ABCA4) continue to emerge as the predominant determinant of a wide variety of retinal degeneration phenotypes. In addition to Stargardt disease, ABCR mutations have shown segregating with several diseases of different phenotypes, such as cone-rod dystrophy (CRD), and retinitis pigmentosa (RP). More importantly, ABCR was identified as the first gene involved in a complex, multifactorial, disorder known as age-related macular degeneration (Allikmets et al., 1997). In summary, ABCR has emerged as the most important gene in retinal disease, since about 1/10 to 1/20 people across all populations carry an ABCR mutation.

This presentation will demonstrate how our current knowledge of genetic variation in genes responsible for monogenic disorders will help to decipher the genetic component of complex traits, and how a combination of genetic and functional research of even a single gene can tremendously advance medical genetics.

PROF. LEENA PELTONEN

Department of Human Genetics, UCLA, USA

EDUCATION
M.D. - 1976 University of Oulu
Ph.D. in Biochemistry - 1978 University of Oulu
Docent in Cell Biology - 1982 University of Oulu
Docent in Molecular Genetics - 1991 University of Helsinki

PROFESSIONAL EXPERIENCE

1973-1976	M.D. Ph.D. Student, Collagen Research Unit (Head Kari Kivirikko), University of Oulu, Finland
1978 -1980	Post-doctoral Fellow, Dept. of Biochemistry (Chair Darwin J. Prockop) Rutgers Medical School, NJ, USA
1981-1984	Acting Associate Professor, Department of Cell Biology, University of Oulu, Finland
1985-1987	Senior Scientist of The Academy of Finland, Recombinant DNA Laboratory, University of Helsinki
1987-1991	Head of the Laboratory, Laboratory of Molecular Genetics, National Public Health Institute, Finland
1991-1995	Professor of Molecular Biology, Director of the Molecular Biology Program, National Public Health Institute
1995 -1998	Professor of Medical Genetics, University of Helsinki and National Public Health Institute (20% time commitment from June 1998)
1998-present	Chairman and Professor of Department of Human Genetics, UCLA (80% time commitment from June 1998)

POSITIONS HELD IN SCIENTIFIC SOCIETIES

1984-1985	Chairman of the Finnish Connective Tissue Society
1990-1992	Chairman, Finnish Society of Medical Genetics
1991 -	European Molecular Biology Organization (EMBO), Member
1991-1998	Human Genome Organization, member of International Council
1992-2000	European Society of Human Genetics, Member of the Council
1993 -	National Academy of Sciences, Finland, Member
1998-2000	American Society of Human Genetics, Member, Board of Directors
1999 -	Hereditary Disease Foundation, Scientific Advisory Board Member
1999 -	European Academy of Sciences (Academiae Europeae), Member
2001 -	American Society of Human Genetics, Member, Board of Directors

ORIGINAL SCIENTIFIC PUBLICATIONS AND PH.D. THESIS SUPERVISION: 339 original publications and several (53) review articles in international scientific journals and books. Supervised 43 Ph.D. theses.

CONTACT INFORMATION
Leena Peltonen, M.D., Ph.D.
Professor and Chair
UCLA Department of Human Genetics
Gonda Neuroscience and Genetics Research Center, Rm. 6506
695 Charles E. Young Drive South, Box 708822
Los Angeles, CA 90095-7088, USA
Tel.: 310-794 5631
Fax: 310-794 5446
e-mail: lpeltonen@mednet.ucla.edu
www.genetics.ucla.edu

Disease Gene Identification Using Tools Produced by the Human Genome Project

PROF. AARNO PALOTIE

Department of Pathology and Laboratory Medicine, UCLA, USA

Present positions :
-Professor, In Residence, Dept. of Pathology and Laboratory Medicine, University of California, Los Angeles, July 1, 1998-
-Joint appointment, Professor, Dept. of Human Genetics, UCLA, October 1, 2000-
-Consultant in Laboratory Medicine (Clinical Chemistry) and head of the Laboratory for Molecular Genetics, Laboratory Department of Helsinki University Central Hospital (tenure position, leave of absence)
- Chair for the Finnish Genome Center, University of Helsinki, September 1, 2001 (leave of absence)

EDUCATION AND TRAINING:
M.D.: September 1981, University of Oulu, Finland
Ph.D.: May 1983, University of Oulu, Finland
Specialist in Clinical Chemistry (Chemical Pathology): Oct 1988, University of Helsinki, Finland
Docent (eqv. to Senior lecturer) in cell biology April 1989, University of Oulu, Finland
PROFESSIONAL APPOINTMENTS:
Scientific training and scientific appointments:
-Research Associate University of Oulu Depts. of Anatomy and Medical Biochemistry, Collagen Research Unit led by Prof. Kari Kivirikko: 1976-1978 and 1980-1984.
-Research Associate University of Medicine and Dentistry of New Jersey, Dept of Biochemistry, in the collagen research group of Prof. Darwin J. Prockop: 1978-1979 (total 16 months).
-Research Fellow, University of Helsinki, Recombinant-DNA laboratory of the University of Helsinki (now Institute of Biotechnology, University of Helsinki), in the human molecular genetic project 1985-1987 (full time, total of 6 month).
-Research Fellow, National Public Health Institute, Laboratory for Human Molecular Genetics, 1989, total of 3 month.
-An independent scientist since 1987 , close collaboration with the Dept. of Human Molecular Genetics of the National Public Health Institute, chaired by Dr. Leena Peltonen.
-A group leader (PI) of the molecular genetic laboratory since 1989, Dept. of Clinical Chemistry, University of Helsinki.

Medical positions:
-Residency training in Departments of Surgery and Pediatrics, Helsinki and Oulu University Central Hospitals in 1984, total 5 months.
-Institute of Occupational Health, Finland, Laboratory of Biochemistry, Acting Chief Physician, 1.7.1985-31.12.1986.
-University Central Hospital of Helsinki, Meilahti Hospital Laboratory, House Officer (residency), 1.1.1987-31.12.1988
-University Central Hospital of Helsinki, Meilahti Hospital Laboratory, (tenure position) Specialist, equivalent to senior consultant 1.4.1989- (presently leave of absence)

CONTACT INFORMATION
Aarno Palotie, M.D., Ph.D.
Professor
Department of Pathology and Laboratory Medicine
UCLA
Gonda Research Center
695 Charles E. Young Drive South
Los Angeles, CA 90095-7088
Tel.: 310 794 5948
Fax: 310 794 5446
e-mail: apalotie@mednet.ucla.edu

Example of a challenging complex trait: Mapping of A Susceptibility Locus for Migraine with Aura on Chromosome 4q24

M. Wessman[1,3], M. Kallela[4], G. Oswell[1], Päivi Tikka [7] M. Kaunisto[3], J. Hartiala[2], P. Broas[2], E. Hämäläinen[2], T. Hiekkalinna[2], G.Joslyn[2], J.Papp[2], S.Leal[5], R. Cantor[2], E. Sobel[2], J. Ott[5], H. Havanka[6], M. Färkkilä[4], L. Peltonen[2], A. Palotie[1,7]. 1) Dept of Pathology, University of California Los Angeles, USA; 2) Dept of Human Genetics, University of California Los Angeles, USA; 3) Dept of BioSciences, University of Helsinki, Finland 4) Dept of Neurology, University of Helsinki, Finland; 5) Lab of Statistical Genetics, Rockefeller University, New York, USA; 6) Dept of Neurology, Länsi-Pohja Central Hospital, Kemi, Finland; 7) The Finnish Genome Center, University of Helsinki, Finland

Migraine is a complex neurovascular disorder with substantial evidence supporting a genetic contribution. Migraine has two main types: migraine without aura (MO) occurring in 85% of patients and migraine with aura (MA) occurring in 15% of patients. Prior attempts to localize susceptibility loci for common forms of migraine have not produced conclusive evidence for linkage or association. Some of the challenges in mapping susceptibility loci in migraine include, the heterogeneity of the disease, no quantitative phenotyping is available and the common nature of the disease results in phenocopies in pedigrees. Our strategy was to collect a large number of well phenotyped multigeneration families (today over 600 families) to provide a sufficient selection for family stratification. To date, no genome-wide screen for migraine has been published. We report results from a genome-wide screen on 50 multi-generational, clinically well-defined, Finnish families showing transmission from generation to generation of MA. The families were screened with 350 polymorphic microsatellite markers, with an average intermarker distance of 11 cM. Significant evidence of linkage was found between the MA phenotype and the marker D4S1647 on chromosome 4q24. Using parametric two-point linkage analysis, assuming a dominant mode of inheritance, and allowing for locus heterogeneity, the maximum lod was 4.20 (under homogeneity p=0.000006). Multipoint parametric (HLOD = 4.45, p=0.0000058) and non-parametric (NPL-all = 3.43, p=0.0007) analyses support this finding. Statistically significant linkage was not observed in any other chromosomal region. The locus on Chromosome 4 is currently been restricted using additional markers and families.

DR. WALDEMAR KÜTT

European Commission, Research Directorate General - Life Sciences Directorates, Belgium

CV

Waldemar Kütt obtained a Ph.D. from the Technical University in Aachen (RWTH) in 1988 in solid state physics and semiconductor technology. He has worked for several years as technology and innovation consultant, with a focus on patent licensing deals and financing of start-ups. In 1997 he joined the Research Directorate General of the European Commission, where he is currently responsible for the co-ordination of innovation and SME policies of the Life Sciences directorates.

CONTACT INFORMATION
Waldemar Kütt, Ph.D.
Co-ordinator of innovation and SME policies
European Commission
Research Directorate General - Life Sciences Directorates
Tel.: +32.2. 299.41.45
Fax: +32-2-299.18.60
e-mail: waldemar.kutt@cec.eu.int

Opportunities for Biotech SMEs in the New Framework Programme

Article 163 of the EU treaty states that the Community has the objective to strengthen the scientific and technological bases of Community industry and encouraging it to become more competitive at international level. The Lisbon European Council in March 2000 adopted conclusions aimed at the rapid establishment of a European research and innovation area with the ultimate goal of enabling the Union to become the world's most competitive and dynamic knowledge economy. Biotechnology and Life Sciences are considered to be one of the frontier technologies that will contribute to this goal.

Strengthening the science base and exploiting the potential of biotechnology in health, food, environment and other areas is one of the major goals of the new framework programme (2002-2006) of the European Community. Specific focus is on the vertical and horizontal integration of different disciplines and players, with a particular emphasise on the important role of small and medium sized enterprises (SMEs) and on increasing the impact on innovation through knowledge, dissemination and exploitation management.

The presentation will give an overview of the major elements of the new framework programme in terms of contents and new instruments. The latter aim specifically at integrating academics, SMEs and large industry, in order to optimise exploration and exploitation of innovative research and new technologies.

Strong and innovative SMEs in the life sciences and biotech sector are, in addition to a high quality science base and market oriented industry, a very important factor for the competitiveness of life sciences and biotech industry in the EU. Therefore, participation of SMEs is particularly encouraged in the new framework programme:

• 15% of the budget of the thematic priorities of the new framework programme is earmarked for SMEs.
• An additional 450 million will be spent on SME specific measures.
• The budget for mobility grants has been doubled, providing further opportunities to SMEs.
• Framework conditions, such as intellectual property rules, have been simplified and made more flexible to encourage innovation.

PROF. BRIGITTE FEUILLET-LE MINTIER

Rennes University, France

FONCTIONS :
- Professeur des Universités, Faculté de Droit et de science politique de Rennes I, spécialiste de Droit des personnes, droit de la famille et droit de la biomédecine.
- Directeur du Centre de Recherche Juridique de l'Ouest (IODE, UMR CNRS n° 6050), laboratoire de recherche spécialisé sur les questions de bioéthique et droit.
- Responsable de deux diplômes de troisième cycle :
* le DESS " Droit-Santé-Ethique " créé en partenariat avec l'Ecole Nationale de la Santé Publique,
* le DU de Responsabilité médicale.
- Membre du Comité scientifique du Groupement d'Intérêt Public " Justice " (Mission " Droit et Justice ", Ministère de la Justice)
- Membre du Séminaire de recherche sur le programme " Ethique médicale " de la MIRE (Mission Recherche du Ministère de l'emploi et de la solidarité).
- Membre du Groupement De Recherche " Sciences et droit " du CNRS
- Membre du comité de rédaction de plusieurs revues : Revue Internationale de Bioéthique, revue " Médecine et droit", Revue Générale de droit médical, Dictionnaire Permanent de bioéthique et de biotechnologies et revue " Responsabilité ".

EXPERTISES :
- Expert auprès du Conseil de l'Europe en 1999 : participation à l'élaboration d'une revue de jurisprudence européenne sur la biomédecine.
- Intervention dans un colloque organisé au Parlement européen sur la thérapie génique en juin 2000 (Bruxelles)
- Audition devant la Commission de réforme des lois " bioéthiques " de l'Assemblée Nationale en juillet 2000
- Audition par la délégation aux droits de la femme aupr?s de l'Assemblée nationale en juillet 2000 sur la réforme de l'interruption de grossesse
- Participation à un colloque interne ? l'Assemblée Nationale, organisé par la Délégation aux droits de la femme auprès de l'Assemblée Nationale, en avril 2001.
- Participation à un Comité des sages créé en mars 2002 auprès de M. Schwartzenberg, Ministre de la recherche , (Comité amené à réfléchir sur l'importation des cellules souches embryonnaires)

PRINCIPALES PUBLICATIONS :
* "L'embryon humain, approche multidisciplinaire", préface A. Kahn, sous la dir. De B. Le Mintier, Economica Paris, 1996.
* "Philosophie, Ethique et droit de la médecine ", sous la codirection de J.F. MATTEI (médecins), D. FOLSCHEID (philosophes), B. LE MINTIER (juristes), ouvrage ayant reçu le prix Le Dissez de Penanrum de l'Académie des Sciences Morales et Politiques (Institut de France) en 1999.
* " Les lois bioéthique à l'épreuve des faits : réalités et perspectives ", sous la direction de B. Le Mintier, PUF, Droit et Justice, 1999, préface du Garde des Sceaux E. GUIGOU
* "Biotechnology and human rights", Rev. Cellular and molecular biology", Décember 2001, vol.47, n°8, p.1361, Offrint.

CONTACT INFORMATION
Prof. Brigitte Feuillet-Le Mintier
Faculté de Droit et de Science Politique
Institut Ouest Droit Europe (IODE)
9 RUE Jean Macé CS 54203 35065 RENNES CEDEX France
Tel : 02 23 23 7694
e-mail: Brigitte.Le-Mintier@univ-rennes1.fr
http://www.droit.univ-rennes1.fr/

Genetics and Protection of Individual Rights

La technologie permet à notre monde d'évoluer. C'est un outil qui sert à mieux comprendre l'humain mais aussi à le faire progresser. Appliquées au vivant, les biotechnologies présentent ces mêmes finalités. Mais parce que leur objet est justement le vivant, les biotechnologies génèrent des dangers spécifiques notamment celui d'utiliser les connaissances sur l'homme pour modifier l'espèce humaine. Le droit des personnes doit donc trouver sa place pour éviter que les droits fondamentaux de la personne humaine subissent des atteintes. Cette mission impartie au droit des personnes est d'autant plus précieuse que les enjeux économiques sont particulièrement importants dans le domaine des biotechnologies.

PROF. ALAXANDRE MAURON

Faculty of Medicine, University of Geneva, Switzerland

CV

Alex Mauron is professor of bioethics at the Faculty of medicine of the University of Geneva. He holds a PhD (Lausanne, 1978) in molecular biology, with research experience in molecular genetics and neurobiology. His professional interests shifted to the field of bioethics in the late eighties. Since then, his scholarly work has included ethical issues in human genetics such as gene therapy, genetic diagnosis, and the social implications of genetic data. He has also had a long-standing involvement with issues concerning the human embryo, including the transplantation of fetal tissue and human embryonic stem cell research. Other topics of interest include biological concepts in ethics, teaching bioethics, and clinical ethics (futility, end-of-life issues).

Alex Mauron has published widely on the ethical issues of genetics and reproduction, as well as on clinical ethics. He has been heavily involved in public debate on genetic engineering and reproductive technologies, and participated in the formulation of ethical guidelines and/or other policy documents on several bioethical issues. In addition, he is a regular columnist on bioethics in the French-language Swiss daily Le Temps. After several years service in the Federal Ethics Commission on genetic engineering, he is now a member of the Swiss National Advisory Commission on Biomedical Ethics. He is also a member of the Central Ethics Commission of the Swiss Academy of Medical Sciences, and several other ethics committees.

CONTACT INFORMATION
Prof. Alexandre Mauron
Unité de Recherche et d'Enseignement en Bioéthique
Villa Thury 8 / Centre Médical Universitaire
1211 Genéve 4, Suisse
Tel.: +41 22 702 57 94
Fax: +41 22 702 57 92
e-mail: Alexandre.Mauron@medecine.unige.ch

The Genome and the Self: Bioethical Reflections

The rise of genomics has renewed popular notions that emphasize the human genome as the hard core of human identity. It has become a kind of conventional wisdom that the genome is what "makes us us". In other words, having a particular genome is commonly believed to be the sufficient reason for being a distinctive individual belonging to the human species. In previous work, I called this set of beliefs "genomic metaphysics". Although this view (or something like it that goes under the popular name of "genetic reductionism") is widely criticised, it remains very influential. This fact is evidenced by exploring several current bioethical debates concerning embryonic stem cell research, or the dispute about the speculations of the German philosopher Peter Sloterdijk's on modifying humans by "anthropotechniques". An analysis of these debates suggests that "genetic metaphysics" and genetic reductionism" are still at work, even among bioethical commentators who purport to be highly critical of genetic explanations of health, disease and behaviour, and who strongly oppose the engineering of human germline genetic material.

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ORGANIZER

Estonian Genome Foundation
Riia 23b, Tartu, 51010,
Estonia
Tel: +372 7 375030
Fax: +372 7 420286
e-mail: info@genomics.ee
www.genomics.ee
www.geneforum.ee

SCIENTIFIC PROGRAMME COMMITTEE

Prof. Andres Metspalu, University of Tartu, Estonia
Dr. Jaanus Pikani, Estonian Genome Foundation, Estonia

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