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EUROPEAN ASSOCIATION FOR THE STUDY OF DIABETES
ASSOCIATION EUROPEENE POUR L'ETUDE DU DIABETE · EUROPÄISCHE GESELLSCHAFT FÜR DIABETOLOGIE
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EASD

News Section
10/2003

2003 Claude Bernard Lecturer

Dr. Michael Brownlee, Albert Einstein College of Medicine, New York, USA

Dr. Michael Brownlee holds the Anita and Jack Saltz Chair of Diabetes Research at the Albert Einstein College of Medicine, where he is a Professor of Medicine and Pathology. He is also Co-Director of the Diabetes Research Center there.

In recognition of his major contributions to understanding the biochemistry, molecular and cell biology of diabetic complications, Dr. Brownlee has received several honours in addition to the Claude Bernard Medal, including the American Diabetes Association's Outstanding Scientific Achievement Award.

Dr. Brownlee is an elected member of the American Federation for Medical Research, the American Society for Clinical Investigation, the Association of American Physicians and the American Society for Biochemistry and Molecular Biology. He has served on the editorial boards of both *Diabetes* and *Diabetes Care* and currently serves on the editorial boards of *The Journal of Biological Chemistry* and *The Journal of Clinical Investigation*.

Dr. Brownlee is the past Chairman of the American Diabetes Association's Council on Complications and has served as a member of the Juvenile Diabetes Foundation's Medical Science Advisory Board.

2003 Minkowski Prize – 38th Minkowski Lecturer

Dr. Michael W. Stumvoll, University of Tübingen Medical Clinic, Tübingen, Germany

As a fellow in the laboratory of John Gerich (La Jolla, CA, and Rochester, NY) from 1993 - 1995, Dr. Stumvoll worked on the mechanism of action of metformin. He was able to show that metformin inhibited excessive endogenous glucose production (in particular lactate conversion to glucose) in patients with Type 2 diabetes.

Dr. Stumvoll's other focus during his fellowship was the quantification of glucose production in the human kidney. He demonstrated that the kidneys contribute approximately 20% to glucose production in the fasting state, a number previously thought be close to zero.

Back in Germany in Hans Häring's laboratory in Tübingen, Germany, he developed a series of methods

to in vivo characterise carriers of genetic variants relevant in the pathogenesis of Type 2 diabetes.

Among these were:
- isotope dilution technique coupled to a stepwise hyper-insulinemic clamp to measure insulin antilipolysis in vivo.
- novel hyperglycaemic clamp technique to assess the beta cell response to a variety of secretory stimuli.
- microdialysis technique (adipose tissue, muscle)
- intramyocellular lipids by magnetic resonance spectroscopy.

Effects of common polymorphisms in candidate genes for Type 2 diabetes on these genotypes were studied.

A further focus of his clinical experimental work was the mechanism underlying the clinical problem of hypoglycaemia unawareness (secondary to intensified insulin therapy in Type 1 diabetes). He studied the role of beta adrenergic sensitivity in the pathogenesis of hypoglycaemia unawareness. In addition to reduced catecholamine response, his group identified a major role of beta adrenergic sensitivity in loss of autonomic warning symptoms during hypoglycaemia in patients with Type 1 diabetes. More importantly, they discovered that prevention of hypoglycaemia seems to primarily improve beta-adrenergic sensitivity.

Michael Stumvoll's articles have been published in ***Diabetes***, ***Diabetes Care, New England Journal of Diabetes, Annals of Internal Medicine, Journal of Clinical Investigation and Journal of Clinical Endocrinology and Metabolism.***

He is a member of the Editorial Board of ***Diabetes*** for a three year term which started January 2003.

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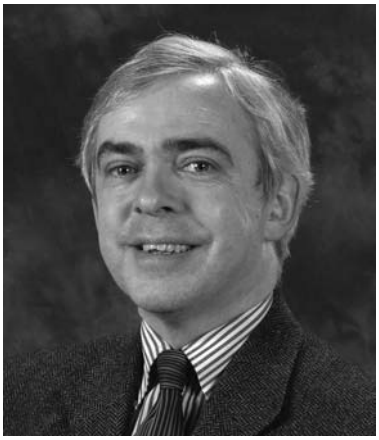
2003 Castelli Pedroli Prize, 18th Camillo Golgi Lecture

Andrew JM Boulton MB BS (Hons) MD FRCP
Professor of Medicine, University of Manchester, Consultant Physician, Consultant, Manchester Royal Infirmary, Manchester, UK
Visiting Professor of Medicine, Division of Endocrinology, University of Miami School of Medicine, Miami, FI, USA



Andrew Boulton attended Medical School at the University of Newcastle-Upon-Tyne, UK and graduated MB BS with honours in 1976. After his internship in Newcastle he moved to Sheffield where he completed his general medical training. During that period of time he worked with Professor John D. Ward who introduced him to the many interesting facets of diabetic neuropathy and foot ulceration. He was subsequently a research fellow at the Royal Hallamshire Hospital in Sheffield and obtained his MD entitled "Diabetic Neuropathy and Foot Ulceration" from the University of Newcastle-Upon-Tyne in 1985. After an 18 month spell as Visiting Assistant Professor of Medicine at the University of Miami, he returned to Sheffield where he completed his medical training as a senior registrar/lecturer in diabetes and endocrinology.

He was appointed as Senior Lecturer and Honorary Consultant to the University of Manchester and Manchester Royal Infirmary in 1986 and was promoted to Reader in 1992 and subsequently Professor of Medicine in 1995.

During the last twenty years his research interests have continued to be in the pathogenesis and treatment of diabetic neuropathy and foot ulceration.

He is a recipient of several scientific awards including the 1990 R.D. Lawrence Lectureship of the British Diabetic Association, the first international award for research into diabetic foot problems in 1995 and the Roger Pecararo Lectureship of the American Diabetes Association in 1996. He is a former Editor of Diabetic Medicine and has served on the Editorial Board of several scientific journals including Diabetologia, Diabetes Reviews and Diabetes Metabolism Research and Reviews.

Professor Boulton has published more than 250 articles, numerous reviews and book chapters and is co-editor of "The Foot in Diabetes" which is now in its 3rd edition.

Report on Research Work

Professor Boulton's research has focussed upon the pathogenesis and management of diabetic neuropathy in foot ulceration. His early observations included, together with Professor John Ward, finding that arteriovenous shunting was commonly present in the neuropathic diabetic foot. Subsequent to this he has demonstrated the importance of abnormal pressures and loads under the diabetic foot during standing and walking, and more recently prescribed the use of ultrasound of the plantar aspect of the neuropathic foot in the determination of risk of foot ulceration. His group was the first to confirm in a prospective study that peripheral nerve dysfunction is the major contributory factor to foot ulceration in diabetic patients. In collaboration with the University of Seattle, he also described causal pathways to foot ulceration. In the area of diabetic neuropathy his group was the first to describe the potential importance of ACE inhibition in the pathogenesis of neuropathy and working with Dr. Rayaz Malik, they more recently described the potential of corneal confocal microscopy as a non-invasive way of assessing peripheral nerve function in diabetes. Lately in the area of diabetic foot ulceration, Professor Boulton has emphasised the need for appropriate control of confounding factors in studies of new treatments for neuropathic foot ulceration.

2003 EASD/GlaxoSmithKline Burden of Diabetes Research Fellowship

Dr. Marit Eika Jørgensen, Steno Diabetes Centre, Gentofte, Denmark

Inuit Health in Transition

Since 1950 the Inuit population of the arctic region in Greenland, Canada and Alaska has undergone rapid sociocultural changes, such as urbanisation, declining dependence on subsistence hunting and fishing, and dietary changes from a sea mammal- and fish-based diet to a diet influenced by typical western dietary habits.

The Inuit population have been shown to have a low risk of developing diabetes and ischaemic heart disease. Recent studies from Alaska and Siberia suggest, that the prevalence of diabetes and CVD may be increasing as a consequence of westernisation of lifestyle. Our study of 1200 Inuit persons in Greenland and Denmark demonstrated age specific prevalence of diabetes as high or higher than what we find among the Caucasoid Danish population. This questions the hypothesis that the traditional arctic diet including high intake of fish and sea mammals protects against development of diabetes and cardiovascular disease.

More knowledge is needed about the determinants of the diseases among the Inuit and about the protective effects of the traditional lifestyle. It is therefore proposed to carry out an epidemiological study among the Inuit and Yupik of Alaska, Canada and Greenland.

A baseline survey will be carried out among people aged 35 and above with Inuit/Yupik ancestry from across the Alaskan, Canadian and Greenlandic North. It is the aim to recruit 10,000 participants. The study will focus on cardiovascular disease and diabetes.

The baseline study will give a description of the disease pattern across the Arctic and a cross-sectional description of the associations between environment, living conditions, lifestyle, risk factors and existing disease. After approximately ten years, a follow-up of the participants will take place including a register-based follow-up and a repeated survey. In a broader context, the project will contribute to a better understanding of the health effects of the transition from a traditional lifestyle to a modern, industrialised life, which takes place in most present day developing countries.

2003 EASD/Amylin-Pharmaceuticals Inc. – Paul Langerhans Research Award

Dr. Jean-Christophe Jonas, Unité d'Endocrinologie et Métabolisme, UCL 55.30, Brussels, Belgium

Brief curriculum vitae

I got my MD degree in 1990 at the Université Catholique de Louvain (UCL) in Brussels. I then joined the group of Prof. J.C. Henquin at the Unit of Endocrinology and Metabolism-UCL as a Research Fellow, then Postdoctoral Fellow, from the Belgian Foundation for Scientific Research (FNRS, Belgium). During that period, within which I spent one year in the group of Prof. C.B. Wollheim at the University of Geneva, I studied various aspects of the pharmacology and physiology of the pancreatic β-cell, e.g. the stimulation of insulin secretion by imidazoline antagonists of α_2-adrenoceptors and the role of cytosolic Ca^{2+} in insulin secretion. I then passed my thesis for the "Agrégation de l'Enseignement Supérieur" in 1996. With the support of several Belgian fellowships (Belgian American Educational Foundation, NATO, Horlait-Dapsens Foundation), and later, as a Harvard Postdoctoral Fellow, I joined the group of Prof. G.C. Weir at the Joslin Diabetes Center in Boston, where I studied the effects of chronic hyperglycaemia on β-cell gene expression. In 1999, I came back to the Unit of Endocrinology and Metabolism-UCL, where, as a Research Associate of the FNRS, I have been studying the effects of hyperglycaemia on the β-cell phenotype. In 2001, I received an award from the Belgian Royal Academy of Medicine for these studies. Since 2001, I have been a part-time Associate Professor at the Faculty of Medicine, UCL.

Brief report on research work

Since 1997, I have mainly been studying the deleterious effects of chronic hyperglycaemia on the β-cell phenotype.

1. **Effects of hyperglycaemia on rat β-cell gene expression**
   We have shown that, in rats submitted to a 90% pancreatectomy, chronic hyperglycaemia triggers β-cell hypertrophy and a loss of β-cell differentiation that is characterised by reduced expression of genes involved in glucose stimulation of insulin secretion (GSIS) and of transcription factors that regulate their expression [1]. Interestingly, chronic hyperglycaemia also increases the expression of several genes repressed in normal β-cells, among which the transcription factor c-Myc and several antioxydant enzymes like heme oxygenase 1 (HO1) [1,2]. Whereas c-Myc may contribute to β-cell apoptosis, loss of differentiation and hypertrophy, HO1 may protect β-cells from oxidative stress. We, therefore, studied the effect of glucose on β-cell c-myc and HO1 expression in vitro, and observed that the expression of both genes is minimal after culture in the presence of 10 $mmol.l^{-1}$ glucose (G10) and strongly increased in either lower (G2-G5) or higher (G20-G30) glucose concentrations [3,4]. We also found that the stimulation of islet c-Myc and HO1 expression by G30 is Ca^{2+} and cyclic AMP dependent and, for HO1 at least, seems to result from an increase in oxidative stress [4]. We are currently investigating the relationship between these changes in β-cell gene expression and other alterations of the β-cell phenotype.

2. **Effects of hyperglycaemia on rat β-cell function**
   It has been previously reported that β-cells chronically exposed to supraphysiological glucose concentrations are either insensitive or, in contrast, more sensitive to subsequent acute glucose stimulation. We have reinvestigated that question and observed that, after 5 days of diet-induced hyperglycaemia in the gerbil *Psammomys obesus*, the lack of GSIS between G5 and G10 results from the combination of two phenomena: a decrease in the maximal rate of insulin secretion likely due to β-cell degranulation, and an increase in glucose sensitivity that leads to an already elevated $[Ca^{2+}]_i$

and insulin secretion at otherwise subthreshold glucose concentrations (≤ G5) [5]. We observed similar alterations of glucose-stimulus secretion coupling events and GSIS in rat islets cultured for 1-3 weeks in a medium containing G30 instead of G10 [6]. Further studies on the mechanism(s) by which chronic hyperglycaemia alters the β-cell phenotype will be supported by the 2003 EASD/ Amylin–Paul Langerhans Research Award, for which I deeply thank the EASD and Amylin Pharmaceuticals.

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2003 ADA-EASD Transatlantic Fellowship

Nina Balthasar, Beth Israel Deaconess Medical Center, Boston, MA

Identifying key neuronal sites mediating melanocortin's effects on energy and glucose homeostasis

Deletion or mutation of the melanocortin-4-receptor (MC4R) in mice or humans leads to obesity with hyperphagia and hyperinsulinemia. MC4R mRNA is expressed in several brain sites, but it is unclear which populations of MC4R neurons are required to mediate melanocortin's effects on energy and glucose homeostasis. Our aim is to identify key neuronal sites mediating the 'anti-obesity and anti-diabetes' actions of MC4Rs.

We have generated mice, in which a lox-modified, null MC4R allele can be reactivated by Cre-recombinase. Mice homozygous for the null MC4R allele display an obesity phenotype identical to previously described MC4R knock-out mice. Reactivation of the MC4R allele in the oocyte, using ZP3-Cre mice, rescued lox-modified, null MC4R mice from their obesity.

Several areas of MC4R expression in the brain will be reactivated using mice with Cre-recombinase expression targeted to specific neuronal groups or by stereotaxic AAV-Cre-injections. Two sites of dense MC4R expression are autonomic preganglionic neurons and the hypothalamic paraventricular nucleus. Here MC4R expressing neurons co-localise with either choline-acetyl-transferase (ChAT) or NPY-Y1-receptors, respectively. We will generate transgenic mice expressing Cre-recombinase under ChAT or NPY-Y1 promoter control on the lox-modified, null MC4R background and analyse physiological phenotypes of mice, expressing MC4Rs in either autonomic preganglionic or hypothalamic PVN neurons or a combination of the two. Stereotaxic injections of AAV-Cre in lox-modified, null MC4R mice will furthermore localise important MC4R regions.

This novel technique of re-expressing a central nervous system receptor region specifically allows us to determine contributions of specific MC4R expressing neuronal groups to the regulation of energy and glucose homeostasis.

European Foundation for the Study of Diabetes (EFSD)

and

Novo Nordisk

Continuing Programme of Support for European Diabetes Research

Request for Applications (RFA)

ANNOUNCING UP TO EURO 2.1 MILLION IN ADDITIONAL FUNDS FOR DIABETES RESEARCH IN EUROPE

Background

The European Association for the Study of Diabetes (EASD) was founded in Montecatini, Italy, in 1965. In 1999, the Association created the ***European Foundation for the Study of Diabetes (EFSD)***. The aims of EFSD are to encourage and support research in the field of diabetes, to rapidly diffuse acquired knowledge and to facilitate its application.

Novo Nordisk is a world leader in insulin and diabetes care and also manufactures and markets a variety of other pharmaceutical products. Headquartered in Denmark, Novo Nordisk has companies and information offices in more than 60 countries.

Plan and Research Focus

The EFSD / Novo Nordisk Programme in diabetes research will accept applications within any area of basic or clinical diabetes research. Those focusing on psycho-social aspects of diabetes management and on prevention will also be most welcome. All applications will be considered on an equal basis and judged on their intrinsic scientific merit,.

Funding

Up to Euro 2.1 million will be made available over 3 years for research in the framework of the Programme and performed in Europe and its associated countries. The awards will be distributed as follows:

2004 – 7 grants, each of Euro 100,000
2005 – 7 grants, "up to" Euro 100,000
2006 – 7 grants, "up to" Euro 100,000

Mechanisms of Support and Review

Research will be supported through the award of fixed grants, each of Euro 100,000. The duration of each award may be one year or longer, depending upon the needs of the project and as justified in the application, so long as the total budget does not exceed the fixed sum of Euro 100,000.

Applications for an EFSD / Novo Nordisk Research Programme Award are invited from single not-for-profit institutions or groups of affiliated institutions from Europe and associated countries. Applications will be subject to a scientific review by a specialised and independent ad hoc committee. Funding will require approval by a joint EFSD and Novo Nordisk Board convened for this purpose. It is anticipated that applications for the grant year 2004 will be received by 1 December 2003 and approved for funding after review by March 2004.

Research Grant Applications

Applications for research grants may be subjected to pre-review (or triage) procedures. In this event, any application rejected at pre-review will not be subject to a complete scientific review.

The deadlines for receipt of research grant applications for funding in 2004 is **1 December 2003.**

For the purpose of this programme, the budget of the research grants is limited to Euro 100,000 per annum. All budgets are to be prepared in Euro. For countries in which the Euro is not yet the common currency, the exchange rate (between the Euro and the local currency in the country where the work is to be performed) used for calculating the Euro budget must be mentioned under "Budget Justification". EFSD and Novo Nordisk reserve the right to increase or decrease approved funding in Euro amounts to compensate for any significant change in the exchange rate.

Application forms are available at:
foundation@easd.org

All applications must be prepared on the official forms and completed in strict accordance with the detailed instructions to be found on these forms. In particular, applicants are reminded that any pages in addition to the maximum of 10 allowed for the scientific section of the application will be deleted prior to review. Similarly, no applications using a font or line-spacing smaller than defined in the instructions will be considered for review. Additional material (in the form of an appendix, attachment, reprints, etc.) is not acceptable and will not be sent to reviewers.

Applications should be submitted by 1 December 2003 (date of receipt) to:

Viktor Jörgens, M.D., Executive Director
European Foundation for the Study of Diabetes
Rheindorfer Weg 3
D-40591 Düsseldorf, Germany

Review Considerations

Completed applications will be evaluated in accordance with the criteria stated below for scientific / technical merit by an appropriate scientific committee convened by EFSD.

Review criteria are as follows:

- Significance: Does the study address an important problem? If the aims of the application are achieved, how will scientific knowledge be advanced? What will be the effect of the proposed studies on the concepts or methods that drive this field?
- Approach: Are the conceptual framework, design, methods and analyses adequately developed, well integrated, and appropriate to the aims of the project? Does the applicant acknowledge potential problem areas and consider alternative tactics?
- Innovation: Does the project employ novel concepts, approaches or methods? Are the aims original and innovative? Does the project challenge existing paradigms or develop new methodologies or technologies?
- Investigator: Is the investigator appropriately trained and well suited to carry out this work? Is the work proposed appropriate to the experience level of the principal investigator and other researchers (if any)?
- Environment: Does the scientific environment in which the work will be done contribute to the probability of success? Do the proposed experiments take advantage of unique features of the scientific environment or employ useful collaborative arrangements? Is there evidence of institutional support?
- Relevance: A brief statement of the impact of the proposed study on diabetes mellitus.

Reporting Requirements

All Investigators funded by this Programme are required to submit a scientific report at the end of the funding period. Investigators must provide EFSD with early notice of papers accepted for publication and must acknowledge the support of the Programme in such papers by use of the phrase: „This work was made possible by an EFSD / Novo Nordisk Research Grant".

Competitive Renewal

Applications for renewal of a Research Programme Award will be accepted on a competitive basis, with the same review process as described in this announcement. Such applications will thus be considered in the same fashion as all other new applications received for review and without any special priority.

Schedule

Announcement:	October 2003 issue of *Diabetologia*
Application Deadline:	1 December 2003
Review Process:	January / February 2003
Anticipated Award:	March 2004

2003 Albert Renold Career development award

Dr. Tim Frayling PhD, Peninsula Medical School, Exeter, UK

Dr Tim Frayling was born in the UK in 1972. He graduated from York University, UK with a 2.1 in biological sciences. He then trained to be a clinical scientist in molecular genetics in the diagnostic genetics laboratory in Oxford. With this excellent grounding he joined Professor Andrew Hattersley and Dr Sian Ellard who were establishing a research team in Exeter working on the genetics of maturity-onset diabetes of the young (MODY) and Type 2 diabetes. The success of his research work leading to 5 peer reviewed publications meant he was awarded his PhD thesis on "The genetics of the beta-cell" after only 2 years of study. On completion of his thesis he was awarded a 5-year NHS career development award for work on the molecular genetics of Type 2 diabetes and birth weight. In this post he has established himself as a leading UK scientist in the genetics of Type 2 diabetes and has trained in epidemiology, statistics, bioinformatics and human physiology as well as state of the art genetic techniques. He has given national and international invited lectures, published 40 peer reviewed articles and 4 chapters/reviews, raised over £600,000 in grants and is supervising 3 PhD students.

Monogenic diabetes

Dr Frayling began his work primarily studying the role of the rare monogenic form of diabetes, Maturity onset diabetes of the young. His work established that mutations in the HNF1alpha gene are the commonest cause of MODY in the UK and that there is no obvious genotype-phenotype relationship. Work continued on MODY, with the identification of ~15% of MODY families that did not have a mutation in any of the known genes. These MODYX families were recently subjected to a genome wide screen led by Dr Frayling and collaborators from Sweden and France. The results from 26 European MODYX families established that there is no one further locus containing a MODY gene and that further genetic heterogeneity exists. Further work is continuing to study the best candidate genes to try and identify additional MODY genes.

Type 2 diabetes

Finding genes for Type 2 diabetes, where multiple genes and environmental factors are involved, has proven a challenging task. However, recent findings, of which some of Dr Frayling's work has been part, provide considerable cause for optimism and suggest that, despite a lot of hype about the power of genetics, geneticists can make a real impact on improving our understanding of Type 2 diabetes. For example, together with collaborators from the DiabetesUK Warren 2 consortium, we have shown conclusively that the K23 allele in the beta-cell potassium channel gene, Kir6.2, predisposes to Type 2 diabetes. Similar work using large case-control studies and a meta-analysis has provided strong evidence that SNP44 in the Calpain 10 gene is associated with Type 2 diabetes. There had been considerable controversy as to the role of Calpain 10, but our work goes some way to confirming that it has a role outside of the Mexican American population in which it was first identified.

One of the most exciting findings resulting from Dr Frayling's work comes from the study of common variation in the Glucokinase (GCK) gene. Using four large normoglycaemic cohorts, we have shown that a G/A variant at position –30 in the islet cell promoter, present in 30% of people, raises fasting blood glucose levels. We are now spearheading efforts to establish the role of this variant in Type 2 diabetes risk and fetal growth. Initial results indicate that the variant alters birthweight in a parent of origin specific way. The presence of the minor allele in the mother raises birth weight but if the offspring inherits the minor allele from their father only, birthweight is reduced.

Together with other recent findings, Dr Frayling's work has provided a number of lessons about finding Type 2 diabetes genes. These include the probability that any single gene variant is likely to have a modest effect on disease risk and, therefore, large numbers of subjects are needed to identify risk alleles. This doesn't lessen the importance of finding these genes: alleles with small predisposing effects may be very common in the population and provide important

knowledge about disease mechanisms. A further important lesson emerging from Dr Frayling's work is that younger onset patients appear to be more powerful for identifying genes by linkage. Together with the Warren 2 consortium, we have shown that patients diagnosed younger provide a disproportionate amount of evidence for linkage in a genome wide scan. In particular, young onset subjects contribute most to loci on chromosomes 1q, 8q and 10q. An additional lesson emerging is that 'monogenic' genes are excellent candidates for a role in Type 2 diabetes. Dr Frayling's work has provided strong evidence that common variation in IPF-1, Kir6.2 and Glucokinase plays a role in Type 2 diabetes susceptibility. This follows on from work of groups in Malmö and Boston which established the role of the PPARG, Pro12Ala variant in Type 2 diabetes. Each of these genes has an example where rare, severe mutations cause a Mendelian form of diabetes or related condition. Further work is continuing to investigate the role of common variation in the HNF-1alpha gene, which falls in a region of chromosome 12 linked to Type 2 diabetes.

Work on the EASD Albert Renold fellowship

Dr Frayling plans to take some of these lessons and resources to one of the leading centres for genetics and genomics, the Centre National de Genotypage, Evry, Paris, run by Prof. Mark Lathrop. There the plan is to use state of the art technology and expertise to attempt to dissect loci mapped by the Warren 2 genome wide scan and identify further loci. In addition to this genetic approach, Dr Frayling will also use the opportunity to improve his knowledge of genomic based approaches to identifying important disease pathways. Dr Frayling would like to thank the EASD for providing this unique opportunity to expand his skills and further his career in diabetes research.

2003 EFSD / Eli Lilly Research Fellowship in Diabetes Microvascular Complications

Dr. Gabriella Gruden, Laboratory of Diabetic Nephropathy, Department of Internal Medicine, University of Turin, Italy

Curriculum vitae and research work

Gabriella Gruden was born in Turin, Italy in 1964. She obtained her MD in 1990 from the University of Turin, her Ph.D in 1997 from the University of Florence, and her specialisation in Internal Medicine in 2001 from the University of Turin.

She has been involved in research in diabetic nephropathy and macroangiopathy, with experience in both clinical and basic science research for over fourteen years. After her graduation, she trained in the Institute of Internal Medicine of Turin (Prof P. Cavallo-Perin and Prof G. Pagano), where she was involved in clinical research in diabetes. In her work, she demonstrated alterations in albumin excretion rate in non-diabetic first-degree relatives of patients with microalbuminuria, providing evidence of a familial susceptibility to kidney disease in Type 2 diabetes mellitus. Furthermore, she has highlighted in both Type 1 and Type 2 microalbuminuric diabetic patients coagulation and lipid abnormalities that may contribute to their greater risk of cardiovascular events.

From 1994 to 2001, she worked in London in the Unit for Metabolic Medicine at Guy's Hospital, King's College London, UK (Prof. GC Viberti) firstly as Research Associate, then as R.D. Lawrence Fellow and finally as Clinical Lecturer. During her time in London, she gained experience in molecular and cell biology techniques and she set up within the unit an *in vitro* system to simulate the haemodynamic insult

in vitro by exposing cultured cells to mechanical stretch. Her research activity focused on basic science aspects of diabetic nephropathy, and, specifically, she studied the mechanisms by which the haemodynamic insult of glomerular capillary hypertension translates into increased glomerular permeability and matrix deposition. In her work, she has demonstrated that stretch induces in mesangial cells overproduction of matrix components, cytokines (VEGF, TGF-β1, MCP-1) and cytokine receptors (AT1, TGF-β, VEGF, GLUT-1) via activation of specific intracellular signalling pathways (PKC, p60src, P38-MAPK, hexosamine biosynthetic pathway). This work has provided a better understanding of the mechanisms whereby the haemodynamic insult of glomerular capillary hypertension enhances the deleterious effects of hyperglycaemia. Back in Turin, she is currently a researcher in the Department of Internal Medicine, University of Turin, Italy, where she is working on the effect of the metabolic and haemodynamic insults on human glomerular epithelial cells.

Dr Gruden's work has yielded more than 30 original publications in diabetes, nephrology and basic science. She has been invited to author several chapters in books, editorials and reviews, including the chapters on the pathogenesis of diabetic nephropathy in the 14th Edition of the "Joslin Textbook of Diabetes Mellitus", the 3rd edition of the "Textbook of Diabetes" edited by Prof J. Pickup and the 3rd edition of the "Diabetes Mellitus: A Fundamental Clinical Text" by D. LeRoith. She was the recipient of the R.D. Lawrence Fellowship of the Diabetes-UK (1998) and the Internal Medicine Society Prize (1995). She has presented in over 40 national and international conferences and has been a reviewer for several scientific journals.

Announcements

The Third Annual Diabetes Technology Meeting

San Francisco, USA, 6–8 November, 2003

This is an opportunity to meet and interact with the world's leaders in glucose and lactate monitoring, closed-loop insulin delivery, new insulin analogues and diabetes databases.

More information, the complete meeting agenda and on-line registration are available on the meeting website: http://www.diabetestechnology.org

Meeting topics will include:

- Technologies for metabolic monitoring (glucose, lactate, markers of glycemic control)
- The artificial pancreas
- Alternate routes of insulin administration (inhaled, oral, transdermal)
- Computers and diabetes
- The annual diabetes technology survey
- Two live demonstrations of continuous glucose monitoring technology

Over 140 Abstracts have been received from 18 countries in North America, Europe, Asia and Africa. There will be two poster sessions / receptions. Sign up now for the meeting and the pre-meeting workshops:

1) "Use of Diabetes Technology in Clinical Practice" and
2) "Connectivity Standards Utilizing Computers for Analyzing Data from Blood Glucose Monitors and Insulin Delivery Systems".

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