

## CURRICULUM VITAE

Professor Michael G Hanna  
MBChB(Hons) BSc(Hons) ECFMG (USA) FRCP(UK) MD

Professor in Clinical Neurology  
Department of Molecular Neuroscience  
Institute of Neurology  
Queen Square  
University College London

Consultant Neurologist and Associate Clinical Director  
National Hospital for Neurology and Neurosurgery  
University College Hospitals NHS Foundation Trust  
Queen Square  
London

## **CV Summary- Professor Michael G Hanna**

### **Professor and Consultant in Clinical Neurology at Queen Square**

Postgraduate training in Neurology in Oxford and Queen Square, London

Published over 100 peer reviewed papers and reviews

Obtained £6.5 million in clinical research funding since 1997

15 book chapters and 1 book in many areas of general clinical neurology including stroke, head injury, epilepsy and headache

Subspecialty interests in neuromuscular diseases and neurogenetics

2003 Youngest Goulstonian Lectureship to the Royal College of Physicians London

Supervised 9 (6 clinical research fellows) Phd students and 3 post doctoral research fellows

Established 2001 the UK National Diagnostic service for Neurological and neuromuscular channelopathies. Obtained recurring funding from DoH [NSCAG] to provide this service ~£250 000 per annum

Commissioned 2006 [to start 2007] the UK Clinical and Diagnostic service for mitochondrial neurological disease in collaboration with Newcastle and Oxford. Funded by NSCAG total value £2.4 million per annum with 1million per annum for the NHNN element of the service lead by Professor Hanna.

Established and Lead the Centre for Neuromuscular Disease at the National Hospital for Neurology Queen Square-assess 2000 patients per year from all UK

Deputy Editor of the Journal of Neurology, Neurosurgery and Psychiatry-London

#### Undergraduate neurology teaching

Established and run new undergraduate clinical neurology teaching course in 1998 based at the National Hospital.

Awarded UCL top undergraduate teacher 2000 by undergraduate medical students

Co-authored 4<sup>th</sup> edition of well known undergraduate text “Tutorials in Differential Diagnosis” sold 6000 copies world-wide since published in 2003

## Clinical activity and management

Associate Clinical Director Neurosciences directorate since 2003

General outpatient neurology practice UCLH NHS Trust

## CURRICULUM VITAE

### 1. Personal Details

Michael G. Hanna 43 years 4.10.63

Present Appointment:

*January 1998-date.* Consultant Neurologist at the National Hospital for Neurology and Neurosurgery (NHNN-UCLH NHS Trust), London and Consultant Neurologist at the Middlesex Hospital, UCLH NHS trust London. Professor in Clinical Neurology, Institute of Neurology, University of London.

### 2. Education/Qualifications

BSc Biochemistry Hons 2.1(Manch)	July 1986
MB ChB First Honours (Manch)	July 1988
ECFMG I&II (USA)	July 1990
MRCP (UK)	March 1991
MD (Manch)	February 1996
FRCP (UK)	May 2002

### 3. Current Post and Professional History

My current Consultant position comprises research-allied to a specialist muscle-genetic service, general neurology and undergraduate neurology teaching.

#### 3a Current Post

##### *General Neurology Service*

I provide a comprehensive general neurology service to the new UCLH hospital and the Heart Hospital, part of the UCLH NHS-trust. This involves an on-site neurology outpatient clinic and a same day neurology ward liaison service to any ward in the hospital. This liaison service allows any inpatient at the Middlesex rapid access to a neurological opinion. Acute neurology care pathways have been developed. I have developed and delivered a new Trust-wide acute Neurology service centered on the new UCH hospital. I am involved in neurological rehabilitation.

##### *Research Programme-Summary*

I have obtained in excess of 6 million pounds sterling in external funding to support my research programmes into mitochondrial disease and human neurological channelopathies. These grants include project grants, MRC cooperative status, MRC cooperative component grants and clinical training fellowships. I have received funding from the MRC, Wellcome Trust, Action Research and NIH-USA. I have established the major clinical research center in the UK for neurological channelopathies with one of the largest clinical databases of channelopathy patients anywhere in the world. All my research efforts are patient-centred and this research has translated directly to the National muscle channel service now funded directly by the Department of Health [250K] on a recurring basis. This funding now provides permanent support for three clinical scientists, genetics lab equipment, a full time clinical nurse specialist and consultant neurology and neurophysiology sessions. I have just successfully obtained a second NSCAG grant commissioning a new UK national service for mitochondrial disease in collaboration with Newcastle and London due to start

2007 with 950kpa recurrent funded for the NHNN part of the service. In recent years I have published in high impact journals including New England Journal of Medicine, Lancet and the American Journal of Human Genetics. I have been invited to give guest Lectures throughout Europe, in North America and in Australia. I have written invited reviews for Lancet Neurology and Nature Neurology in Clinical Practice. My research goals remain to improve understanding of the molecular mechanisms in human mitochondrial and ion channel diseases and, wherever possible, to translate my findings into clinical practice.

#### ***Undergraduate medical student clinical neurology teaching course***

In 1998 I established a new two week medical student neurology programme. Prior to this although special module neurology teaching occurred for those students who selected it (Prof AJ Lees) no formal neurology teaching existed for all UCL medical students. The course I established initially took place on the Middlesex Hospital site but subsequently I was able to transfer it to the Queen Square site, which had traditionally only taken postgraduate neurology trainees. This has proved very successful. I have recently extensively revised this course which is now five weeks long and incorporates all the requirements for the “New Curriculum” for the training of UK doctors. The new course is summative towards the final MB and therefore involves organizing and coordinating a written exam and an OSCE exam each term. I am a member of the medical school neuroscience undergraduate planning committee. I also act as an academic advisee for four undergraduate medical students at any one time. This involves regular meetings offering various forms of support throughout their clinical three year course. My work in undergraduate teaching was recognized by the award of “Top clinical teacher” in 1999-2000 voted for by the clinical medical students. In 2002 Queen Square voted best undergraduate teaching site –UCL medical students. I have recently co-authored the fourth edition of the well known textbook “Tutorials in Differential Diagnosis”

#### ***Specialist Clinical Service-The National Hospital Centre for Neuromuscular Disease***

I have recently established a centre for neuromuscular disease with colleagues at the National Hospital in order to enhance services to patients with muscle and peripheral nerve diseases. The center comprises a critical mass of clinical neurologists with expertise in muscle and nerve disease, neurophysiologists, specialist nursing staff and a state of the art computerized myometry system as well as support staff. I run the weekly muscle-genetic clinic which has a regional and national referral base for patients with acquired and genetic muscle disease. I have obtained funding from the Department of health [National Specialist Commissioning Agency] to support the muscle channel component of this muscle service. This now amounts to £250 000 per annum on a recurring basis. In addition I have successfully constructed capital bids for DNA equipment and clinical neurophysiology workstations amounting to an additional £350k This NSCAG funding allows me to provide a comprehensive, clinical electrophysiological and genetic service to this group of patients from anywhere in the UK without cost implications to the local referring centre. The NSCAG service I offer is part of a National consortium for the diagnosis of rare neuromuscular diseases which I established with colleagues in Oxford, Newcastle and London. Neurological trainees as well as consultant colleagues from the UK and internationally frequently attend my clinic. I run a joint Inflammatory muscle disease clinic with Professors Isenberg and Schapira for complex cases. With charity and private partners I am currently raising funds in order to develop the physical location for the Centre for Neuromuscular Disease.

### **3b Professional History**

***Aug 88-July 89***

#### Preregistration Positions

Professorial House Physician General Medicine and Neurology  
Professor D Neary & Professor S Tomlinson, Manchester Royal Infirmary  
Professorial House Surgeon  
Professor Sir Miles Irving, Hope University Hospital, Manchester

***Aug 89-Jan 92***

#### Senior House Officer Positions

Newcastle-upon-Tyne central teaching medical rotation.  
General medicine & endocrinology. Dr WMG Tunbridge, Newcastle General hospital  
General medicine & gastroenterology. Dr C Record, Royal Victoria Infirmary  
Cardiology Professor F Campbell, Freeman Hospital  
Chest medicine Professor J Gibson & Professor P Corris, Freeman Hospital  
Neurology Dr P Hudgson & Dr J Foster, Newcastle General Hospital  
Renal medicine Professor R Wilkinson, Freeman Hospital

Oxford Department of Clinical Neurology

Neurology Professor Newsom-Davis, Drs R Greenhall, D Hilton-Jones, C Fursden-Davis, G Wright, J Oxbury, N Hyman and M Donaghy, Radcliffe Infirmary, Oxford

***Feb 92-July 92***

#### Registrar/Clinical Lecturer

General medicine & geratology, Nuffield Department of Clinical Medicine, Oxford University  
Professor J Grimley-Evans, John Radcliffe Hospital & Radcliffe Infirmary.

***Aug 92-July 94***

#### MRC Research Fellow

Medical Research Council clinical training fellow,  
Mitochondrial DNA in human mitochondrial disease  
University Department of Clinical Neurology, Institute of Neurology, Queen Square, London;  
Supervisor *the late* Professor Anita E Harding

***Aug 94-April 96***

#### Registrar in Clinical Neurology

University & NHS Departments of Clinical Neurology, Radcliffe Infirmary, Oxford  
Drs R Greenhall, M Donaghy, D Hilton-Jones, N Hymen, J Oxbury, C Fursden-Davis, G Wright, P Davis, P Matthews & Professor Newsom-Davis.

***May 96-Nov 96***

#### Registrar in Clinical Neurology

The National Hospital for Neurology and Neurosurgery, Queen Square, London  
Professors Shorvon, Duncan, Fish, Marsden, Frackowiak, Schapira Quinn, Wood and Goadsby

*Nov 96-January 98*

Senior Registrar in Neurology and Clinical Lecturer in Neurogenetics

The Institute of Neurology and The National Hospital for Neurology and Neurosurgery  
Queen Square and St Mary's Hospital, Paddington, London  
Professors Rossor and Wood and Drs Farmer, Thomas and Ball

#### **4. Other Appointments and Affiliations**

Associate Clinical Director, National Hospital for Neurology and Neurosurgery since June 2003.  
Responsible for clinical management of all inpatient and outpatient neurology activity at NHNN.

Deputy Editor, Journal of Neurology, Neurosurgery and Psychiatry since January 2004. Involves daily running of Journal and handling 2000 manuscripts per year with the Editor and 3 associate editors. Regular editorial meetings.

Membership of Societies-advisory panels

Association of British Neurologists, World Muscle Society, European Neurological Society  
Centre lead-National Specialist Commissioning Agency funded National muscle channelopathy service, National Hospital Neurology, UCLH NHS Trust 2002-present  
Oxford University Wellcome Trust Initiative in Channelopathies-co investigator and collaborator 2003-present  
North American Muscle Interest Group member and Scientific Advisor 2003-present  
On steering group for "Immuno-suppression in myositis" MRC trial 2002-present

I regularly review papers and books for the following journals: Brain; Human Molecular Genetics; Journal of Neurology; Journal of Neurology, Neurosurgery and Psychiatry; Journal of Medical Genetics; Movement Disorders; European Journal of Neurology; Genomics, Annals of Human Genetics, Annals of Neurology, European Journal of Human Genetics, Journal of Neurological Sciences, Neuroscience, American Journal of Human Genetics, Neuropediatrics, American Journal of Medical Genetics, Journal of Clinical Investigation and Nature Genetics.

Grant reviewer for: The Wellcome Trust, MRC, Telethon (Italia), Action Research, Woolfson Foundation.

Institute, University, and Hospital Committees

*Institute of Neurology:* Academic Board, Education subcommittee

*National Hospital:* Medical Committee (Secretary 2000-2003), Neurology directorate committee

*University College Hospital Trust:* UCLH-trust special trustees research award committee

*University College London:* Neurosciences new curriculum undergraduate planning committee

*University College London NHS Trust:* member of the use of medicines committee

## **5. Prizes, Awards and other Honours**

Neurology: The Dorothy Clarke Memorial Prize University of Manchester. Based on final year clinical examination in Neurology (1988)

Mabel Harriet Florence Smith travel scholarship (1987)  
Awarded by Leeds City Council on the basis of an oral presentation .

Top teacher award, University College London Medical school. Voted best clinical teacher by clinical medical students year 2000

### **Goulstonian Lectureship to the Royal College of Physicians 2003**

Awarded to the youngest elected fellow after assessment of achievements by the senior college officers.

Lecture delivered Nov 2003 at Royal College of Physicians, Regents Park, London  
“Neurological Channelopathies: a new field”

## **6. Grants**

### **1992**

Medical Research Council Training Fellowship-1992-1994

The study of the molecular pathogenesis of primary defects of mtDNA using a human myoblast culture system

MG Hanna-supervisor Prof AE Harding  
£60,000

### **1996**

Joint Research Advisory Committee Institute of Neurology-1996-1997

Mechanisms of phenotypic diversity associated with the mitochondrial A3243G point mutation  
Collaborator with Dr IP Nelson

£35,000

### **1997**

Brain Research Trust-1997-1999

Clinical and Genetic studies of human neurological channelopathies  
MG Hanna Principal applicant

£80,000

Brain Research Trust -1997-1999

Expression studies of human neurological channelopathies  
MG Hanna co-applicant with Professor DM Kullmann

£90,000

### **1998**

Wellcome entry level fellowship for medical research fellow-1998-1999

Studies of mtDNA in human Neurological disease

MG Hanna sponsor and supervisor  
£57,000

**1999**

Wellcome entry level fellowship for medical research fellow-1999-2000

Molecular genetic studies of human skeletal muscle channelopathies

MG Hanna sponsor and supervisor

£59,000

Epilepsy Research Foundation-1999-2001

Clinical, Genetic and Expression studies of the voltage gated calcium channel (CACNA1A) in complex human epilepsy phenotypes

MG Hanna, principal applicant

£50,000

Brain Research Trust-1999-2001

Molecular basis of phenotypic heterogeneity associated with mtDNA mutations

MG Hanna principal applicant

£55,000

**2000**

Wellcome training fellowship-2000-2003

MG Hanna, sponsor and supervisor for N Davies

Molecular genetic and expression studies on muscle chloride channelopathies

£120 000

MRC mitochondrial cooperative: mitochondria in health and disease

Cooperative status awarded 1999-2004

MG Hanna co-principal applicant with Prof JB Clarke, Prof M Duchen, Prof Wood, Prof Rich, Prof Crompton and Prof Moncado-UCL

MRC mitochondrial cooperative –component grant-2000-2003

MG Hanna-principal applicant one component grant

Identifying nuclear genes which influence the expression of mtDNA mutations

£180 000

Special Trustees of the UCLH NHS trust 2000-2002

MG Hanna principal applicant

Clinical, genetic and expression studies of the voltage gated calcium channel CACNA1A in neurological disease-£69000

**2001**

National Institutes of Health [Bethesda USA] 2001

Research proposal planning grant

An international trial of treatment in skeletal muscle channelopathies

USA PI-Professor RC Griggs and UK Co PI-MG Hanna \$25 000

**2002**

Competitive NHS-service related grants 2002-recurrent

National Specialist Commissioning Agency [NSCAG]

Principal applicant.

Recognized by the Department of Health as a National Centre for DNA-diagnosis in muscle

channel disease. Permanent funding of £250 000 {2005} per annum to provide this service.  
Funding for DNA-scientist, consultant sessions and DNA equipment.  
[2002-3 £150 000, 2003-4 £170 000, 2004-5 £180 000 2005-5 £250 000]  
Additional successful NSCAG capital bids for DNA and EMG equipment [350K]

### **2003**

Kennedy's disease research fund grant-2003

£50 000 awarded to Dr MG Hanna. commencing October 2003 for a clinical research fellow to undertake molecular genetic research into Kennedy's disease

MRC Cooperative-Epilepsy-2003-2005

Component grant £397 000

Commenced July 2003-2006

Awarded to DM Kullmann, NW Wood and MG Hanna

Ion channels in epilepsy

### **2003 contd**

National Institutes of Health Bethesda [USA]-2003-2007

Clinical Investigations into Neurological Channelopathies "CINCH"

UK Centre Co PI on International multicentre study in neurological channelopathies

Funds one clinical research fellow salary per year for 5 years-£200 000

Wellcome Integrative Physiology Ion Channel Programme grant to Oxford University

OXION 2003-2007 2million

Co-Investigator on grant

Entitled to provide projects each year for PhD students

### **2004**

National Institutes of Health [Bethesda USA] awarded 2004

An international trial of pharmacological intervention in periodic paralysis

\$1.1million US USA PI and Coordinator-Professor RC Griggs- only UK centre Co-PI MG Hanna

[Trial to commence UK 2006]

Guarantors of Brain 2004-2005

MG Hanna Supervisor for Dr Tracey Graves

Research fellowship

£55 000

UCL special Trustees-Fast track grant application 2004 £29000

MG Hanna Principal applicant and supervisor [1 post doc]

"Nuclear genes and mitochondrial disease"

### **2005**

Medical Research Council Clinical Research training fellowship 2005-2007

Molecular studies of mouse fetal motor neurons in Kennedy's disease

MG Hanna and L Greensmith joint co-supervisors-£135 000

Action Research-Clinical Training fellowship 2005-2007  
MG Hanna sponsor and supervisor  
Brain calcium channel as and neurological disease  
£113 000

MRC component grant 2005-2008  
MG Hanna Co-applicant with Dr S Rahman  
“Nuclear genes and mitochondrial disease”  
£80 000

UCLH CRDC clinical training fellowship  
£75000  
Awarded 2005-2006  
Supervisors Dr MG Hanna, Prof Unwin and Prof Duchen  
For Dr Andrew Hall-“A molecular study of renal dysfunction in human mitochondrial disease”

## **2006**

Competitive NHS-service related grants 2007-recurrent  
National Specialist Commissioning Agency [NSCAG]  
Principal applicant.  
Recognized by the Department of Health as a National Centre for Mitochondrial clinical and diagnostic service in conjunction with Newcastle and Oxford.-diagnosis in muscle channel disease. Permanent funding 2.1 million across 3 centre pa of which £950 000 per annum for NHNN to provide this service. Funding for DNA-scientists, clinical nurse specialists, consultant sessions and DNA equipment.

## **2006**

MRC translational research centre for neuromuscular disease  
£3.5 Million Sterling

## **7. Invited National and International Lectures**

### **1995**

1. April 1995: Oxford University Department of biochemistry invited seminars  
*“New mitochondria DNA mutations and myoblast studies on their molecular pathogenesis”*
2. Sept 1995: Oxford University, Nuffield Department of Pathology, invited seminar  
*“The emerging role of mitochondria in human disease”*

### **1997**

3. April 1997: Department of Clinical Neurology, University of Queensland, Brisbane, Australia  
*“Channelopathies: A new name for old diseases”*
4. May 1997: Institute of Neurology short course in Neurogenetics  
*“Channelopathies”*
5. Nov 1997: Recent advances in Epilepsy, Glaxo Wellcome, Paris  
*“Modern Genetics of Epilepsy”*

6. Nov 1997: Institute of Child Health, UCL- research seminar  
*"Ion channel disorders of skeletal muscle"*
7. Dec 1997: UCL centre for human genetics annual meeting  
*"Ion channels and epilepsy"*
- 1998**
8. Jan 1998: Department of Neurology, Kings College Hospital research seminar  
*"Mitochondrial genetics: focus on myopathies"*
9. March 1998: Glaxo Wellcome centre for neuromuscular disease annual meeting, Liverpool  
*"Recent advances in the genetics of neuromuscular diseases"*
10. March 1998: Annual Neuromuscular Symposium, Walton Centre for Neurology, Liverpool  
*"Skeletal muscle channelopathies"*
11. Sept 1998: Annual meeting of the European Federation of Neurology, Seville, Spain, Scientific symposium  
*"Channelopathies: a new field"*
12. Sept 1998: Association of British Neurologists autumn meeting, scientific symposium  
*"Ion channels and neurological disease"*
13. Oct 1998: International league against epilepsy, Annual Scientific Meeting, Oxford  
*"Ion channels and paroxysmal disorders"*
14. Oct 1998: Oxford clinical genetics seminars  
*"Developing a skeletal muscle ion channel DNA diagnostic service"*
15. Nov 1998: Department of Neurology, Leeds University  
*"Skeletal muscle ion channel disorders"*
- 1999**
16. Feb 1999: Annual Salpetriere Queen Square Neurology meeting, Paris  
*"New mutational mechanisms in mitochondrial diseases"*
17. March 1999: Dept Neurology, Addenbrooke's Hospital, Cambridge  
*"Neurological channelopathies-the future"*
18. March 1999: Neurology for Neuroscientists, Magdalen College Oxford  
*"Ion channels and Neurological Disease"*
19. April 1999: Annual Clinical Genetics Day, Institute of Child Health, Great Ormond Street  
*"Mitochondrial Deafness"*
20. April 1999: International League against Epilepsy, British branch, annual meeting, Birmingham,  
*"Ion Channels and Epilepsy-the future"*
21. June 1999: Muscle Course, Hammersmith Hospital, London

*“Molecular genetics of inherited myotonic disorders*

”

22. June 1999: Dept Neurology, Western General Infirmary, Edinburgh  
*“Neurological Channelopathies”*
- 2000**
23. Jan 2000: British Paediatric Neurologists Association annual meeting, Glasgow  
*“Ion channel dysfunction-a common problem in epilepsy”*
24. Jan 2000: Institute of Neurology-UCL-Annual Glaxo Lecture  
*“Ion channels and neurological disease”*
25. March 2000: University of Sheffield, Dept of Neurology  
*“Neurological channelopathies”*
26. April 2000: National neurology meeting Glaxo Wellcome-Stratford  
*“Molecular mechanisms in paroxysmal neurological disease”*
27. May 2000: University of Birmingham, Dept of Neurology  
*Ion channels and Neurological diseases”*
28. June 2000: University of Birmingham, Dept Clinical Genetics  
*“The genetic ataxias”*
29. Sept 2000: Salpetriere Hospital, Dept Neurology, Paris  
*“Molecular mechanisms in mitochondrial disease”*
30. October 2000: University of Bologna, Dept of Neurology, Italy  
*“Brain potassium channel dysfunction and neurological disease”*
- 2001**
31. Feb 2001: Institute of Child Health, Dept metabolic medicine, UCL  
*“Paediatric channelopathies”*
32. April 2001: Advanced Neuromuscular course, Hammersmith Hospital  
*“Skeletal muscle channelopathies”*
- 2001 contd**
33. July 2001: University of Sheffield, Channelopathies 2001  
*“Human neurological disease and ion channel dysfunction”*
34. Oct 2001: Dept Clinical Neurology, University of Oxford  
*“Molecular Mechanisms in neuronal calcium channelopathies”*
- 2002**
35. April 2002: University of Milan, Dept Neurology  
*“Calcium channels and epilepsy”*
36. July 2002, International Congress on Neuromuscular disease, Vancouver Canada workshop-  
*“Painful muscle channelopathies”*
37. September 2002, Birmingham Heartlands Hospital NSCAG meeting  
*“The National diagnostic service for muscle channelopathies”*
38. October 2002, Atkinson’s Morley’s Hospital, Dept of Neurology,

*“An Update on Brain Channelopathies”*

**2003**

- 39 March 2003, Royal Society Medicine, London  
*“Episodic Ataxias-mechanisms in human cerebellar channelopathies”*
- 40 March 2003 University of Oxford Wellcome Trust ion channel initiative  
*“Human brain channelopathies”*
- 41 November 2003 Bath Advanced Neurology course  
*“Neurological channelopathies”*
- 42 November 2003 Goulstonian Lectureship  
Royal College of Physicians, London  
*“Neurological channelopathies”*
- 43 March 2003 UCL annual rheumatology course  
*“Inflammatory myopathies”*
- 44 May 2003 Dept Neurology University Nottingham  
*“Muscle channelopathies”*

**2004**

- 45 June 2004 Dept Neurology, University of Bonn  
*“Nuclear Mitochondrial disease”*
- 46 September 2004 EFNS Paris  
Invited to organize workshop  
*“Neurological channelopathies”*
- 47 October 2004 NIH-CINCH-grant collaborators’ symposium  
University of Rochester Medical School, Rochester, New York  
*“Molecular genetic basis of Periodic Paralysis in the UK”*

**2005**

- 48 April 2005 Dept Neurology, University of Bristol  
*“Neurological channelopathies”*
- 49 April 2005, Dept of Neurology, University of Newcastle  
*“Brain paroxysmal disorders”*
- 50 May 2005, Dept Paediatrics, Alder Hay Hospital, Liverpool  
*“Paediatric channelopathies”*
- 51 May 2005 Short course on Muscle Disease, Institute of Neurology, London  
*“Inflammatory myopathies”*

**2006**

- 52 Feb 2006 NIH-CINCH collaborators’ symposium UCLA-SanDiego USA  
*“Molecular mechanisms in Episodic ataxia”*

- 53 Jan 2006-Irish National Annual Neuromuscular Symposium-Cork, Ireland  
*Guest Lecture “ Human skeletal muscle channelopathies-mechanisms and treatment”*
- 54 June 2006-Dept of Neurology, St George’s Hospital, London  
*“ Neuronal channelopathies”*
- 55 April 2004 Neurology for Neuroscientists, Guarantors of Brain-Oxford  
*Neurological channelopathies*
- 56 Sept 2006 -International Society of Neurophysiology annual conference, Edinburgh  
*Invited lecture- “Genetic neurological channelopathies”*  
*Workshop organizer: “Channelopathies”*

## **8. Academic Supervision and Muscle Disease Clinical Attachments:**

### **1997-2000**

Ms Louise Eunson BSc

3 years funding BRT and ERF (1997-2000)

“Molecular genetic studies on brain channelopathies”

*Queen Square essay prize 2000 [the enigma of paroxysmal disorders in neurology-the role of ion channels”]*

Graduated PhD August 2001. Currently Genetics Lecturer University of Colchester”

### **1999-2000**

Dr A Siddique 1999-2000 medical research fellow

Wellcome entry level fellowship-mitochondrial disease 1999-2000

Transferred to MRC funded “Genetics of epilepsy project” [Prof Wood]

Currently SpR Neurology-pan-Thames rotation

### **1998-2001**

Dr T Pulkes MD

3 years funding BRT 1998-2001

“Molecular mechanisms in mitochondrial disease”

PhD graduated University of London 2004

Currently Consultant Neurologist and associate Chair neurology, Bangkok, Thailand

### **1999-2001**

Ms Ruth Rea BSc

3 years funding Wellcome Trust

Co-supervised with Prof Kullmann

“Molecular expression in neurological channelopathies”

Graduated PhD University of London 2003

### **1999-2002**

Dr NP Davies MBBS

Wellcome research training fellow commenced 1999 for 4 years [PhD]

“Skeletal muscle channelopathies”

PhD in preparation

Currently Consultant Neurologist, Birmingham.

**2001-2004**

Dr D Liolitsa PhD

Postdoctoral research assistant commenced 2001 for 4 years

Funding MRC coop component grant

“Nuclear genes and mitochondrial disease”

Currently doing degree in medicine UCL

**2002-2004**

Dr P Imbrici PhD

Post doctoral research assistant

Special trustees grant commence 2002 2 years

Functional expression studies of calcium channel mutations causing human neurological disease

Currently post-doc in ion channel research Rome.

**2004-2007**

Dr Tracey Graves medical research fellow 2004-2007

Brain Research Trust-Calcium channelopathies

NIH –USA-CINCH Fellow

Action Research Clinical training fellowship

Registered for PhD-UCL

**2004-2007**

Dr Doreen Fialho medical research fellow 2004-2007

NIH –USA-Muscle channelopathies

NSCAG Molecular expression scientist grant

Registered for PhD-UCL

**2004-2007**

Dr Niranjanan Nirmalanathan

Medical research fellow 2004-2007

Kennedy’s research donation-Molecular aspects of Kennedy’s

Medical Research Council Clinical Training Fellowship 2005-2007

Registered for PhD-UCL

**2004-2006**

Dr Charunghai Dejthevaporn 2004-2006

Neurology National Scholarship Thailand

Clinical studies on the natural history of mitochondrial disease

**2006-2008**

New NIH CINCH clinical research fellow post 3 years 2005-2007

Recently appointed Dr Sanjeev to start Feb 06

**2006-2007**

New NIH-CINCH clinical fellow post 2 years 2005-2007

Recently appointed Dr Emma Matthews start Jan 06

**2006-2009**

Dr Susie Tomlinson

Human peripheral nerve excitability measurements to diagnose CNS channelopathies

Australian neurology fellowship

**Clinical/research attachments to my specialist muscle disease clinic**

The colleagues listed below received 4 to 6 month training senior SpR training attachments with in my muscle service. They have all now been appointed to senior genetic/muscle consultant posts as indicated.

**2001**

Prof Patrick Chinnery, Neurogenetics, University of Newcastle upon-Tyne

**2002**

Dr Kevin Talbot, now Neuromuscular Consultant neurologist Oxford

**2003**

Dr Paul Maddison Neuromuscular Consultant Neurologist, Nottingham,

**2004**

Dr John Cole, now Muscle Disease -Consultant Neurologist Manchester

Dr Charlotte Brierly, now Muscle Disease- Consultant Neurologist Cambridge

**2005**

Dr Veronica Tan, now Consultant Neurophysiologist London

Dr Aisling Ryan, Consultant Neurologist, Cork, Ireland

**2006**

Dr Singh-Senior SpR genetics Manchester

Dr Smith-Senior neurology SpR, Bristol

**9. Teaching Activity*****Undergraduate teaching***

University College London, Medical student Neurology Course Organizer

In 1999 I established and was responsible for running a completely new two week course based for the first time on the Queen Square site. I am actively involved in the Neurosciences planning group and have developed a new five week neurology course in line with the new curriculum which commenced in September 2002 at Queen Square. This new course is summative for the final MB and significantly enhances the training of UCL undergraduates in clinical neurology. In 2004 Dr Jarman joined me and we now co-run the course. I received UCL top clinical teacher prize in 2000 'voted for by medical students] and the undergraduate teaching course received best clinic teaching site.

***Postgraduate teaching***

Recognized teacher status at the University of London (since 1998).

I have an active and varied teaching role at the Institute of Neurology/National Hospital. These include:

Clinical teaching: Regular outpatient, case demonstrations, ward and chairmanship of the neurology grand round.

Formal lecturing: I have lectured at international meetings, many neurology departments around the country and numerous in-house lectures, including the MSc Neuroscience course.

I contribute to the Institute of Neurology, Diploma in Clinical Neurology course.

### ***PhD Examiner***

Between 1997 and 2005 I have been appointed as an examiner for eleven PhD theses for the Universities of London, Oxford and Newcastle upon Tyne.

### ***Lay audiences***

I also give lectures and occasional tutorials to a wide range of audiences including medical, paramedical, lay and scientific.

## **10. Enabling Activity**

### **Local**

The Institute of Neurology/UCL:

As a Professor my research involves mentoring, supervising and overseeing the training and development of clinical and non-clinical PhD students and Post-doctoral research workers. I have supported the progression of all trainees who have left my group. Two of my PhD students have now graduated PhD UCL [Louise Eunson and Tee Pulkes]. Louise gained the prestigious Queen Square Essay prize, 2000, for her work on neuronal channelopathies. Tee Pulkes was a co-author of our work published in the New England Journal of Medicine and is now assistant Professor of Neurology in Department of Neurology University of Bangkok. Dr Nick Davies spent four years with us doing a PhD on muscle channelopathies and is now consultant Neurologist in Birmingham and has set up the Birmingham Muscle and Nerve Centre. Dr Liolitsa was my post-doc on my mitochondrial MRC cooperative component grant. She published several papers with me including in Annals of Neurology and is a coauthor on work we have just submitted to the Lancet. She became so interested in clinical neurology she obtained a place at UCL medical school and is now in her second year. Dr Paola Imbrici worked with me and Professor Dimitri Kullmann as a post-doc on a CRDC grant I obtained. She successfully obtained further evidence for a role of neuronal calcium channels in epilepsy and we published this work in Brain 2004 and we also worked on potassium channel dysfunction in periodic paralysis recently published in Neurology 2005. In addition I contribute to the neurogenetics unit and collaborate closely with Professor NW Wood. This has two main functions DNA service and research. I am responsible for coordinating the DNA based diagnostic work for muscle genetic disorders such as mitochondrial disorders and for channelopathies. I integrate this with the specific training needs of highly competent clinical scientists, many of whom will move back into clinical practice as neurologists with a primary interest in neurogenetics. I established the current UCL undergraduate neurology teaching course and moved the course to be based at Queen Square in 2000. I was awarded UCL top clinical teacher in 2000 by undergraduate medical students. I now co-run the course which continues to be very successful [Queen Square recently voted best clinical teaching location by UCL medical students].

### **National**

In 2001 in open competition we obtained recurring funding [currently £250 000 per annum] from the Department of Health through National Specialist Commissioning to run a National Clinical and DNA-based diagnostic service for patients with skeletal muscle channelopathies. This funding now supports three clinical scientists [2 DNA 1 molecular expression], consultant sessions, a full time clinical nurse specialist, and consumables. In addition I made successful capital bids amounting to an additional £350K for DNA and electrophysiology equipment. This national service now in its fifth year has strengthened the position of the National Hospital and the Institute of Neurology as a leader in this area in the UK and recognized internationally. A unique database of brain and muscle channel patients has been established and has been a major resource facilitating both internal collaborations in the Institute eg Professor Kullmann and International collaborations eg grants from NIH [USA] in collaboration with Professor Griggs, University Rochester USA The muscle clinics I run in the Centre for Neuromuscular disease have attracted trainees from all over the UK; many are now neuromuscular consultants all over the UK and beyond [see list of individuals in section 8]. I have just 2006 obtained a second NSCAG commissioned service for mitochondrial disease due to commence 2007. This is a collaboration with Oxford and Newcastle and is funded 2.1 million per annum across the three centres [950k pa for NHNN]

## **International**

My work in establishing the UK national clinical and genetic centre for channelopathies has stimulated international research collaborations [see grants NIH USA in collaboration with Professor Griggs-University Rochester USA]. I am a scientific advisor for the North American Muscle Study Group. This group established by Professor Griggs involves many of the key international figures in muscle research and has an important goal of developing new treatments through basic research and clinical trials. I have organized workshops and been invited to lecture at meetings in USA, Europe and Australia. I am Deputy Editor of the Journal of Neurology, Neurosurgery and Psychiatry, an internationally recognized Journal. I co-authored the fourth edition of the well known undergraduate text book "Tutorials in differential diagnosis" published in 2003 and now on its third print run having sold over 6000 copies world-wide and translated into several languages.

## **11. Research Activity**

The neurogenetics research group in the Department of Clinical Neurology was established in 1985 (by the late Professor AE Harding) and is now headed by Professor Nick Wood. Anita Harding supervised my original research higher degree and inspired my interest in studying the molecular basis of neuromuscular disease. I undertake clinical/molecular genetic research into mitochondrial and ion channel disorders.

### **Human Mitochondrial Diseases**

- My group continues to define new mutations in mtDNA associated with human neurological disease which permits new insights into pathogenetic mechanisms. I have spent several years defining new mitochondria DNA mutations and investigating the mechanisms of pathogenicity using a different primary and transformed cell systems. More recently I have studied the role of nuclear mitochondrial interactions as a disease mechanism in human mitochondrial disease. We developed a cell model which allows nuclear-mitochondrial genetic interactions to be studied, with the aim of identifying important nuclear genes.
- I published in high impact journals such as New England Journal of Medicine, the Lancet and American Journal of Human Genetics. I have written invited reviews and book chapters in this area. Recently, I was a principal applicant on a successful five year MRC cooperative application "Mitochondria in Health and Disease". I have received two components grants from this cooperative. Currently I am actively pursuing the role of nuclear genes in mitochondrial disease [the second component project grant] in collaboration with Dr Rahman in the Institute of Child Health. Recent collaborations with Prof Chinnery and Turnbull in Newcastle have allowed us to define new phenotypes associated with mitochondrial nuclear gene mutations. I collaborate closely with Professor Michael Duchon in Physiology UCL. Through a jointly funded post-doc position we have recently provided evidence for a nuclear role in the expression of a mitochondrial DNA mutation and obtained data that suggest mutant mitochondria not only fail to produce ATP but also consume cellular ATP thereby suggesting a new mechanism of cellular pathophysiology-work submitted to the Lancet. All my basic research work in mitochondrial disease is allied to a large clinical mitochondrial service based in the National Hospital.

### **Human Neurological Channelopathies**

- There are an increasing number of neurological conditions caused by abnormalities of ion channel function. I established a National database for patients with neurological channelopathies in 1996 with the Association of British Neurologists Surveillance Unit. This data-base is now one of the largest collections of such patients in the world and has enabled collaborations with colleagues locally [Professor Kullmann and Wood], nationally [as a co-investigator on the Oxford ion channel initiative funded by the Wellcome Trust-Professor Francis Ashcroft and Professor Kay Davies] and internationally [eg NIH grants with Professor RC Griggs North America]. The setting up of an interdisciplinary group in ION/UCL with cellular physiologists (Prof DM Kullmann and Prof A Dolphin) and geneticists (Prof Wood) has allowed my group to undertake molecular genetic and cellular electrophysiological studies. We have extensively studied clinical and molecular aspects of muscle channelopathies and some neuronal channelopathies. We have defined the range of clinical phenotypes associated with neuronal potassium channel dysfunction and related this to the cellular electrophysiological phenotypes. We have

shown that there is an increased risk of epilepsy in patients with neuronal potassium channel dysfunction [Annals of Neurology, Brain]. We have provided evidence that the brain P/Q-type calcium channel may have a role in human absence epilepsy [Lancet, Brain]. In collaboration with Prof Wood, Dr Sisodiya and Prof Goldstein [Duke USA] we are currently addressing the role of calcium channel variation as a risk factor in common forms of epilepsy. This ion channel work has led directly to the establishment of the UK national channelopathy centre for diagnosis and treatment currently funded £250 000 per year by the UK Department of Health. I have obtained funding from the NIH-USA, MRC-UK, Action Research UK and the Wellcome Trust UK, to support basic science and clinical research into channelopathies. I am a co-investigator on the recent successful Oxford-based Wellcome funded integrative physiology programme grant on ion channels and human disease. It is probable that some other neurological disease areas (most notably the epilepsies, migraine and paroxysmal movement disorders) are also due to channels. This functional work will complement our positional cloning strategies once these genes are cloned. I have published original channel research widely in international journals including Lancet, Annals of Neurology, Brain, Journal of Physiology, and Neurology. I have published several reviews in this area, most recently I have been invited to provide a review for Nature Neurology in Clinical Practice.

#### **Clinical Aspects of Human Muscle Diseases**

- I am actively involved in developing better ways to measure disease activity, disease damage and response to treatment in patients with inflammatory muscle disease. I published new scales to analyze these parameters with colleagues from UCL and NIH -Bethesda in the Journal Rheumatology 2004. I am adapting these scales to use in treatment of certain dystrophies with the intention of using new agents such as myostatin antibodies [through collaboration with Wyeth]. I am on the steering committee of a current MRC funded trial of treatment in myositis.

## 12. Publications

### Five Key Papers

Andreu AL, **Hanna MG**, Reichman H, Bruno C, Penn AS, Tanji K, Palloti F, Iwata S, Shanske S, Bonilla E, Morgan-Hughes JA, DiMauro S (1999) Aches, pains and cramps: Exercise intolerance due to mutations in the cytochrome b gene of mitochondrial DNA.

*New England Journal of Medicine* 341: 1037-1078

Cited 96 times [Google scholar] Impact Factor 34.833

This work published in the New England Journal of Medicine was the first demonstration that somatic mutations in the protein encoding gene cytochrome b in human mitochondrial DNA could associate with a commonly encountered clinical phenotype of exercise intolerance and myalgia. This was a collaborative research project with colleagues in USA and Germany. I undertook total mtDNA sequence analysis in a group of patients and identified cytochrome b mutations in mtDNA which were only detectable in muscle [not in blood]. Prior to these findings point mutations in human mtDNA which were only confined to single somatic tissue had not been fully recognized. This suggested that the mutational event causing this form of human mitochondrial disease must have occurred in a cell line already destined to differentiate into muscle. Such late mutational events [ie not germline] had not been recognized previously for point mutations. We undertook detailed biochemical experiments to confirm a specific defect in complex III of the respiratory chain. This work served to initiate the area of somatic mtDNA point mutations in human disease. Subsequently my group and others have identified further somatic mutations in other mtDNA encoded genes in patients with a similar phenotypes confirming this is a new category of mtDNA mitochondrial disease [see ref 54 and 70 ]. From a clinical viewpoint this work emphasized the need to not rely on analysis of mtDNA point mutations in blood when assessing such patients. This is in contrast to germline mtDNA point mutations which are always detectable in blood. There was an accompanying Editorial Review in the New England Journal of Medicine by Professor RC Griggs (Head of Department of Neurology, University of Rochester New York and Professor George Karpati, (Head of the Montreal Institute of Neuromuscular disease).

In addition this work generated subsequent correspondence in the New England Journal of Medicine.

N Engl J Med. 1999 Sep 30;341(14):1077-8.

N Engl J Med. 2000 Feb 10;342(6):438-9; author reply 439-40.

**Hanna MG**, Nelson IP, Rahmann S, Schapira AHV, Morgan-Hughes JA Wood NW (1998) Cytochrome c Oxidase deficiency associated with the first stop codon mutation in human mitochondrial DNA *American Journal of Human Genetics* 63:29-36  
Cited 40 times [Google scholar] Impact Factor 11.602

This paper reports some of our findings resulting from a larger body of work studying mitochondrial DNA in human disease. At the time of this report although a number of pathogenic mutations in human mtDNA had been identified it was notable that mutations in protein coding genes that caused premature truncation of protein synthesis had never been reported despite being common in lower organisms. In this study I analyzed the entire human mitochondrial genome by direct DNA sequence analysis in a patient with a severe reduction in mitochondrial complex IV activity. I identified the first stop codon mutation described in human mitochondrial disease. The mutation occurred in subunit III of the cytochrome oxidase protein and resulted in loss of a large part of the C terminal region of the protein which is key for the catalytic activity of cytochrome c oxidase. Subsequently we and others identified additional similar mutations [see reference 70] Soon after this discovery I was involved in the identification of the first initiation codon mutation discovered in human mitochondrial DNA also published in American Journal of Human Genetics (see ref 19)

Pulkes T, Eunson L, Patterson V, Wood NW, Nelson IP, Morgan-Hughes JA, **Hanna MG** (1999) The mitochondrial DNA G13513A transition in ND5 is associated with a LHON/MELAS overlap syndrome and may be a frequent cause of MELAS. *Annals of Neurology* 46;916-919.  
Cited 36 times [Google scholar] Impact Factor 8.71

At the end of 1998 only one common mutation in human mtDNA had been described in association with the MELAS stroke phenotype [A3243G] in a tRNA gene. My group identified patients with MELAS who did not harbour the A3243G mutation. We showed that a mutation in the protein encoding ND5 (G13513A) gene was causative and we suggested that this may be a common cause of the MELAS phenotype and that it could cause a MELAS/LHON overlap syndrome. Several subsequent studies, including further work from my group also published in Annals of Neurology 2003 (see reference 54), and others have subsequently demonstrated that this mutation is indeed an important cause of the MELAS phenotype and also of Leigh's disease. Other workers have also subsequently found an association with LHON.

Zuberi S, Eunson L, Spauschus A, DeSilva R, Wood NW, McWilliam RC, Stephenson JPB, Tolmie J, Kullmann DM and **Hanna MG** (1999) A new potassium channel mutation associates with episodic ataxia type I and epilepsy *Brain* 122:817-825  
Cited 65 times (Google Scholar) Impact factor 9.16

Jouvencaeu A, Eunson LH, Spauschus A, Ramesh V, Kullmann DM and **Hanna MG** (2001) Human absence epilepsy associates with dysfunction of the brain P/Q type calcium channel CACNA1A *Lancet* 34:45-51  
Cited 70 times (Google Scholar) Impact Factor 18.316

I established the UK national database of patients with suspected brain and muscle channelopathies at the end of 1996. This subsequently evolved into the current UK national clinical and diagnostic service funded directly by the UK department of Health [following my application in open competition]. The two papers cited above published in *Brain* and in the *Lancet* stemmed initially from clinical observations I made in patients with episodic ataxia. It was evident that some of these patients had epilepsy in addition to the ataxia phenotype. However, it was not clear if this was a chance association or if the epilepsy was generated by the dysfunctional brain ion channels I suspected these patients must have. In collaboration with Professor Dimitri Kullmann and Professor Nicholas Wood we studied such families in detail from a clinical, genetic and molecular expression view point. I undertook extensive DNA sequence analysis of candidate channel genes. New mutations in the neuronal potassium channel KCNA1 gene and the brain calcium channel CACNA1A gene were discovered. We went on to prove molecular mechanisms of pathogenicity of identified mutations through molecular expression experiments. In the paper published in *Brain* 1999 we provided strong evidence that in the patients with neuronal potassium channel mutations there is an increased risk of epilepsy as a direct result of the potassium channel dysfunction. This has subsequently been confirmed by others and is now generally accepted. In addition, we went on to define new phenotypes of human disease associated with the new KCNA1 mutations we identified. We showed that the range of phenotypes was from mild isolated neuromyotonia through to severe drug resistant episodic ataxia with epilepsy [See ref 32 published in *Annals of Neurology*]. The *Lancet* publication provides the first evidence for a link between human brain calcium channel dysfunction and epilepsy. My first Phd student Ms Louise Eunson obtained the Queen Square prize 2000 [graduated UCL PhD 2001] for this work published in *Brain* and the *Lancet*. We have recently described a significant body of evidence strengthening the link between calcium channel dysfunction and human absence epilepsy. Part of this evidence is now published in *Brain* 2004 see ref 64. Further evidence in the form of new CACNA1A mutations and an extensive review of all EA2 cases published is in preparation. Recently, Professor Geoffrey Noebels who first identified spontaneous CACNA1A mutant mice with absence epilepsy in 1979 [*Science* 204;1334-1336] has published a detailed commentary on our *Brain* 2004 paper supporting the role of CACNA1A in human epilepsy see Noebels JL *Epilepsy Current* [Literature in Basic Science] 2005: 5; 95-7

## A. Books/Thesis

### A1

**Hanna MG**, co-authored with Holdright D, Beck E, Souhami R-Tutorials in differential diagnosis 4<sup>th</sup> Edition Publishers Harcourt London 2003 pp245. [6000 copies sold worldwide upto November 2005]

**Hanna MG** MD thesis University of Manchester 1996, “Studies on the molecular genetics and molecular pathogenesis of the mitochondrial encephalomyopathies”. Supervisor *the late* Professor Anita Harding

### A3 Chapters

#### 1999

- 1 Rudel R, **Hanna MG**, Lehmann-Horn F (1999) Muscle ion channelopathies: Malignant Hyperthermia, Periodic Paralysis, Paramyotonia congenita and Myotonia. In muscle Diseases; Butterworth Heinemann Ed Schapira AHV and Griggs B. *pp 134-154*

#### 2000

- 2 **Hanna MG**. 50 (2000) cases from the National Hospital. Ed; CD Marsden and A Wills. Martin Dunitz, London (*two cases pp23-26&pp56-59*)

#### 2001

- 3 Davies NP **Hanna MG** (2001) Genetic neurological channelopathies. In; New treatments in Neurology Ed Scolding N Butterworth Heinemann London. *pp234-247*
- 4 Kinton L, **Hanna MG**, Wood NW (2001) Genetics of Epilepsy and Paroxysmal Movement Disorders. Epilepsy and Movement Disorders. Ed Guerinni, Aicardi, Andermann and Hallet. Cambridge University Press. *pp67-79*

#### 2003

- 5 Davies NP **Hanna MG** (2003). Myopathies and Neurorehabilitation. In Textbook of neurorehabilitation Editor; Greenwood R *pp256-274*
- 6 Pulkes T **Hanna MG**. Mitochondrial diseases (2003). In; Mitochondrial DNA and Human disease Ed Holt IJ Butterworth Heinemann *pp57-75*
- 7 Liolitsa D **Hanna MG**. Cell Models in mitochondrial disease. (2003) In Mitochondrial function and dysfunction in human disease. Ed Schapira AHV, DeLauro S; Butterworth Heinemann, London *pp89-110*
- 8 **Hanna MG** Peripheral neuropathy and mitochondrial diseases (2003) In Peripheral Neuropathy Eds Dyck D and Thomas PK; Saunders *1937-1949*

#### 2004

- 9 **Hanna MG**. Disorders of Voluntary muscle. Oxford Textbook of Medicine 2004 (4<sup>th</sup> Ed). *pp1344-1346*

- In press**
- 10 **Hanna MG** Neurogenetics in The Oxford Handbook of Molecular medicine Editor D Lo, Oxford University Press *in press*
  - 11 **Hanna MG** Fialho D;-Muscle channelopathies-in Paediatric channelopathies; Butterworths, Editors Zuberi S *in press*
  - 12 Fialho D **Hanna MG**-Periodic Paralysis-in Handbook of Neurology, Editors Hilton Jones DA, Laing D. Heinemann *in press*
  - 13 Graves T **Hanna MG**- Channelopathies causing movement disorders in Paediatric Channelopathies *in press*
  - 14 **Hanna MG** Kullmann DM- Neurological channelopathies- a clinicians guide in Neurogenetics. Cambridge University Press-Ed NW Wood *in press*
  - 15 **Hanna MG**-Muscle diseases in Queen Square Text book of Neurology-Editors Shorvon, Howard, Rossor, Clarke-*in preparation*.

## **B. Peer reviewed original publications**

### **1989**

- 1 Selam J, Kayshap M, **Hanna MG**, Albertii KGMM, Lozano J, Turner D, Jeandidier N, Chan E, Charles MA (1989) Comparison of intraperitoneal and subcutaneous insulin administration on lipids, apolipoproteins, fuel metabolites and hormones in type I diabetes mellitus. *Metabolism* 38: 234-244

### **1995**

- 2 **Hanna MG**, Nelson I, Sweeney MG, Cooper M, Watkins PJ Morgan-Hughes JA Harding AE (1995) Congenital myopathy, adult onset myopathy and diabetes mellitus: different phenotypic associations of a new heteroplasmic mitochondrial tRNA glutamic acid mutation. *American Journal of Human Genetics* 56: 1025-1030
- 3 **Hanna MG**, Nelson I, Morgan-Hughes JA, Harding AE (1995) Impaired mitochondrial translation in myoblasts harbouring the mitochondrial DNA tRNA lysine 8344 A->G (MERRF) mutation. *Journal of the Neurological Sciences* 130: 154-160
- 4 **Hanna MG** (1995) Vitamin E deficiency. *British Medical Journal* 310: 1673
- 5 Nelson I, **Hanna MG**, Alsanjari N, Scaravilli F, Morgan-Hughes JA, Harding A (1995) A new mitochondrial DNA mutation associated with progressive dementia and chorea: a clinical, pathological and molecular genetic study. *Annals of Neurology* 37: 400-403
- 6 Hammans SR, Sweeney MG, **Hanna MG**, Brockington M, Morgan-Hughes JA,

Harding AE (1995) The mitochondrial DNA transfer RNA<sup>Leu(UUR)</sup> A->G<sup>(3243)</sup> mutation: A clinical and genetic study. *Brain* 118: 721-734

**1996**

7 **Hanna MG**, Papanastassiou V, Greenhall RCD (1996) Parafalcine Meningioma. *British Medical Journal* 313: 502

**1997**

8 **Hanna MG**, Vaughan J, Silburn P, Renowden S, Poulton J, Squire M, Davis P, Greenhall RCD (1997). Two unusual presentations of the A3243G mitochondrial DNA mutation in adult neurological practice. *Journal of Neurology, Neurosurgery and Psychiatry* 62:544-546

9 **Hanna MG**, Mills KR, Newsom-Davis J (1997). Primary orthostatic tremor associated with prominent muscle hypertrophy *Neurology* 49:872-874

10 Nelson IP, **Hanna MG**, Wood NW, Harding AE (1997) Mitochondrial DNA depletion of untransformed fibroblasts with ddC: A model for nuclear-mitochondrial interactions. *Somatic Cell Genetics* 23:287-290

11 **Hanna MG**, Bhatia K (1997) Movement disorders and mitochondrial dysfunction. *Current Opinion in Neurology* 10:351-356

**1998**

12 **Hanna MG**, Sweeney MG, Davis MB, Noursadeghi M, Ellis CJ, Wood NW, Marsden CD (1998). Generalized chorea in two patients harbouring the Friedreich's ataxia gene expansion. *Movement Disorders* 13:2;339-340

13 Leff A, McNabb A, **Hanna MG**, Clarke C, Larner AJ (1998) Complex partial status epilepticus in a case of MELAS *Epilepsia* 39:4;438-441

14 **Hanna MG**, Nelson IP, Rahmann S, Schapira AHV, Morgan-Hughes JA Wood NW (1998) Cytochrome c Oxidase deficiency associated with the first stop codon mutation in human mitochondrial DNA *American Journal of Human Genetics* 63:29-36

15 **Hanna MG**, Nelson IP, Morgan-Hughes, and Wood NW (1998) MELAS: A new disease associated mitochondrial DNA mutation and evidence for further genetic heterogeneity *Journal of Neurology Neurosurgery and Psychiatry* 65:512-517

16 **Hanna MG**, Stewart J, Wood NW Murray NMF (1998) Treatment of hyperkalaemic periodic paralysis associated with the 704 mutation with salbutamol *Journal of Neurology Neurosurgery and Psychiatry* 64:77-79

17 **Hanna MG**, Wood NW, Kullmann DM (1998). Ion channels and neurological disease: DNA diagnosis is now possible and ion channels may be important in common paroxysmal disorders. *Editorial review, Journal of Neurology, Neurosurgery and Psychiatry* 65:427-431

**1999**

18 Marques W, **Hanna MG**, Marques SR, Sweeney MG, Thomas PK Wood NW (1999). Phenotypic variation of a new P0 mutation in genetically identical twins.

- 19 Clarke KM, Taylor RW, Johnson MA, Chinnery PF, PJ Lamont, NW Wood, Nelson IP, **Hanna MG**, Lightowlers RN, Turnbull DM (1999) An mtDNA mutation in the initiation codon of the cytochrome c oxidase subunit II gene results in lower levels of the protein and a mitochondrial encephalomyopathy. *American Journal of Human Genetics* 64:1330-1339
  - 20 Elliot P, **Hanna MG**, Chinnery PF, Turnbull D, Wood NW, McKenna W (1999). Diagnostic utility of metabolic testing in a patient with cardiovascular disease. *Heart* 81: 441-443
  - 21 Nelson IP, **Hanna MG** (1999) Genetics and molecular pathogenesis of mitochondrial respiratory chain diseases. *Cellular and Molecular Life Sciences* 67:45-60
  - 22 **Hanna MG**, Morgan-Hughes JA (1999) Mitochondrial encephalomyopathies. The enigma of genotype versus phenotype. *Biochimica Biophysica Acta* 1410:125-145
  - 23 Zuberi S, Eunson L, Spauschus A, DeSilva R, Wood NW, McWilliam RC, Stephenson JPB, Tolmie J, Kullmann DM and **Hanna MG** (1999) A new potassium channel mutation associates with episodic ataxia type I. and epilepsy *Brain* 122:817-825
  - 24 Spauschus A, Eunson L, **Hanna MG**, Kullmann DM (1999) Functional characterization of a novel mutation in KCNA1 in episodic ataxia type I associated with epilepsy. *Annals of the New York Academy of Science* 868:442-6
  - 25 Rahman S, Taanman JW, Cooper JM, Nelson IP, Capaldi RA, Lake BD, **Hanna MG**, Leonard JV, Schapira AHV (1999) A missense mutation of cytochrome oxidase subunit II causes defective assembly and myopathy. *American Journal of Human Genetics* 65:1030-1039
  - 26 Andreu AL, **Hanna MG**, Reichman H, Bruno C, Penn AS, Tanji K, Palloti F, Iwata S, Shanske S, Bonilla E, Morgan-Hughes JA, DiMauro S (1999) Aches, pains and cramps: Exercise intolerance due to mutations in the cytochrome b gene of mitochondrial DNA. *New England Journal of Medicine* 341:1037-1044
  - 27 Vergani L, Rossi R, Brierly CH, **Hanna MG**, Holt IJ (1999) Introduction of heteroplasmic mitochondrial DNA (mtDNA) from a patient with NARP into two human rho degrees cell lines is associated either with selection and maintenance of NARP mutant mt DNA or failure to maintain mtDNA. *Human Molecular Genetics* 8:1752-1755
  - 28 Pulkes T, Eunson L, Patterson V, Wood NW, Nelson IP, Morgan-Hughes JA, **Hanna MG** (1999) The mitochondrial DNA G13513A transition in ND5 is associated with a LHON/MELAS overlap syndrome and may be a frequent cause of MELAS. *Annals of Neurology* 46:916-919.
- 2000**
- 29 Munchau A, Valente EM, Shahidhi GA, Eunson LH, **Hanna MG**, Bhatia KP (2000) A new family with paroxysmal exercise induced dystonia and migraine: a clinical and genetic study *Journal of Neurology Neurosurgery Psychiatry* 68:609-14

- 30 Rahman S, Lake BD, J-W Taanman, Cooper JM, **Hanna MG**, Leonard JV, Schapira AHV (2000) Patterns of subunit loss in cytochrome oxidase deficiency. *Brain* 123: 591-600
- 31 Cottrell DA, Ince PG, Chinnery PF, **Hanna MG**, Turnbull DM (2000) Neuropathological and histochemical changes in a multiple mitochondrial DNA deletion disorder. *Journal of Neuropathology and Experimental Neurology* 59:621-7
- 32 Eunson LH, Spauschus A, Rea R, Zuberi SM, Youroukos S, Panayiotopoulos CP, Wood NW, Liguori R, Avoni P, **Hanna MG**, Kullmann DM. Clinical, Genetic and Oocyte (2000) Expression Studies on Four Families with Point Mutations in the Human Voltage-Gated Potassium Channel Gene (KCNA1) Reveal New Phenotypic Variation. *Annals of Neurology* 48: 647-656.
- 33 Davis NP, Eunson LH, Gregory RP, Mills KR, Morrison PJ, **Hanna MG** (2000) Clinical , electrophysiological and molecular genetic studies in a new family with paramyotonia congenita. *Journal of Neurology, Neurosurgery and Psychiatry* 68:504-7
- 34 Pulkes T, Sweeney MG, **Hanna MG** (2000) Increased risk of stroke in patients with the A12308G polymorphism in mitochondria *Lancet* 356;2068-9
- 35 Davis NP and **Hanna MG** (2000) Neurological channelopathies: diagnosis and therapy in the new millennium. *Annals of Medicine* 31:406-20
- 36 Pulkes T, Siddiqui A, Morgan-Hughes JA **Hanna MG** (2000) A novel mutation in the mitochondrial tRNA[tyr] gene associated with exercise intolerance. *Neurology* 55:1210-2
- 2001**
- 37 Jouvencaeu A, Eunson LH, Spauschus A, Ramesh V, Kullmann DM and **Hanna MG** (2001) Human absence epilepsy associates with dysfunction of the brain P/Q type calcium channel CACNA1A *Lancet* 34:45-51
- 38 Davies NP, Eunson LH, Samuels M, **Hanna MG** (2001) A molecular genetic study of hypokalaemic periodic paralysis in the UK. *Neurology* 2001;57:1323-5.
- 39 Davis NP **Hanna MG**. (2001) Therapy in neurological channelopathies. *Neurotherapeutics* 21;32-38
- 40 Davies NP **Hanna MG**. (2001) Skeletal muscle channelopathies: basic science, clinical genetics and treatment *Current opinion in Neurology* 34;42-49
- 41 Pulkes T, **Hanna MG** (2001) Human mitochondrial disease. *Advanced Drug Delivery Reviews* 49:27-43
- 42 Zuberi SM **Hanna MG** (2001) Ion channels and Neurology. *Archives of Diseases in Childhood* 84:277-280
- 2002**
- 43 Rea R, Spauschus A, Eunson LH, **Hanna MG**, Kullmann DM (2001). Cellular electrophysiology of mutant potassium [kv1.1] channels *Journal of Physiology* 538;5-23

- 44 Chinnery PF, **Hanna MG**, Walls T, Bates D (2002). Normokalaemia periodic paralysis; does it exist? *Annals of Neurology* 52;251-2
- 45 McCabe D, Wood NW, **Hanna MG** Ryan F, Connolly S, Redmond J Barton DE, Murphy R (2002). Phenotypic variability in patients harboring the FA genetic defect. *Archives of Neurology* 59;296-300
- 46 Hanna MG and **Wood NW**(2002). Running a Neurogenetic Clinic. *Journal of Neurology, Neurosurgery and Psychiatry.* 73;ii2-5
- 47 Reilly MM and **Hanna MG**. Genetic Neuromuscular Disease (2002). *Journal of Neurology, Neurosurgery and Psychiatry.* 73;ii12-22
- 48 **Hanna MG** and Kullmann DM (2002). Neurological channelopathies. *Lancet Neurology* 43;43-48
- 49 Jacques TS, Holton J, Watts AJ, Wills AJ, Smith SE, **Hanna MG** (2002). Tubular aggregate myopathy with abnormal pupils and skeletal deformities. *Journal of Neurology, Neurosurgery and Psychiatry.* 73;324-6
- 50 Garrard P, Blake J, Stinton V, **Hanna MG**, Reilly MM, Landon DN, Honan WP (2002). Distal myopathy with tubular aggregates; a new phenotype associated with multiple deletions in mitochondrial DNA? *Journal of Neurology, Neurosurgery and Psychiatry.* 73;207-8
- 51 Littleton ET, Man WD, Holton JL, **Hanna MG**, Polkey MI, Taylor GP (2002). Human T cell leukaemia virus type 1 associated with neuromuscular disease causing respiratory failure. *Journal of Neurology, Neurosurgery and Psychiatry.* 72;650-2
- 2003**
- 52 Rakowitz V, **Hanna MG** (2003) Neurological Channelopathies-review. *Advances in Neurology and Clinical Rehabilitation.* 21:45-54
- 53 Miller R, Unwin R, Schapira A, **Hanna MG**, Weller R (2003) Polyphenotypic expression of mitochondrial toxicity caused by nucleoside reverse transcriptase inhibitors. *Journal Antiviral Therapy* 8;253-7
- 54 Liolitsa D, Rahman S, Carr L, Benton S, **Hanna MG**. (2003) Is the mtDNA ND5 gene a hotspot for MELAS mutations? *Annals of Neurology* 53;128-32
- 55 Elliot P, **Hanna MG**, Sweeney MG Chalmers RM, Wood NW, McKenna W(2003) Cardiac abnormalities in patients with Leber's hereditary optic neuropathy. *Heart.* 2003 89(7):791-2.
- 56 Brown K, White R **Hanna MG** (2003) HSV7 associates with myelitis in a bone marrow allograft patient. *Journal of bone marrow transplantation* *Transplantation.* 8; 253-7
- 57 Isenberg DA, **Hanna MG** and international consortium on myositis (2003). Developing clinical measures of disease activity and tissue damage in myositis. *Journal of Rheumatology.*43: 49-54

- 58 Pulkes T, Liolitsa D, Nelson I, **Hanna MG** (2003) Classical mitochondrial phenotypes without mtDNA mutations. *Neurology* 61;1144-7
- 59 Hargreaves IP, Heales SJ, Briddon A, Lee PJ, **Hanna MG**, Land JM (2003) Primary pyruvate dehydrogenase E3 binding protein deficiency with mild hyperlactatemia and hyperalaninaemia. *Journal of Inherited and Metabolic Diseases* 26(5) 505-6
- 60 Davies NP, **Hanna MG** (2003) The skeletal muscle channelopathies. *Current opinion in neurology* 16;559-68
- 61 Mundy HR, Jones SJ, Hobart JC, **Hanna MG**, Lee PJ (2003). A randomized controlled study of modified cobra toxin in adrenomyeloneuropathy. *Neurology* 26;61;528-30
- 62 Brancati F, Valente EM, Davies NP, Sarkozy A, Sweeney MG, Lo Monaco M, Pizzuti A, **Hanna MG**, Dallapiccola B. (2003) Severe infantile hyperkalaemic periodic paralysis and paramyotonia; broadening the clinical spectrum associated with the T704M mutation in SCN4A. *Journal of Neurology, Neurosurgery and Psychiatry* 74;1339-41
- 2004**
- 63 McKenzie M, Liolitsa D, **Hanna MG** (2004)-Mitochondrial disease mutations and mechanisms. *Neurochemical Research* 589-600
- 64 Roedling S, Pearl D, Manji H, **Hanna MG**, Holton JL, Miller RF (2004) Unusual muscle disease in HIV infected patients *Sexually Transmitted Infection* 80 315-7
- 65 Kinali M, Jungblath H, Eunson LH, Sewry CA, Munzur AY, Mercuri E, **Hanna MG** Muntoni F (2004) Expanding the phenotype of potassium channelopathy : severe neuromyotonia DNA skeletal deformities without prominent episodic ataxia. *Neuromuscular Disorders* 14 689-93
- 66 Imbrici P, Jaffe S, Eunson LH, Davies NP, Herd C, Robinson R, Kullmann DM, **Hanna MG** (2004) Dysfunction of the brain calcium channel CaV2.1 in absence epilepsy and episodic ataxia *Brain* 127 2682-92
- 67 Nirmalanathan N, Holton J and **Hanna MG** (2004) Is it really myositis? A consideration of the differential diagnosis. *Current opinion in Rheumatology* 16 684-91
- 2005**
- 68 Graves TD, **Hanna MG** (2005)-The neurological channelopathies- *Postgraduate Medical Journal*; 81(951):20-32.
- 69 Murphy RT, Mogensen J, McGarry K, Bahl A, Evans A, Osman E, Syrris P, Gorman G, Farrell M, Holton JL, **Hanna MG**, Hughes S, Elliott PM, Macrae CA, McKenna WJ (2005). Adenosine monophosphate-activated protein kinase disease mimicks hypertrophic cardiomyopathy and Wolff-Parkinson-White syndrome: natural history *Journal of the American collage of cardiology* 15 45 922-30
- 70 Pulkes T, Liolitsa D, Wills A, Hargreaves I, Heales S, **Hanna MG** (2005)

- Nonsense mutations in mitochondrial DNA associated with myalgia and exercise intolerance *Neurology* 22 64 1091-2
- 71 Pulkes T, Liolitsa D, Eunson LH, Rose M, Nelson IP, Rahman S, Landon DN, Debono AG Morgan-Hughes JA, **Hanna MG**-New phenotypic diversity associated with the mitochondrial tRNA serine gene mutation (2005) *Neuromuscular Disorders* 15 364-371
- 72 **Hanna MG**, Graves TD, Jaffe S, Imbrici P, Kullmann DM (2005) Dysfunction of the brain calcium channel in absence epilepsy and episodic ataxia *Brain* 128 letter
- 73 Gioltzoglou T, Cordivari C, Lee PJ, **Hanna MG**, Lees AJ (2005). Problems with botulinum toxin in mitochondrial cytopathy; case report and review of the literature *Journal of Neurology, Neurosurgery and Psychiatry* 76:1594-6
- 74 Davies NP, Imbrici P, Fiahlo D, Herd C, Ealing J, Hilton-Jones, D, Rose M, Jurkat-Rott K, Lehmann-Horn F, Chinnery PF, Kullmann DM, **Hanna MG** (2005) Andersen Tawil syndrome- new potassium channel mutations and possible phenotypic variation *Neurology*;65;1083-9
- 75 Imbrici P, Eunson LH, Graves TD, Bhatia KP, Kullmann DM, **Hanna MG** (2005). Late-onset episodic ataxia type 2 due to an in-frame insertion in CACNA1A *Neurology* 65:944-6
- 76 Eunson LH, Graves TD, **Hanna MG** (2005) New calcium channel mutations predict aberrant RNA splicing in episodic ataxia *Neurology* 65:308-310
- 77 Venance SL, Canon SC, Fialho D, Fontaine B, **Hanna MG**, Ptacek L, Tristani-Firouzi M, Tawil R, Griggs RC (2005). The primary periodic paralyses: diagnosis, pathogenesis and treatment. *Brain* oct 24 epub ahead of print
- 78 Abou-Sleiman PM, **Hanna MG**, Wood NW(2005) Genetic association studies in complex neurological disease *JNNP* review in press
- 79 **Hanna MG** (2006) Human genetic neurological channelopathies *Nature Neurology in Clinical Practice* invited review in press
- 80 McKenzie M, Liolitsa D, Hargreaves I, Sisodiya S, Wood NW, **Hanna MG**, Duchon M. Mutant mitochondria consume ATP in young onset stroke *under review Lancet*

### C. Other publications selected abstracts, posters and oral presentations 1994-2005

I have published 79 abstracts from posters and platform presentations at National and International learned societies and meetings.