NE Thames Regional Genetics Service Annual Report

2011-2012

Great Ormond Street Hospital for Children

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EXECUTIVE SUMMARY

Angela Barnicoat stepped down from her role as Lead Clinician in October 2011 and was succeeded by Jane Hurst. We would to thank Angela for her leadership over the years and her key role in establishing Trust support for in-patient ward work, consolidation of the peripheral genetics clinical service and transition to paperless, electronic patient notes.

During the year, the service has continued to exhibit growth in all areas – clinical appointments were up by 11%, cytogenetics service work load units increased by 30% (mainly attributable to the ongoing uptake of chromosomal microarray testing) and molecular genetics service reports increased by 8%. New clinical services include a renal genetics clinic and a multi-disciplinary neurogenetics clinic both based at GOSH. Clinical Research Network funding for three genetic counsellors has enabled us to expand and improve patient recruitment to numerous clinical studies including Deciphering Developmental Disorders. The translational research and development activities of the service were further enhanced by new grant funding and capital equipment and infrastructure investment supporting the non-invasive prenatal diagnosis and next generation DNA sequencing programmes.

Dr Jane Hurst
Lead Clinician

Dr Nick Lench
Director

1. INTRODUCTION

The NE Thames Regional Genetics Service at Great Ormond Street Hospital comprises the Clinical Genetics Department and the Laboratories for Cytogenetics and Molecular Genetics and is commissioned to provide a service to a population of approximately 4.5 million people including the whole of the North East of London and extends as far as Hertfordshire to the North and Essex to the South and East. The Unit also receives nationally commissioned funding for a number of specialised services including Bardet-Biedl syndrome, craniosynostoses, lysosomal storage disorders and severe combined immunodeficiencies. The laboratories provide an extensive range of diagnostic testing services and have full clinical pathology accreditation (CPA) status. The service is a member of the South East of England Genetics Network (SEEGEN) and the United Kingdom Genetics Testing Network (UKGTN).

Research and development is a key objective of the Unit, a number of staff having joint academic appointments with University College London. The service has a strong commitment to education and training and public and patient engagement and participates in clinician, scientist and technologist training programmes. A number of staff are also actively involved at a regional and national level in policy development, training and examination.

2. CLINICAL GENETICS

The Clinical Genetics service is headed by Dr Jane Hurst (from October 2011). Ten consultant staff (7.2FTE) provide services across a range of general, cancer and specialist clinics in hospitals throughout north east London and Essex. The Clinical Nurse Specialists and Genetic Counsellors team has a total of 8 staff providing a total of 5.8 FTEs.

2.1 Staff List

Clinical Geneticists and Consultant Academic Staff	
Jane Hurst	Lead Clinician (from October 2011) Consultant and Honorary Senior Lecturer, ICH
Maria Bitner-Glindzicz	Consultant and Reader, ICH
Angela Barnicoat	Consultant, Lead Clinician (to September 2011)
Ajith Kumar	Consultant

Melissa Lees	Consultant
Alison Male	Consultant
Elisabeth Rosser	Consultant
Richard Scott	Consultant and Honorary Senior Lecturer, ICH
Lucy Side	Consultant, Senior Lecturer UCL, Lead Cancer Genetics Service
Louise Wilson	Consultant
Honorary Staff	
Phil Beales	Professor, Molecular Medicine, ICH
Lyn Chitty	Professor, Genetics and Fetal Medicine, ICH
Gudrun Moore	Professor, Clinical and Molecular Genetic, ICH

Clinical Nurse Specialists and Genetic Counsellors	
Cheryl Berlin	The Royal Free Hospital
Anita Bruce	South Essex
Bernadette Farren	Great Ormond St Hospital, North Middlesex Hospital, Newborn CF Screening
Kelly Loggenberg	Bart's and The London Hospital
Kate Simon	South Essex
Sally Taffinder	Great Ormond St Hospital and UCLH
Emma Williams	Great Ormond St Hospital
Administrative and Clerical Staff	
Chris Skilbeck	Project Manager
Nasrin Khalique	Office Manager
Laura Boddy	Medical Secretary
Jacqueline Charles	Medical Secretary
Jill Corneille	Medical Secretary

Parveen Akhtar	Administrative Assistant
Paul Gough	Administrative Assistant
Elizabeth Sturges	Administrative Assistant
Research/CLRN Staff	
Kate Brunstrom	CLRN Genetic Counsellor (General)
Cecelia Compton	CLRN Genetic Counsellor (Craniofacial, GOLD, IMPACT)
Elizabeth Tidey	CLRN Genetic Counsellor (Deciphering Developmental Disorders)

2.2 General Clinics

General Clinics	
Basildon Hospital	
Broomfield Hospital, Chelmsford	
Chase Farm Hospital	
Colchester Hospital	
Harlow Hospital	
Homerton Hospital	
Great Ormond Street Hospital	
Queens Hospital, Romford	
St Ann's Hospital	
West Ham Lane Child Development Centre	
Wood Street Child Development Centre	

2.3 Cancer Clinics

Specialist Cancer Clinics	
Neuroendocrine	Bart's and The London

Retinoblastoma	Supra-regional Service, Bart's and The London
Von-Hippel Lindau	The Royal Free Hospital
Breast, ovarian and colon cancers	Orsett Hospital
Breast, ovarian and colon cancers	St Margaret's Hospital, Epping
Paediatric cancers	Great Ormond St Hospital

2.4 Specialist Clinics

Specialist Clinics	
Cardiac Genetics	The London Chest Hospital
Regional Cleft Lip and Palate	Great Ormond St Hospital and The Broomfield Hospital
Craniofacial	Great Ormond St Hospital
Deafness	The Nuffield Hospital
Dual Sensory Impairment	National Hospital for Neurology and Neurosurgery
Di George Syndrome	Great Ormond St Hospital
Disorders of Sexual Development	Great Ormond St Hospital
Dysmorphology	Great Ormond St Hospital
Endocrine (adult)	St Bartholomew's Hospital
Fetal Medicine	UCLH
Neurogenetics	National Hospital for Neurology and Neurosurgery
Renal Genetics	Great Ormond St Hospital

2.5 Activity

Non-Cancer Clinic Appointments 2011-2012		
Region	Baseline	Actual
Bedfordshire and Hertfordshire	177	172

Essex	1185	1228
North West London	129	193
North Central London	684	832
North East London	1154	1276
South East London	28	50
South West London	55	45
Kent and Medway	48	49
Surrey and Sussex	46	57
Total	3506	3902

Cancer Clinic Appointments 2011-2012		
Region	Baseline	Actual
Bedfordshire and Hertfordshire	62	45
Essex	612	634
North West London	31	29
North Central London	384	451
North East London	409	510
South East London	18	6
South West London	5	9
Kent and Medway	13	6
Surrey and Sussex	5	13
Total	1539	1703

General clinic appointments and cancer clinic appointments were both 11% above baseline level in 2011-2012. We continue to monitor and seek ways to improve Failure to Attend (FTA) rates. Services continue to be offered in areas with high social deprivation including some with high transient refugee populations. Communication with patients can be challenging - interpreters are often required and many families are relocated during the time between referral and appointment.

2.6 Universal Newborn Screening Service – Cystic Fibrosis

We are commissioned to organise the genetic follow-up service to the parents of children identified to be carriers of cystic fibrosis on behalf London, Kent, Essex, E and W Sussex, Surrey, Hertfordshire and Bedfordshire.

2.7 Patient and Public Involvement

2.7.1 Patient Survey

We participated in a patient survey of our service which gave one of the best overall satisfaction scores of any of the GOSH Trust specialities.

2.7.2 Patient Information Evening

A patient information evening was held in September 2011at the Broomfield Hospital, Chelmsford, for patients who are carriers of *BRCA* mutations: over 40 carriers, family members, and friends attended the evening. Breast and ovarian cancer charities provided information for the participants and Breakthrough Breast Cancer sent a representative to attend the evening to answer questions.

The information evening consisted of five presentations. The evening started with Jackie Harris from Breast Cancer Care speaking briefly about the services they provide. Lucy Side spoke about managing ovarian cancer risk, which prompted many questions. Sylvia Young's presentation focused more on the psychosocial side of being a carrier and sharing carrier status with children. Alison Shaw gave insight into the multidisciplinary approach for women who are seeking risk reducing procedure. The night ended in Lucy Side presentation on the IMPACT study which is a prostate cancer screening study available to the male carriers.

Overall, the feedback was good with everyone stating that they would be "very likely" or "likely" to attend a future event. Most of the presentations were ranked "excellent" or "good" with a few "average" rankings. Suggestion for future meetings included: patient led presentation, ovarian cancer treatment, more research updates and information on prostate screening for carriers. Many participants stated that meeting other carriers was one of one of the most valuable aspects of the evening.

2.8 Training and Teaching

The department undertakes a wide range of teaching activities, contributing to the medical undergraduate course at University College London and providing extensive postgraduate and health professional teaching within the department and at local NHS Trust sites. Teaching is offered to GP trainees and district hospitals in paediatric, obstetric and adult genetics. The department provides teaching for the Clinical Pediatrics MSc, UCL Institute of Child Health. Informal teaching was also carried out in schools under the Jeans for Genes initiative. We are particularly involved with the Molecular and Genetic Basis of Paediatrics module of the UCL MSc in Child Health. Dr L Wilson is co-organiser and lecturer with Hannah Mitchison (ICH). There are lectures from other Consultant members of staff.

The department also provided a significant amount of informal teaching to observers sitting in on clinics over the course of the year. Local consultants and registrars regularly attend peripheral clinics as well as

Fetal Medicine Unit trainees, GOSH and UCLH junior staff from other specialties and laboratory staff wanting to learn about the clinical service. The department also provides taster weeks for F1 and F2 trainees – a clinic visit is often a starting point for junior doctors and medical students who wish to consider clinical genetics as a career option.

Clinical Genetics Trainees	
Janna Kenny	
Helen Moody	
Shereen Tadros	
Visitors	
Clinical Fellows	3
Electives	3
Essential Training	9
MSc Student (Counsellor)	1
Observers	8
Taster Sessions	9
Work Experience	4

2.9 Professional Duties

Selected Responsibilities	
Jane Hurst	Member Clinical Reference Group, Clinical Genetics SEEGEN South East England Genetics Clinical Network Clinical Genetics Society Lead Clinicians Group UK Dysmorphology Club Co-organiser (with Dr R Scott) SWAN, syndrome without a name, Specialist Medical Advisor
Angela Barnicoat	Forum for Clinical Effectiveness, Royal College of

	Physicians - CGS Representative Clinical Governance Committee, CGS Fragile X Syndrome Society, Specialist Advisor Jewish Genetic Disorders UK, Scientific and Medical Advisor
Maria Bitner Glindzicz	SENSE, Medical Advisor Jeans for Genes Small Grants Panel Deafness Research UK, Medical Advisor RNID Research Grants Advisory Panel, Member Human Tissue Act Licence for Research, ICH Representative
Anita Bruce	AGNC Committee Member
Melissa Lees	Pre-implantation Genetic Diagnosis Clinical Group, Clinical Advisor
Alison Male	Smith-Magenis Foundation, Medical Advisor
Elisabeth Rosser	Secretary, CGS Retinoblastoma Society, Research Committee Member National Organisation for Fetal Alcohol Syndrome, Trustee
Lucy Side	BSHG Scientific Committee Member for Conference Steering Group Member Cancer Genetics Group BSHG Genetics representative North London Cancer Network Tumour Board Advisor Cancerkin Charity London Genetics Consortium Advisory Group for Familial Breast Cancer Management
Sally Taffinder	Antenatal Results and Choices, Trustee
Louise Wilson	Skeletal Dysplasia Group, CGS Representative

2.10 Research Studies

Clinical Research Network (CLRN) funding was received for 3 new members of staff to facilitate patient recruitment to a number of clinical studies:

- EMBRACE - Epidemiological study of familial breast cancer
- BOCS – Identification and molecular analyses of families with susceptibility to breast and/or ovarian cancer
- CORGI – The Genetic Study of Colorectal Cancer Families without known inherited predispositions
- IMPACT – Identification of Men with a genetic predisposition to ProstAte Cancer: Targeted Screening in *BRCA1/2* mutation carriers and controls
- COPE – Diagnostic and therapeutic insights into breast cancer from morphological and molecular profiling of breast tumours in patients with germline p53 mutations (Li Fraumeni Syndrome)
- GOLD - Investigation of the role of genomic deletions and duplications of a X chromosomes as a cause of X-linked learning disabilities
- The genetic basis of craniofacial malformations
- DDD – Deciphering Development Disorders

3 REGIONAL GENETICS SERVICE LABORATORY

Management	
Nick Lench PhD FRCPath	Director and Honorary Reader, ICH
Jon Northfield	Finance Manager
Mike Tinsley	IT and Data Analyst Specialist
Gillian Hendry	Secretary and Office Administrator
Alicia Hudson	Administrator
Mhairi Irvine	Administrator
Rebecca Kingston	Administrator
Tony Paul	Administrator
Bola Olayinka*	Administrator

Fatima Sonawar*	Administrator
*Leavers	
Research Staff	
Suzie Drury PhD	Post-doctoral Scientist, Translational Research
Angela Barrett PhD	Post-doctoral Scientist, RAPID Project
Tina Baker	Research Technician, RAPID Project
Tom McDonnell	Research Technician, RAPID Project
Anthony Gait	Research Technician, FH CPSS Project

3.1 Cytogenetics Service Staff List

Cytogenetics Staff 2011-12	
Jonathan Waters PhD FRCPath	Head of Service - Consultant Clinical Scientist
Ann Jackson FRCPath	Head of Section – Principal Clinical Scientist
Rodger Palmer	Head of Section – Principal Clinical Scientist
Tom Spencer	Head of Section – Principal Clinical Scientist
Lee Grimsley	Senior Clinical Scientist
Deborah Morrogh	Senior Clinical Scientist
Lucy Platts	Senior Clinical Scientist
Monika Augustynowicz	Clinical Scientist
Kamila Jagiello	Clinical Scientist
Denise Rooney PhD	Clinical Scientist
Paula Stubbs	Clinical Scientist
Rubin Wang PhD	Clinical Scientist
Qian Zheng	Clinical Scientist
Jennifer Carter	Pre-registration Scientist
Drew Ellershaw	Pre-registration Scientist

Joanne Gilmore*	Trainee Scientist
Tanja Fiegel*	Trainee Scientist
Evangelia Karampetsou	Trainee Scientist
Oliver Spasic-Boskovic*	Trainee Scientist
Celia Brown	Scientist Trainee (Modernising Scientific Careers)
Rebecca Franses	Scientist Trainee (Modernising Scientific Careers)
Ahinora Dimitrova	Senior Genetic Technologist
Claire Jones	Senior Genetic Technologist
Harvinder Bangar	Genetic Technologist
Olugbenga Bashorun	Genetic Technologist
Eleanor Helmore	Genetic Technologist
Anisa Jimalle	Genetic Technologist
Alvin Michael	Genetic Technologist
Nomfuneko Nosilela	Genetic Technologist
Karolina Pawliczak*	Genetic Technologist
Katarzyna Rzepa	Genetic Technologist
Remben Talaban	Genetic Technologist
David Conner	Assistant Genetic Technologist
John Lane	Laboratory Assistant
*Leavers	

3.2 Cytogenetics Service Activity

Genetics Consortium Activity 2011-2012	Work Load Units
Chromosomal microarray	6376
Bloods	2770
FISH	326

Solid tissues	613
Chorionic villus	580
Amniotic fluid	448
TOTAL	**11,114**

Workload activity for the Genetics Consortium showed a major increase during 2011-2012, with a 30% rise in total workload units against baseline. This increase in activity was a direct result of the introduction of chromosomal microarray analysis as a first line test for patients with multiple congenital anomalies, developmental delay and mental retardation for all Service Users. Sample turnaround times were within the defined national targets, with the exception of urgent/routine bloods (72%/94.9%) and tissues (92%).

Turnaround Times 2011-2012	Days to Report	National Target
Bloods	21.3	28.0
Urgent bloods	5.7	10.0
Solid tissues	19.3	28.0
Chorionic villus	10.2	14.0
Amniotic fluid	11.6	14.0

3.3 New Service Developments

3.3.1 Chromosomal Microarrays

2011-12 was the first full year for which microarray was offered as a first line test for all suitable postnatal referrals - a comprehensive service for all service users having been introduced in March 2011. The diagnostic yield at ~10%, for this wider referral group, continues to be significantly higher than for karyotyping. This major transformation in our diagnostics provision (from karyotyping to microarray) is a major driver in integrating our genetics laboratory workflow and importantly continues to result in a reduction patient testing pathway times. A significant majority of postnatal samples received for testing are now analysed by chromosomal microarray.

3.3.2 Recurrent Miscarriage - Karyotyping of parental samples

In October 2011 the laboratory ceased to routinely offer karyotyping for the above cohort in line with RCOG – 2011 Guidelines and after consultation with service commissioners and notification of users. Instead combined molecular cytogenetic testing was offered for all pregnancy loss samples using quantitative fluorescent PCR (QF-PCR) and multiplex-ligation dependent primer amplification

(MLPA) service was offered. The improvements in tissue success rates and reporting times following the introduction of this methodology last year have continued to be maintained.

3.4 Quality

The laboratory participated in all available Cytogenetics EQA schemes including a chromosomal microarray pilot scheme and a scheme for solid tissue molecular cytogenetic investigation. No performance issues were identified. The laboratory has maintained its UKGTN registered laboratory status.

3.5 Molecular Genetics Service Staff List

Molecular Genetics Staff 2011-12	
Lucy Jenkins FRCPath	Head of Service - Consultant Clinical Scientist
Sam Loughlin	Deputy Head of Service, Principal Clinical Scientist
Emma Ashton PhD	Head of Section - Principal Clinical Scientist
Ann-Marie Differ	Head of Section - Principal Clinical Scientist
Fiona McKay	Head of Section – Senior Clinical Scientist
Alison Taylor FRCPath	Head of Section - Principal Clinical Scientist
Clare Beesley PhD	Clinical Scientist
Shahnaz Bibi	Clinical Scientist
Sarah Fielding	Clinical Scientist
Cathy Meaney	Clinical Scientist
Kirsty Stewart	Clinical Scientist
Natalie Trump PhD	Clinical Scientist
Valerie Witt PhD	Clinical Scientist
Bethan Hoskins PhD	Pre-Registration Scientist
Kunjan Patel	Trainee Scientist
Leesa Morris*	Practitioner Trainee (Modernising Scientific Careers)
Lighta Godinho	Senior Genetic Technologist
Brendan Martin	Senior Genetic Technologist

Solmaz Oskooei	Senior Genetic Technologist
Neesa Bhudia	Genetic Technologist
Rebecca Lewis	Genetic Technologist
Tom Linton-Willoughby	Genetic Technologist
Bhaneeta Mistry	Genetic Technologist
Toulla Ryan	Genetic Technologist
Yara Shamsah	Genetic Technologist
Louisa Steel	Genetic Technologist
Lech Stepkowski	Genetic Technologist
Joseph Tsedeke	Genetic Technologist
*Leavers	

3.6 Molecular Genetics Service Activity

Samples 2011-12	Number
Samples received	15,096
Samples extracted	13, 137
Samples exported	3,043
Reports Issued 2011-12	**Number**
Deafness	1340
Fragile X	1176
Cardiac genetics	740
Cystic fibrosis	538
Metabolic/Renal disease	471
Immunodeficiencies	324
Surfactant disease	233

Bardet-Biedl syndrome	198
Craniosynostoses	189
Imprinting disorders	186
Cancer	149
Free fetal DNA analysis	124
Skeletal dysplasias	111
Other	275
***TOTAL**	6054
*Excluding Store Letters	2689

Commissioned activity increased during the year with a 2% and 84% rise above baseline for non-cancer genetic testing and cancer genetic testing respectively. Total laboratory activity saw a 21% increase in samples received compared with 2010-11 and 8% increase in reports generated. A significant proportion of the increase includes NCG service activity for Bardet-Biedl syndrome, craniosynostoses, immunodeficiencies and lysosomal storage diseases.

Report Category	Description	Mean Turnaround Time (Days)	Reports within Turnaround Time*
3 Day	Prenatal Diagnosis	2.6	80%
10 Day	Familial Mutation / Urgent Targeted Test	8.6	90%
20 Day	Non-Urgent Targeted Test	14.0	81%
40 Day	Full Gene Sequence	33.7	83%

* National guideline is to achieve 95% of reports within target turnaround time

3.7 New Service Developments

Five gene dossiers were submitted and approved by UKGTN enabling the laboratory to expand its UK wide services.

Gene	Disorder

ITK	EBV-associated autosomal lymphoproliferative syndrome
POU3F4	X-linked deafness
SPINK5	Netherton syndrome
FGFR3	Non-invasive prenatal diagnosis for achondroplasia
FGFR3	Non-invasive prenatal diagnosis for thanatophoric dysplasia

3.8 Quality

The Molecular Genetics Laboratory underwent a full CPA inspection in November 2011 and successfully maintained full accreditation status.

3.9 Continuing Professional Development (Genetics)

3.9.1 Modernising Scientific Careers

The laboratory participates jointly in the Department of Health pilot scheme for Modernising Scientific Careers. Led by the Chief Scientific Officer, this key work programme has been created to ensure flexibility, sustainability and modern career pathways for the healthcare science workforce and fit to address the needs of the future NHS. In a joint application with the NW Thames Regional Genetics Service, Northwick Park, two scientists were appointed to the Scientist Training Program (STP). One Practitioner Training Program (PTP) trainee was recruited to GOSH.

3.9.2 Teaching and Training

Genetics Laboratory Staff contributed to various formal teaching programmes e.g. MSc courses in Fetal Medicine and Clinical Biochemistry (UCL) and an intercalated BSc course in Genetics for Paediatricians (ICH, UCL). Staff also hosted laboratory visits from students on these courses as well as visits from obstetrics trainees and midwives with the NE Thames region as part of their laboratory practice training requirements.

RNID Summer Studentship/Action on Hearing Loss Award

Janice Lee, a University College London medical student was presented with an award for her successful summer research project into hearing loss, which was funded by Action on Hearing Loss. The charity invited budding young undergraduate scientists from across the UK to take part in the grant scheme, with the aim of introducing them to an exciting field of work and encouraging them to consider it for their future careers. As part of the project, Janice designed and validated a diagnostic assay for *POU3F4*, a gene that causes X-linked non-syndromic deafness. She was able to identify *POU3F4* mutations in a number of different patients and her work has formed the basis of a gene dossier submission to the UK Genetic Testing Network that will enable the NE Thames Regional Genetics Service at GOSH to offer a fully accredited POU3F4 gene testing service for patients and families.

MSc Medical Immunology - Outstanding Research Project Award

Claire Escaron, a King's College MSc Medical Immunology student, received the Award for Outstanding Research Project for her work in the Regional Genetics Laboratories on the development of a diagnostic test for haemophagocytic lymphohistiocytosis. Haemophagocytic lymphohistiocytosis (HLH) encompasses a heterogeneous group of disorders, which warrant urgent diagnosis. In HLH the unchecked immune response can quickly progress with characteristic lymphohistiocytic infiltration of tissues, organ failure and death. HLH occurs in sporadic and inherited forms. Mutations in the IL-2 inducible T cell kinase (ITK), which is associated with EBV precipitated HLH, and the familial HLH (FHL) 5, due to mutations in syntaxin binding protein 2 (*STXBP2*, *Munc 18-2*), are the most recent forms of HLH to be defined. The aim of the project was to develop robust diagnostic tests for definitive diagnosis of HLH caused by mutations in the STXBP2 and ITK genes.

ACC/CMGS Meeting, Durham April 2012 - Trainee Award

Eva Karampetsou was awarded the prize for the best presentation for a clinical scientist trainee research project – "Analysis of copy number change using quantitative real-time PCR".

3.9.3 Meetings Attended

Date	Conferences	Location	Attendees
April 2011	CMGS/ACC Spring Conference	Durham	5
July 2011	European Cytogenetics Conference, Porto	Portugal	1
April 2011	ACC/CMGS	Durham	
April 2011	South West and Wessex Spring Regional ACB Meeting	Southampton	1
April 2011	SGPPH Spring Conference: Clinical and Public Health Implications of Cutting Edge Genomic Advances	Cardiff	1

May 2011	Molecular Diagnostics and Personalised Medicine	London	1
May 2011	Wellcome Trust Decipher Symposium	Hinxton Genome Campus	1
June 2011	Health Care Science Advisory Group	London	1
September 2011	BSHG	Warwick	7
September 2011	European Neuromuscular Disease Consortium Meeting	UCL, London	4
October 2011	Circulating Nucleic Acids and Proteins VII, Madrid	Spain	2
October 2011	Familial Hypercholesterolaemia Study Day	QMUL	2
October 2011	International Congress of Human Genetics Montreal	Canada	
November 2011	3rd Annual Next Generation Sequencing Conference	London	1
November 2011	DMD registry steering committee meeting	London	1
January 2012	EuroGenTest, Nijmegen	Netherlands	1
February 2012	Emerging Technologies in Prenatal Diagnosis	UCL, London	8

March 2012	Illumina seminar series - Using new technologies to study the genetics of disease	UCL, London	3
March 2012	Wellcome Trust Genomic Disorders Conference 2012	Hinxton Genome Campus	1
March 2012	The 13th International Conference on Neuronal Ceroid-Lipofuscinoses	Royal Holloway, London	1
Date	**Training Meetings**	**Location**	**Attendees**
May 2011	London Labs' meeting	GOSH	8
May 2011	Affymetrix Cytochip Users' Group meeting	Hinxton Genome Campus	1
June 2011	Nimblegen Users' Meeting	London	3
October 2011	Roche/Fluidigm NGS Users' Meeting	Birmingham	3
November 2011	London Labs' Meeting	KGC, Northwick Park	1
March 2012	London Labs' Meeting	St George's Hospital	3
March 2012	Agilent Genomics Users' Meeting	Cambridge	1
May 2011	NOWGEN Bioinformatics course	Manchester	1

May 2011	MSC Assessor training	Birmingham	1
July 2011	FRCPath Part 1 Study Group	Birmingham	2
July 2011	NHS London – Life Sciences STP meeting	London	2
September 2011	MSC STP Training for Trainers	London	1
September 2011	Bioinformatics for Cytogeneticists	Manchester	2
November 2011	Genetic Technologists' Meeting	Newcastle	3
November 2011	NOWGEN Bioinformatics course	Manchester	1
February 2012	Laboratory Accreditation for Beginners	Istanbul	1

3.10 Professional Duties

Selected Responsibilities	
Nick Lench	NIHR Programme Grant (RAPID project) Steering Group
Lucy Jenkins	FRCPath Genetics, Course Facilitator

Lucy Jenkins	CMGS Executive Committee
Lucy Jenkins	Assessor, Association of Clinical Scientists
Jonathan Waters	RCPath Council
Jonathan Waters	Chair, RCPath Specialist Advisory Committee, Genetics and Clinical Embryology
Jonathan Waters	RCPath Genetics Curriculum Lead: Higher Specialist Scientific Training (HSST)
Jonathan Waters	RCPath Examiner (FRCPath)
Jonathan Waters	UKGTN Clinical and Scientific Advisory Group (CSAG) – RCPath representative
Jonathan Waters	Joint Committee on Medical Genetics (JCMG) - RCPath representative
Sam Loughlin	UKNEQAS Steering Committee
Alison Taylor	FRCPath Genetics, Course Facilitator
Ann Jackson	Assessor, Association of Clinical Scientists

4 RESEARCH AND DEVELOPMENT

4.1 RAPID (Reliable accurate prenatal non-invasive diagnosis)

The service is working with Professor Lyn Chitty, UCL Institute of Child Health to further develop non-invasive prenatal diagnosis. The RAPID project is funded by a 5 year NIHR programme grant and the main aim of the study is to improve the quality of NHS prenatal diagnostic services by evaluating early non-invasive prenatal diagnosis (NIPD) based on cell free fetal (cff) DNA and RNA in maternal plasma.

4.1.1 Technology Development

An assessment of transport and storage effects on sample viability and a detailed evaluation of extraction methods for cffDNA from maternal plasma has been conducted. The results of this work have highlighted the need for processing samples collected into EDTA shortly after collection as prolonged transfer times (>8 hours) result in a significant decrease in the proportion of fetal DNA present. In addition, we have shown that the DNA extraction kit and/or volume of plasma extracted can influence the reliability of diagnostic tests (Barrett et al, 2011).

A cffDNA extraction workshop involving 13 NHS laboratories from around the UK is now complete- the results of the workshop support the use of a larger starting volume of plasma with the cffDNA extraction kits for sex determination by real-time PCR and digital PCR assays, with the latter assay shown to be more reliable.

A key achievement of the RAPID programme to date has been our collaborative work with the NHS service laboratories to achieve widespread introduction of NIPD for fetal sex determination into routine clinical practice in the UK. Approval by the UKGTN and recognition by commissioners is a crucial step to allow NIPD to enter mainstream clinical care. Gene dossiers for fetal sex determination for congenital adrenal hyperplasia (CAH) and X-linked disorders (excluding haemophilia) were approved by the UKGTN for three laboratories (GOSH, Birmingham and Manchester) in April 2011. The RAPID Programme has worked with the service laboratories to facilitate this process and the application was supported by the development of care pathways and best practice guidelines as well as the PROOF audit and an economic analysis. Papers describing the process followed for implementing NIPD for fetal sex determination in the UK and the role of the RAPID programme have been published (Hill et al. 2011, 2012).

4.1.2 Diagnosis of Single Gene Disorders

NIPD for skeletal dysplasias (achondroplasia and thanatophoric dysplasia) is currently offered on a research basis. Gene dossiers for these tests were submitted to the UKGTN in January 2012. To date, 21 pregnancies have been tested for achondroplasia using cffDNA. NIPD results were validated by audit of pregnancy outcomes. Overall, six mutation positive, 14 mutation negative and one inconclusive result was reported giving a sensitivity of 100% (6/6) and specificity of 100% (14/14). Development of this test and the clinical role of NIPD testing for achondroplasia has been published (Chitty et al, 2011).

4.2 FH Child-Parent Screening Study

In collaboration with Dr. David Wald (Queen Mary University London) we are participating in a MRC-funded study to screen 10,000 children for familial hypercholesterolaemia (FH) by measuring cholesterol levels and mutation screening. The aim is to determine if cholesterol level at 1 year of age is a reliable

indicator of FH. The laboratory screens for 48 common *LDLR, APOB* and *PCSK9* mutations to provide genotype data for the study.

4.3 Chromosomal Microarrays

A number of collaborative and in-house projects have focussed on the use of standard, high-density and custom microarrays to define specific chromosomal anomalies including:

- Adult and childhood epilepsies
- Rett-like phenotypes with seizures
- Schizophrenia
- Neurodegeneration and movement disorders
- Hyperinsulinaemia
- Congenital melanocytic nevus

5 SELECTED FULL PUBLICATIONS

1 Allali S, Le Goff C, Pressac-Diebold I, Pfennig G, Mahaut C, Dagoneau N, Alanay Y, Brady AF, Crow YJ, Devriendt K, Drouin-Garraud V, Flori E, Geneviève D, Hennekam RC, Hurst J, Krakow D, Le Merrer M, Lichtenbelt KD, Lynch SA, Lyonnet S, MacDermot K, Mansour S, Megarbané A, Santos HG, Splitt M, Superti-Furga A, Unger S, Williams D, Munnich A, Cormier-Daire V. Molecular screening of ADAMTSL2 gene in 33 patients reveals the genetic heterogeneity of geleophysic dysplasia. J Med Genet. 2011 Jun;48(6):417-21. Epub 2011 Mar 17.

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6 NON-INVASIVE PRENATAL DIAGNOSIS

6.1 Invited Presentations

AGNC Spring Meeting, April 2011, Belfast, Northern Ireland
Hill M: Non-invasive prenatal diagnosis using cell free fetal DNA: Current status, future applications and the role of the RAPID programme.

National Congress on 'Controversies in Modern Obstetrics,' June 2011, St Petersburg, USSR
Chitty LS: Non-Invasive prenatal diagnosis in clinical practice.

10th World Congress in Fetal Medicine, June 2011 Malta
Chitty LS: Non-invasive prenatal diagnosis using cffDNA: background; Routine fetal Rhesus typing in the first trimester.

Hill M: Determination of fetal sex.

European Society of Human Reproduction and Embryology Annual Meeting, July 2011, Stockholm, Sweden
Chitty LS: Medical and scientific aspects of NIPD.
Chitty LS: Developing standards to implement NIPD

International Conference on Circulating Nucleic Acids in Plasma and Serum (CNAPS) October 2011, Madrid, Spain
Chitty LS: Implementing non-invasive prenatal fetal sex determination using cell free fetal DNA.

Antenatal Results and Choices (ARC) Annual General Meeting, October 2011 London
Chitty LS: Information about non-invasive prenatal diagnosis research.

Brocher Foundation: Symposium on New Developments in Non-Invasive Prenatal Genetic Testing November 2011, Hermance, Switzerland

Advances in Fetal Medicine, Fetal Medicine Foundation, November 2011, London
Chitty LS: Non-invasive prenatal diagnosis.

Emerging Techniques for Prenatal Diagnosis – Implications for Patients, Practitioners and Service Delivery, February 2012, London
Chitty LS: Non-invasive prenatal diagnosis (NIPD) using cell free fetal DNA: principles and implications for RhD negative mothers and use of anti-D.

Clinical Biochemistry and Adverse Pregnancy Outcome, Association for Clinical Biochemistry Meeting, May 2012, London
Chitty LS: Fetal DNA – ready for prime time?

6.2 Abstracts and Oral presentations

AGNC Spring Meeting, April 2011, Belfast, Northern Ireland
*Compton C, Hill M, Lewis C, Chitty L: Determination of fetal sex in pregnancies at risk of haemophilia: A qualitative study exploring health professional attitudes and practices.

Institute for Women's Health Annual Meeting, May 2011 London, UK
Khalil A, Barrett AN, Pakrt E, Griffin DR, Chitty LS: New aids to the prenatal diagnosis of thanatophoric dysplasia.

Compton C, Hill M, Lewis C, Chitty L: Determination of fetal sex through non-invasive prenatal diagnosis in pregnancies at risk of haemophilia: The health professional perspective.

*Forya F, Compton C, McCall K, Lewis C, Hill M, Chitty LS: Non-invasive prenatal diagnosis of single gene disorders: An exploration of views and preferences gathered from consumers and health professionals.

British Society of Human Genetics, September 2011, University of Warwick, UK
Barrett AN, McDonnell T, Chitty LS: Digital PCR analysis of maternal plasma for non-invasive Detection of Sickle Cell Anaemia. J Med Gen 2011; 48: Supple 1; S39.

Dent C, Chitty LS, Crolla J, White HE: Non-invasive prenatal detection of aneuploidy by targeted next generation sequencing. J Med Gen 2011; 48: Supple 1; S54.

Hill M and Chitty LS on behalf of the RAPID team: Non-invasive prenatal diagnosis using cell free fetal DNA – how far have we got? An update from the RAPID programme. J Med Gen 2011; 48: Supple 1; S81.

International Conference on Circulating Nucleic Acids in Plasma and Serum (CNAPS) October 2011, Madrid, Spain
*Barrett AN, McDonnell TCR, Chitty LS: Further developments in the use of cell-free fetal DNA for non-invasive prenatal diagnosis of single gene disorders: digital PCR allows diagnosis of sickle cell disease. CNAPS VII: J Nucleic Acids Invest 2011; 2: Suppl 1; 5.

White E, Dent CL, Hall VJ, Crolla JA, Chitty LS: Facilitating implementation of NIPD: a modified protocol to detect the universal fetal DNA marker RASSF1A. J Nucleic Acids Invest 2011; 2: Suppl 1; 33.

Hill M, Barrett A, Meany C, Lench N, Chitty LS: Implementing non-invasive prenatal diagnosis for genetic disorders using cell free fetal DNA into clinical practice acceptability and impact on pregnancy management. J Nucleic Acids Invest 2011; 2: Suppl 1; 38.

AGNC Spring Meeting, April 2012, Cambridge, UK
Karunaratna M, Lewis C, Hill M, McCall K, Forya F, Chitty L: Non-invasive prenatal diagnosis for single gene disorders: An exploration of service users' and providers' views and preferences.

ESRC Genomics Network Annual conference, April 2012, London, UK
Lewis C: Non-invasive prenatal testing - a new dawn in antenatal care.

Joint ACC/CMGS Genetics Spring Meeting April–May 2012 Birmingham UK
*Dent CL, Chitty LS, Crolla JA, White HE: Non-invasive prenatal detection of aneuploidy by targeted next generation sequencing.

McDonnell T, Barrett A, Baker T, Chitty LS: The use of formaldehyde to stabilise the percentage of fetal DNA from cell-free DNA.

White HE, Dent CL, Hall VJ, Crolla JA, Chitty LS: Evaluation of a novel PCR assay for the detection of the universal fetal DNA marker RASSF1A for use in clinical practice: facilitating improved diagnostic reliability of non-invasive prenatal diagnosis.

Institute for Women's Health Annual Meeting, May 2012, London, UK
*Barrett AN, McDonnell TCR, Chan A, Petrou M, Chitty LS: Further developments in the use of cell-free fetal DNA for non-invasive prenatal diagnosis of single gene disorders: digital PCR allows diagnosis of sickle cell disease.

Barrett AN, Lench N, Chitty LS: Non-invasive prenatal diagnosis for thanatophoric dysplasia.

Hill M, Fisher J, Morris S, Chitty LS: Towards implementation of non-invasive prenatal diagnosis for Down's syndrome: what do women and health professionals want?

Karunaratna M, Lewis C, Hill M, McCall K, Forya F, Chitty LS: Non-invasive prenatal diagnosis for single gene disorders: an exploration of service users' and providers' views and preferences.

White HE, Dent CL, Barrett A, Brugger K, Chitty LS: Comparison of multiplexed maternal plasma DNA sequencing and targeted (chromosome specific) next generation sequencing approaches for the non-invasive prenatal detection of trisomy 21.

*Oral presentations

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