



**National Centre for Medical Genetics**  
Dublin, Ireland



National Centre for Medical Genetics  
Ionad Náisiúnta Gineolaíocht Leighis

# National Centre for Medical Genetics

## 5 year report

### 2007-2011

National Centre for Medical Genetics  
Our Lady's Children's Hospital  
Crumlin  
Dublin 12

[www.genetics.ie](http://www.genetics.ie)

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



<b>1</b>	<b>FOREWORD BY PROFESSOR ANDREW GREEN</b>	<b>3</b>
<b>2</b>	<b>INTRODUCTION</b>	<b>3</b>
<b>3</b>	<b>DIVISION OF CLINICAL GENETICS</b>	<b>3</b>
3.1	Referrals	3
3.2	Triage	3
3.3	Clinical Activity	3
3.4	Staffing levels	3
3.5	Training in Clinical Genetics	3
3.6	New Staff posts	3
3.7	Prenatal testing	3
3.8	Genetic Counsellors	3
3.9	Clinical links with other genetic & other specialist departments	3
<b>4</b>	<b>DIVISION OF CYTOGENETICS</b>	<b>3</b>
4.1	Overview	3
4.2	5 year Statistics and Trends	3
4.3	Service Changes	3
4.4	Accreditation	3
4.5	Quality Assurance	3
4.6	Teaching and Education	3
4.7	Collaborations	3
4.8	Future Outlook	3
<b>5</b>	<b>DIVISION OF MOLECULAR GENETICS</b>	<b>3</b>
5.1	Sample Numbers, Reports & Staff numbers	3
5.2	CPA Accreditation	3
5.3	Audits	3
5.4	User Survey	3
5.5	External quality assessment (EQA) reports	3
5.6	Training & Education in Molecular Genetics	3
5.7	Molecular Genetics changes in service 2007-2011	3
5.7.1	Suspension & temporary cessation of services.....	3
5.7.2	New services.....	3
5.7.3	Cystic Fibrosis Service – New Born Screening (NBS) and a new assay .....	3
5.7.4	Prenatal diagnostic service .....	3
5.7.5	DNA Preparation.....	3
5.7.6	Genetic & Rare Disorders Organisation (GRDO).....	3
5.8	Molecular Genetics plans for 2012 & onwards	3
5.8.1	Service planning & implementation of copy-number variation analysis.....	3
5.8.2	Breast Cancer (BRCA) service .....	3
5.8.3	Service planning & implantation of Next Generation Sequencing .....	3
<b>6</b>	<b>ADMINISTRATION</b>	<b>3</b>

<b>Clinical Authors:</b> Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. <b>Cytogenetics Authors:</b> David Betts. <b>Molecular Authors:</b> Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt. <b>Admin Authors:</b> Lisa Malone, Sally Ann Lynch, Damien Moyles.	
<b>Collated by:</b> Christine Brady, Sally Ann Lynch, Alana Ward	<b>Authorised by:</b> NCMG Mgt
<b>Page 2 of 90</b>	



# National Centre for Medical Genetics

Dublin, Ireland

7	IT SYSTEMS	3
7.1	iGene Database	3
7.2	Electronic Data transfer	3
8	ENGAGEMENT WITH HSE & DOH	3
9	PREMISES AND ENVIRONMENT	3
10	PROCUREMENT & MANAGEMENT OF EQUIPMENT	3
11	NCMG SPECIMEN RECEPTION COMMITTEE	3
12	NCMG SAMPLE IDENTIFICATION POLICY	3
13	CONTINUING PROFESSIONAL DEVELOPMENT	3
14	TEACHING	3
15	NCMG COMMITTEE REPRESENTATION	3
16	RESEARCH	3
16.1	The Genetics of Vesicoureteric Reflux	3
16.2	SNiP2CHIP	3
16.3	Group of Dr Sean Ennis	3
16.4	Group of Dr Sally Ann Lynch	3
17	PAPERS	3
18	PUBLICATIONS	3
19	SUBMITTED ABSTRACTS	3
20	PLATFORM PRESENTATIONS	3
21	ABSTRACT FROM MEETINGS	3
22	POSTER PRESENTATIONS	3
23	RESEARCH GRANTS AWARDED	3

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## 1 Foreword by Professor Andrew Green

I am delighted to introduce the 5 year report of the activities of the National Centre for Medical Genetics. This report gives a description of the clinical and laboratory work of the centre, as well as the active research and teaching programmes in the Centre. It reflects the changing economic circumstances in which health care has been delivered from 2007 through to the difficult financial climate of 2011.

Despite the 15% reduction in staff of the NCMG over the 5 years of the report, the centre has maintained its clinical and laboratory activity, seeing over 27,000 patients, carrying out over 60,000 genetic tests in that period, and coping with a 15% annual increase in the numbers of molecular genetic tests requested. The laboratories have also successfully introduced newborn screening for cystic fibrosis in 2011, and funding for in-house high resolution chromosome array testing in 2011.

Both cytogenetic and molecular genetic laboratories can be justifiably proud in achieving external accreditation from CPA (UK) in 2010. Both laboratories were highly commended for their work, and I congratulate all the laboratory staff, especially the quality managers Adam Dunlop and Christine Brady for their hard work in achieving and maintaining standards.

The NCMG can also be congratulated for obtaining a 5 million euro grant from the Health Research Board for research into the genetics of autism, held jointly with University College Dublin and Trinity College Dublin, which has led to a series of landmark publications in the top ranking scientific journal *Nature*. The NCMG has also been instrumental in developing a successful program with UCD for the identification of the genetic mechanisms behind rare single gene disorders.

Nonetheless, there is much more that could be done. The clinical service of the NCMG is deeply under-resourced, with only 15-20% of the staffing levels of other European genetic centres serving a similar population size. Waiting times for families to be seen in the genetics clinic are unacceptably far too long. There are many samples being sent abroad for genetic testing from Irish patients costing well over 1 million euro, when those samples could be tested in the NCMG at a lower cost, if the NCMG had adequate staff and equipment resources to carry out those tests. Repatriation of those tests would be of benefit both to the exchequer, and to Irish patients with genetic diseases, as their clinical geneticists are dealing directly with the laboratories carrying out the tests.

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

The NCMG has close links with the many support groups for families with genetic disorders, and in particular with GRDO, the Irish Genetic and Rare Disease Organisation. We are grateful for their support, and look forward to continued close relationships with these groups, particularly leading into 2013, when the EU directive on Rare Diseases must be implemented.

I would like to thank in particular all the staff of the NCMG who have helped put together this report, in particular Dr Sally Ann Lynch, Dr Alana Ward, and Christine Brady. I would also personally like to thank all the administrative, laboratory and clinical staff of the NCMG for all their unstinting hard work over the last 5 years for patients and families affected by genetic disorders.

Andrew Green

Director, National Centre for Medical Genetics, November 2012.

## 2 Introduction

This comprehensive report provides an insight into the specialist work carried out in the National Centre for Medical Genetics (NCMG) between 2007 and 2011. The data was compiled by nominated staff members from each division who felt it important to highlight our work & achievements and make it available to our users. It shows the changes in demand and highlights the challenges that our national service has had and continues to face. It has now been endorsed and supported by the Director and the laboratory heads of NCMG

The NCMG has been based in Our Lady's Children Hospital in Crumlin (OLCHC) since its inception in 1994. Since this time, the NCMG has obtained its funding directly from OLCHC and its staff form part of the overall staff numbers of the Hospital. Therefore, despite having the responsibilities of a National service, our funding has not been ring-fenced. Overall funding for the NCMG has not been related to the year on year increases in clinical or laboratory activity. Recruitment and retention of NCMG staff numbers is outside the control of the Centre. This has had a significant impact on the services offered by the NCMG, both in the past and especially in recent years due to the economic climate and employment moratorium. These factors have resulted in the cessation and/or reduction of specific services. In response, there has been ongoing discussion by the NCMG with OLCHC, the Health Service Executive (HSE) and especially with the National Hospital's Office (NHO) (which

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

was disbanded in 2009) at the HSE to highlight and address these service difficulties. This has resulted in engagement with the NHO/HSE for a 'Needs Assessment' for Medical Genetics services in Ireland and an assessment of the resources required for the proper provision and organisation of a national medical genetics service.

The years 2007-2011 have been challenging for any service trying to provide health care within the Republic of Ireland. NCMG is no exception particularly as we are the only centre providing Clinical Genetics services in the Republic of Ireland. NCMG strives to follow best practice as outlined by the Public and Professional Policy Committee (PPPC) of the European Society of Human Genetics (ESHG). However, we have experienced staff cutbacks of between 15-25% throughout these years and have had to curtail some services as a result.

A policy document published in the European Journal of Human Genetics in 2003 outlined recommendations from the PPPC of the ESHG on the Provision of genetic services in Europe. *European Journal of Human Genetics (2003) 11, Suppl 2, S2-S4. doi:10.1038/sj.ejhg.5201110*. This document outlined 34 aims and recommendations for the safe provision of genetics care. NCMG does its best to adhere to the recommendations outlined in this document.

The PPPC described a Clinical Genetics service as *"A specialized service provided in tertiary centres, accessed by self-referral or referral from consultant physicians and others including general practitioners, for patients and relatives with complex or rare conditions, and serving a wide geographic area. A genetic service is distinguished by the fact that diagnosis, investigations, counselling, and support is given for disorders affecting any organ system or at any age and records are sometimes kindred based and multigenerational, which requires extra-care for data protection. This imposes unique disciplines and requirements on the molecular & cytogenetic diagnostic laboratories, which distinguish them from other categories of clinical laboratories. The family is the unit of study in contrast to the individual. Furthermore, inheritance across generations and in the extended kindred gives the information generated by the genetic laboratory a lasting relevance. It places on a laboratory a responsibility for long-term and careful storage and retrieval of clinical information"*.

Safe practice is of utmost importance. NCMG has had to limit what it can offer in terms of genetic testing whilst our resources have been cut. Whilst reducing what we can offer in terms of service and testing has been a difficult decision to make, it has only been undertaken when the volume of requests became so overwhelming that patient safety was being compromised.

Currently, there are approximately 60 employees working in NCMG. This includes 9 administrative staff members who provide essential support to our team. There are three

<b>Clinical Authors:</b> Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. <b>Cytogenetics Authors:</b> David Betts.
---

<b>Molecular Authors:</b> Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.
--

<b>Admin Authors:</b> Lisa Malone, Sally Ann Lynch, Damien Moyles.
--

<b>Collated by:</b> Christine Brady, Sally Ann Lynch, Alana Ward
--

<b>Authorised by:</b> NCMG Mgt
--------------------------------



## National Centre for Medical Genetics

Dublin, Ireland

divisions in the NCMG (<http://www.genetics.ie>); each is individually distinct and unique. These are:

- Clinical Genetics (<http://www.genetics.ie/clinical/>)
- Cytogenetics (<http://www.genetics.ie/cytogenetics/>)
- Molecular Genetics (<http://www.genetics.ie/molecular/>)

### 3 Division of Clinical Genetics

The Clinical Genetics team consists of Consultants in Clinical Genetics and Genetic Counsellors who are experienced practitioners with a scientific or nursing background and a Professional qualification in Genetic Counselling. Consultants see all cases where a diagnosis is still being sought and complex cases. Genetic counsellors see families where the diagnosis is already established to discuss recurrence risks, possible preventative or reproductive options and any implications for more extended family members. A significant proportion of the Genetic Counsellor case-load involves predictive testing for certain later-onset conditions. In addition, Genetic counsellors coordinate specific pre-natal tests in families known to our service. As a national service, the clinic appointments and any genetic testing arising is free. The NCMG holds clinics in two major paediatric hospitals in Dublin - Our Lady's Children's Hospital Crumlin, where the centre is based, and The Children's University Hospital, Temple Street. Peripheral clinics in Cork, Galway, and Limerick are held regularly throughout the year. Cardiac genetic clinics are held at Heart House (Mater campus) and Tallaght Hospital, as well as in the NCMG.

The Clinical Genetics Committee of the Royal College of Physicians in London defined three objectives of a clinical genetic service: (1) for persons who are affected or who are referred because of a genetic risk - to make the genetic diagnoses, provide pedigree analyses and assess the transmission risk. These are necessary for genetic counselling and to guide preventive and therapeutic actions; (2) to support the identification and surveillance of relatives who are at risk for serious genetic disorders, but who may not have been directly referred, so that they may receive well informed genetic counselling and guidance on preventive and therapeutic actions if required; and (3) to provide support to family members, both to those affected and unaffected.

The British Clinical Genetics Society (2000) outlined in detail the responsibilities of a clinical geneticist. Particular emphasis was placed on follow-up, support, coordination of health surveillance, and services to extended families. Unfortunately, with staffing levels at 80-90% below other centres in Europe NCMG has had to focus on our core role, that of diagnosis,

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

pedigree analyses and estimate of transmission risk. Most UK units have disease specific registries to help coordinate the care of patients with rare diseases but a database manager is a requirement and NCMG, with limited administrative support, cannot provide this.

### 3.1 Referrals

Clinical Genetics (<http://www.genetics.ie/clinical/>) as a speciality, involves the care of both children and adults with over 40% of our referrals being for adults. The NCMG has a broad referral base with referrals from a wide range of specialties including obstetricians; surgical specialities such as orthopaedics, plastic surgery, general surgery, ophthalmology, ENT; paediatric specialities such as metabolic medicine, neonatology, neurology, endocrinology, cardiology, immunology, dermatology and gastroenterology; the adult equivalents of each of these specialities; GPs and allied health professionals. Around 70-80% of rare diseases are genetic and we are cognisant of the EU recommendation on the treatment of patients with rare disease which Ms Mary Harney signed in 2009 and which comes into place in 2013.

The use of genetic techniques and approaches is increasing in all clinical specialties, but the recent report prepared by the Royal College of Physicians of London indicated that many primary care physicians and specialists in other fields do not feel confident to handle genetic issues and greatly value the support of clinical geneticists. The number of genes available to test has risen exponentially over the last ten years (see Fig1). As the technology increases in sensitivity so more genetic variants are being identified including those of uncertain clinical significance requiring specialist knowledge. This has been reflected in the nature of our referrals and we have noted a concurrent increase in the number of referrals generated by clinicians (paediatricians, cardiologists & obstetricians) asking us to help with interpretation of laboratory results. This has been noted by Genetics centres throughout Europe (Figure 1)

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

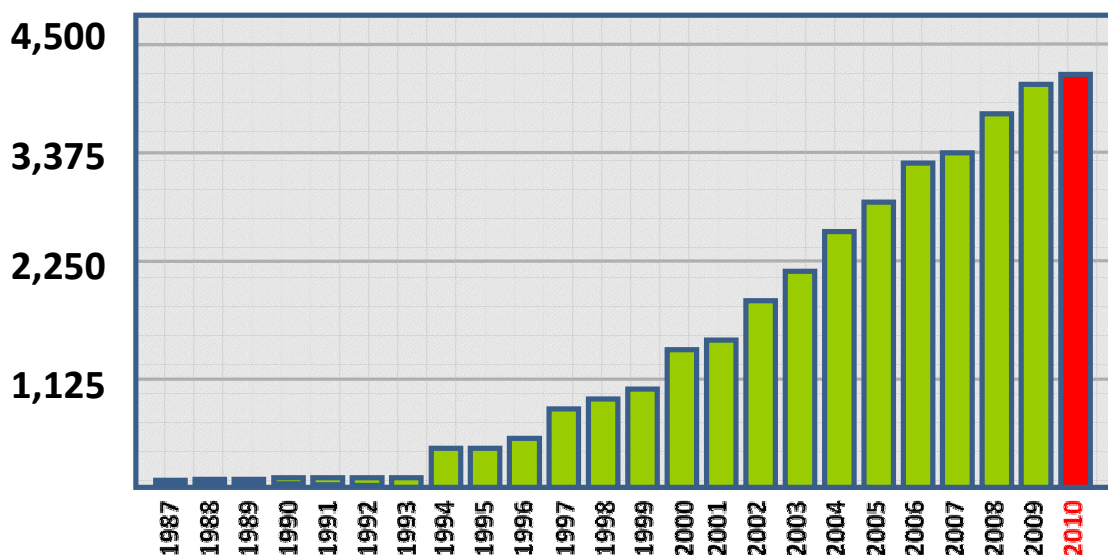
**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt





Figure 1: Identification of Disease Genes <http://omim.org/statistics/>



### 3.2 Triage

In order to minimize waiting times, referrals are triaged and priority given to certain patients; a) those who are critically ill b) those at high risk of recurrence and c) those who are pregnant. Pre-clinic work up is undertaken in certain conditions, with requests to the referrers and the families to arrange for blood tests to be carried out prior to clinic appointments. This new development commenced in 2011 in an attempt to cope with the overwhelming number of referrals. For certain genetic conditions individuals concerned about a family disorder are now being dealt with initially by letter or telephone. Testing is arranged via the GP and NCMG only offers appointments to those who are found to have a genetic alteration. Please note, for predictive testing an appointment and consent is still required before testing is offered as in accordance with European Guidelines. Arranging blood samples via GPs & allied health professionals carries a clinical risk as blood samples are being sent in from all over Ireland and many samples have to be rejected because of discrepancies in patient identifiers. Despite the drawbacks to this practice, anecdotal feedback from our patients and referrers, suggests that they would prefer us to operate in this manner if it means they get their risk status resolved in a timely manner. However, this process is under close review.

### 3.3 Clinical Activity

Between 2006 and 2010 the number of referrals for the NCMG Clinical service has increased by 27%. This represents an average yearly increase in referrals of 6.75% per year between 2006

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

and 2010. We have seen a drop in 2011 which may reflect the introduction of our triage system in this period. These figures are outlined in Table 1

**Table 1**

	2007	2008	2009	2010	2011
NCMG Referrals	4,175	4,433	4,919	4,862	4,580

This increase in referrals is due in part to the identification of new genes. This has prompted not only new referrals but the need to re-visit previously seen families. However, despite reductions in HSE funded staffing, the number of patients attending the NCMG clinics has been maintained and indeed slightly increased in 2011, as outlined in Table 2.

**Table 2:**

	2007	2008	2009	2010	2011
NCMG OPD appointments attended	2,195	2,372	2,334	2,287	2,483
OLCHC	1,241	1,256	1,191	1,278	1,438
Temple St	407	450	389	408	308
Cork	235	286	282	302	251
Limerick	138	170	187	170	211
Galway	135	144	177	129	122
Other	39	66	108	0	153
In-patient consultations					
OLCHC	194	168	195	237	179
Temple St	73	72	72	75	61
Maternity Hospitals	41	68	36	29	42
Total patients seen	5,151	5,350	5,568	5,648	5,937

Genetics clinics are unique as we deal not only with the individual patient referred but with the family unit and our clinics include family appointments. Therefore OPD clinic numbers refer to the numbers of appointments attended, and not the number of patients seen. On average, 2.5 family members are seen at each clinic appointment. The number of patients seen annually is shown on the final row of figures for each year.

### 3.4 Staffing levels

The Royal College of Physicians UK recommend a minimum of 3 Consultant Geneticists per million and the Association of Genetic Nurse and Counsellors UK (AGNC) recommend 1 full-time Genetic Counsellor per 100,000 population. Based on these for a population of 4.6

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

million the Republic of Ireland should have 14 Consultant Geneticists and 46 Genetic Counsellors. Staffing level comparisons with many European countries are detailed in Table 3 with The Republic of Ireland has the worst staffing quotient.

**Table 3** demonstrating staffing levels in Clinical genetics across many European countries.

	Rep of Ireland	Northern Ireland	Finland	Norway	France	Czech Republic	Wales	Scotland	England	Portugal
Total population (million)	4.6	1.7	5.3	5	65	10	3	5	52	10.7
Live births	78,000	22,000	60,000	62,000	800,000	100,000	36,000	58,592	687,000	96,856
No of WTE clinical consultant geneticists	4	6	23	28	160	54	9	12.28	115 + 4.5 vacant	23
No of WTE research consultants	0	0	15-18	0			1.1	2.2	14.2	0
No. of genetic counsellors	5.6	6		15	80	0	22.3	21.4	256	2
No of specialist registrars	0	2	7	12	90	10	4	2	56	15
No of genetic staff per population	1 per 500,000	1 per 121,428	1 per 176,000	1 per 90,000	1 per 196,000	1 per 156,788	1 per 85,000	1 per 140,134	1 per 120,500	1 per 266,290
No of clinical consultants per population	1 per 1,150,000	1 per 285,000	1 per 176,000	1 per 180,000	1 per 406,000	1 per 185,000	1 per 325,000	1 per 407,000	1 per 435,146	1 per 463,114

In comparison with the Great Ormond Street Hospital's (GOSH) genetics service (Annual Report 2008 – 2009) which serves a similar population (4.5 million) the NCMG staffing levels fall far short. They sent out 4,457 appointments in a 12 month period from 2008-2009. Despite having only 50% of GOSH staff numbers, we sent out 3,553 appointments (80% of GOSH levels) in 2010, 2,628 patients/families attended, 427 cancelled and rescheduled their appointment, 260 failed to attend, 160 cancelled and said they no longer required an appointment. Each clinic appointment in the NCMG generally takes between 45-60 minutes of patient contact. Approximately 75% of these contacts are new referrals which are in

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

contrast to many other outpatient clinical services where a significant proportion are follow-up appointments. Our failure to attend rate (8.9%) is well below the national average (15%).

We are currently making up >2000 new Clinical Genetics charts per annum. This is in addition to trying to slot in re-referrals and follow-up family clinic appointments. We now have over 21,000 family charts. It is expected that demands on our service will continue to rise as new appointees in other specialities result in additional requests for our service. However, the clinical team is at full capacity now and it is impossible to envisage us seeing any more patients' year on year without a significant increase in clinical staff.

### 3.5 Training in Clinical Genetics

We have considerable concerns about the long term viability of our speciality within the Republic of Ireland. We, along with Cyprus, are the only countries in Europe not to have a Specialist training programme for Clinical Genetics. Initial attempts to set up a training scheme started in February 2008 but the Irish Medical Council stalled the development of any new schemes due to legal issues arising from the Medical Practitioners Act 2007. In October 2010 the Irish Medical Council announced that these issues had been largely resolved. However, negotiations between the Royal College of Physicians and the HSE are ongoing. We are hoping these issues will finally be settled in 2012 to avoid any further delay to the commencement of this essential scheme. The NCMG training programme, if granted, will liaise closely with the UK training programme. Dr Sally Ann Lynch has involved Dr Alex Magee, Consultant Clinical Geneticist in Belfast and Dr Sarah Smithson, Chair of Clinical Genetics SAC, in the application process to commence training at NCMG. Dr Lynch will be the National Speciality Director once approval has been granted. We plan to offer dual training in both Clinical and Biochemical Genetics. The trainee will spend time in the metabolic unit at Temple Street working with Prof Eileen Treacy and her team. This decision was reached because of similar recruitment difficulties in Biochemical Genetics.

Workforce planning: recruitment to Clinical Genetics has always been difficult as it is highly specialised. Therefore training is imperative to ensure the long term viability of Clinical Genetics service in Ireland. The three consultants appointed prior to Dr Gill are all due to retire within the next ten years. As a minimum period of four years is required for Clinical Genetics training, it is vital that a training scheme commences imminently to ensure sufficient time for the present consultants to train appropriate staff. EU recommendation (due 2013) on the treatment of patients with rare diseases may require us to refer patients abroad should we not be able to provide the required standards of care. In 2011 the European Parliament voted in favour of the EU Directive on Patients' Rights in Cross-border Healthcare. *'The legislation concerns the application of patients' rights in cross-border healthcare and seeks to eliminate obstacles*

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

hindering patients from seeking treatment in another Member State. This is especially important for rare disease patients who cannot find diagnosis locally or want to access a centre of expertise based in another country.' The European Society of Human Genetics is aware of our concerns and is planning a work-shop on inequity in Genetic Health Care in Europe.

**Table 4: Meetings to initiate Specialist training in Clinical Genetics**

27/02/08	Prof J McKenna RCPI Prof A Green NCMG SA Lynch NCMG	Proposal to start training programme in Clinical Genetics
17/11/08	SA Lynch NCMG G Turner RCPI B Silke RCPI L Kearns RCPI	Proposal to start training programme in Clinical Genetics
25/01/09	SA Lynch NCMG A O'Shaughnessy RCPI	Developmental of curriculum for Clinical Genetics training programme
30/01/09	SA Lynch NCMG Grace Turner RCPI	Proposal to start training programme in Clinical Genetics
12/03/10	Prof G Bury Met B Unit HSE C Mellett Met B unit SA Lynch NCMG	Proposal to start training programme in Clinical Genetics
20/05/10	Prof W Powderley IMC A Keane IMC SA Lynch NCMG	Proposal to start training programme in Clinical Genetics
29/10/10	Harinder Gill NCMG IMC staff	Information session on the recognition of new specialties, new programmes and bodies
26/11/10	Jennifer Shiels RCPI Ann O'Shaughnessy RCPI SA Lynch NCMG	Towards development of training programme
06/12/10	Jennifer Shiels RCPI Bernard Silke RCPI SA Lynch NCMG	Proposal to start training programme in Clinical Genetics
20/05/11	Kellie Myers RCPI John Magner RCPI Eileen Treacy NCIMD SA Lynch NCMG	Proposal to start training programme in Clinical Genetics

### 3.6 New Staff posts

Our service has struggled over the five year period due to embargos on HSE staff recruitment meaning that we were unable to fill staff posts to cover for extended periods of leave. However, despite these restrictions, we managed to secure a new consultant post, Dr Harinder Gill, a Consultant Geneticist, joined NCMG in August 2010. This brings the total number of Clinical Geneticists to four.

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

We also managed to secure a new full-time Genetic Counsellor, Dr Alana Ward to deal with the issues arising from the introduction of newborn screening for Cystic Fibrosis which commenced in July 2011. In addition, Prof Green together with cardiology colleagues, Dr Joe Galvin Mater & Dr Deirdre Ward successfully secured funding from cardiology charities Heart House, CRY Ireland, and also the Children's Medical and Research Foundation (CMRF) to fill a two year cardiac genetic counsellor position which Ms Nicola Harper commenced in February 2011. This new development means that those families at risk of sudden adult death resulting from a genetic cause can be seen within six months. Ms Harper holds clinics in Tallaght and Heart House at the Mater in addition to clinics at NCMG.

Prof Green together with the Neurofibromatosis association, and NF Ireland CEO Paddy Griffin also secured funding for a part-time Genetic Counsellor to help manage families who have or are at risk of Neurofibromatosis type 1 and 2 (NF1 & NF2). A fortnightly NF clinic is held in NCMG. Links have been made with a number of Consultant specialists (neurosurgery, dermatology, neurology, ophthalmology and oncology) to allow for rapid onward referral should the need arise. Previously these patients suffered from poor co-ordination of care and whilst further development is required, we hope the patients have seen a real improvement in this service. Alana Ward who initially took up this position in December 2010 moved over to the CF post in October 2011. Ms Claire Kirk was subsequently appointed to the NF post and is due to start in 2012.

Therefore we now have 5 WTE genetic counsellors employed by the HSE and 1.5 WTEs employed through charity funding.

### *3.7 Prenatal testing*

Prenatal testing is available in 6 fetal medicine units in the Republic of Ireland (the 3 Dublin maternity hospitals, Cork, Limerick & Galway). NCMG are closely involved in those families at increased risk of a specific genetic condition. We co-ordinate approximately 100 tests per annum in conjunction with the 3 Dublin maternity hospitals and we expect this to rise significantly as the availability of testing increases. It is not feasible to arrange prenatal tests for rare disorders outside of Dublin as co-ordination of sample collection and timely transport (sometimes through customs) for subsequent analysis by NCMG or laboratories abroad precludes this. The work-load involved in these cases is significant requiring close and sensitive liaison between the Genetic Counsellor, the family, the obstetric team, the NCMG laboratory and the testing laboratory (if the samples are being sent abroad). Many of these cases are co-ordinated by phone and letter and therefore this clinical activity remains largely uncaptured.

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

In 2007, a new test, foetal sexing from maternal blood, was offered to those families seeking prenatal testing for X-linked conditions. This allows the gender of the pregnancy to be determined by testing the mother's blood from around 9 weeks of pregnancy. The test has been shown to be over 99% accurate. As this is non-invasive to the pregnancy it allows those women carrying a female pregnancy to be reassured without having to proceed with a more invasive CVS or amnio sampling. Those carrying a male pregnancy can then consider whether to proceed with diagnostic prenatal testing. Between 2007 and 2011, 27 such tests were managed by the clinical team.

A recent audit of prenatal cases by Ms Rosie O'Shea, Genetic Counsellor, showed that the most common reasons for prenatal testing were for Cystic Fibrosis, Sickle Cell Disease, Duchenne Muscular Dystrophy and chromosomal abnormalities. Whilst the majority of couples proceeding with testing had recurrence risks of 25% or over it was noted that approximately 20% of prenatal tests were taken up by couples with a less than 5% risk.

### 3.8 Genetic Counsellors

The following Genetic counsellors received full registration with the Association of Genetic Counsellors and Nurses (AGNC): Rosemarie Kelly (2007), Nuala Cody (2008) & Marie Meany in 2011. Registration is an ongoing process with renewal required every 5 years and Cliona deBaroid & Jackie Turner successfully re-registered with the AGNC in 2010. Rosemarie Kelly, our Principal Genetic Counsellor, is a registered Mentor with the AGNC.

The NCMG Genetic Counsellors liaise closely with the British Association of Genetic Nurse and Counsellors (AGNC) and attend yearly meetings in the UK to ensure that professional working practices are adhered to. Our colleagues in Belfast hosted the annual conference of the AGNC in 2011 and Ms Marie Meany as our AGNC representative chaired sessions at this meeting.

The Genetic counsellors welcomed a number of students for clinical attachments from the Manchester & Cardiff MSc Genetic Counselling training programmes. We have had the pleasure of having Sarah Gibson (2007), Tara O'Neill (2008), Laura Zahavich (2009) & Claire Gibney (2010). Ms Lindy Hodgkin, an Associate Genetic Counsellor from Australia joined us for a 3 months locum in 2007.

### 3.9 Clinical links with other genetic & other specialist departments

The clinical team at NCMG have two joint meetings annually with the Clinical Genetics department in Belfast. Presentations are made by staff from both genetic teams. Initially these meetings alternated between both centres but since 2010 the meetings have been held at the

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

paediatric department at Daisy Hill Hospital Newry with the kind assistance of Dr James Hughes. All meetings receive Continuing Medical Education (CME) approval.

Additionally from 2008 to the present day, both Professor Andrew Green and Dr Sally Ann Lynch attended the multidisciplinary paediatric endocrine meetings held three times a year and hosted by the paediatric endocrinology teams at OLCHC and Temple Street Children's Hospital. Bi-annual joint meetings are also held with the Paediatric Dermatologists. In addition, Dr Lynch attends the cross city paediatric neurology meetings held quarterly.

## 4 Division of Cytogenetics

### 4.1 Overview

During this period the Division has provided a cytogenetic (G-band and FISH) service for constitutional, prenatal, haematological-oncology and paediatric solid tumours. The results generated by these cytogenetic techniques continue to play a major role in clinical decisions at both the constitutional and haematological-oncology level. The aim of the Division would be to provide a true National service whereby all the cytogenetic needs can be covered in a full and fair manner for the whole of Ireland. However, the years 2007 - 2011 have been characterised by the need to manage sample numbers and reductions in staff numbers. Therefore, service restrictions in terms of numbers and types of samples have been a factor since 2008.

In the period 2000 - 2007 the Division experienced an almost doubling of the sample number that the laboratory received. For a 5 year overview, in many ways 2007 represents the atypical year as it was the only time in this period where there were no staff or sample restrictions.

Sample number would have continued to grow in 2008, but by mid 2008 the Division was forced to impose severe restrictions on the samples that we could accept. This was in part to allow us to reduce the backlog that had arisen, but also to maintain a high standard of service for the urgent samples received.

The fluctuation in staff numbers has been a particular challenge with the numbers in 2009 - 2011 being 15-30% down on 2007 levels. Hence the Division has strived to maintain and modify services rather than to expand.

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

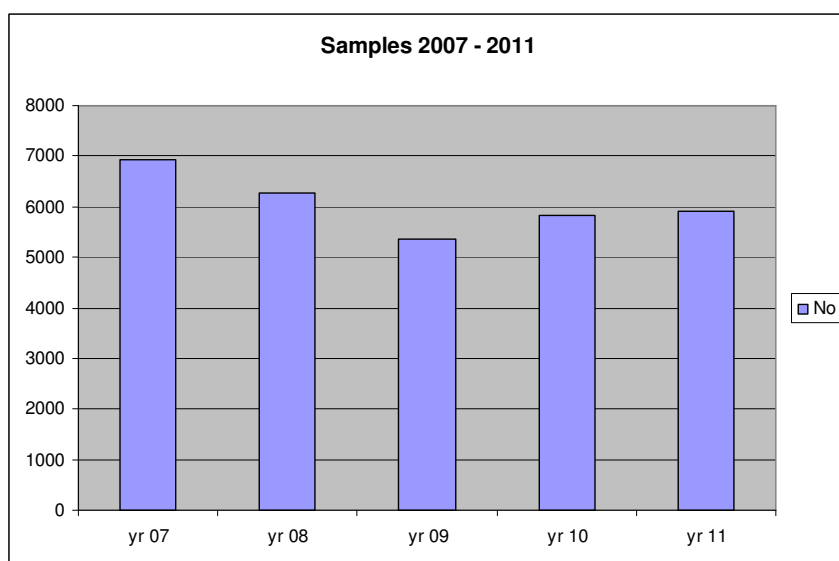
**Authorised by:** NCMG Mgt





### 4.2 5 year Statistics and Trends

The overall number of samples (see fig. 2) has effectively been controlled by the extent of restrictions that have been imposed. While almost 7,000 samples were received in 2007, this raises to 7,500 if the period July 2007 to Jun 2008 is considered. The graph demonstrates the full impact of the restrictions in 2009. Subsequent to 2009 the restrictions were slightly softened with the aim that the laboratory had the capacity to process 6000 samples per annum. As can be seen the number of samples received in 2011 very closely matched this goal.



**Fig 2:** Number of total samples received in the Division of Cytogenetics by year 2007 - 2011

The Division receives three main sample types; peripheral blood for constitutional analysis, neoplastic related samples, and prenatal samples. Over the 5 year period dramatic differences can be seen in the distribution of these sample types. By individual sample type peripheral blood for constitutional analysis is sent in the largest numbers. However, this sample type demonstrates the largest fluctuation in numbers (see fig. 3), a situation that can be fully explained by the impact of the restrictions. Prior to 2007 there had been a gradual yearly increase in the number received, rising from 2,400 in 2000 to the 3,800 in 2007. The impact of this was initially so severe that the sample number in 2009 dropped to below the number received in 2000.

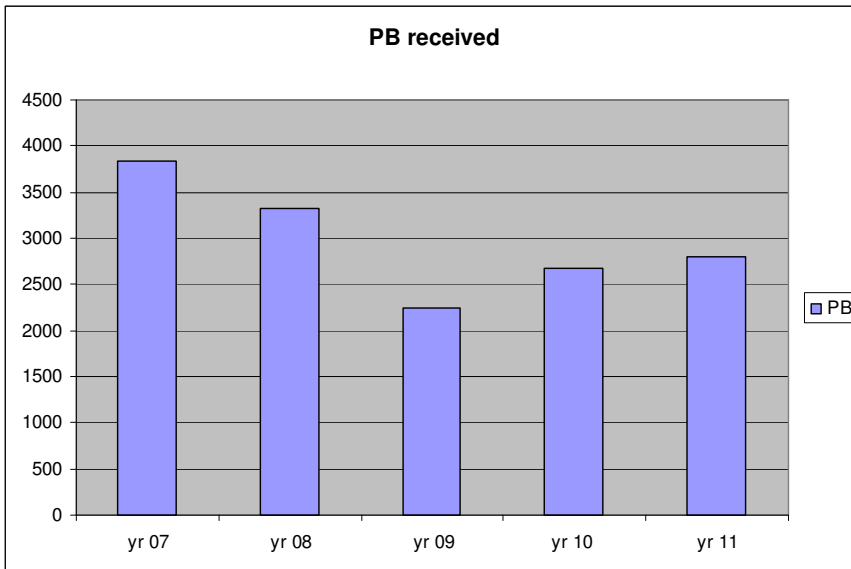
**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

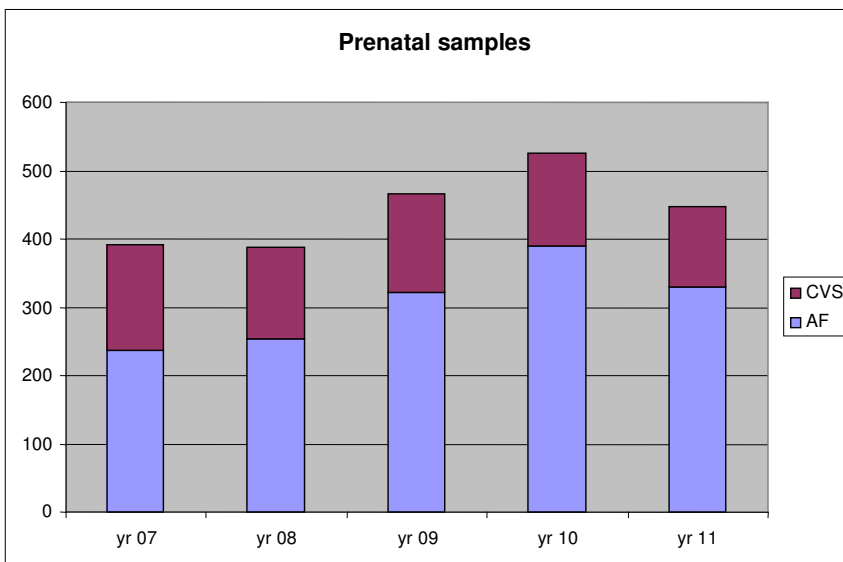
**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



**Fig 3:** Number of peripheral blood samples received in the Division of Cytogenetics during the years 2007 - 2011

As with peripheral blood samples the total number of prenatal samples had shown a gradual increase from 2000 onwards, primarily due to increasing numbers of chorionic villus samples (CVS). Until 2010 this sample number increase continued (see fig. 4), although in the latter years as the result of increases in amniotic fluid (AF) samples. This increase was halted in 2011 with a notable decrease in both sample types, although the total sample number was still in excess of 2008.



**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

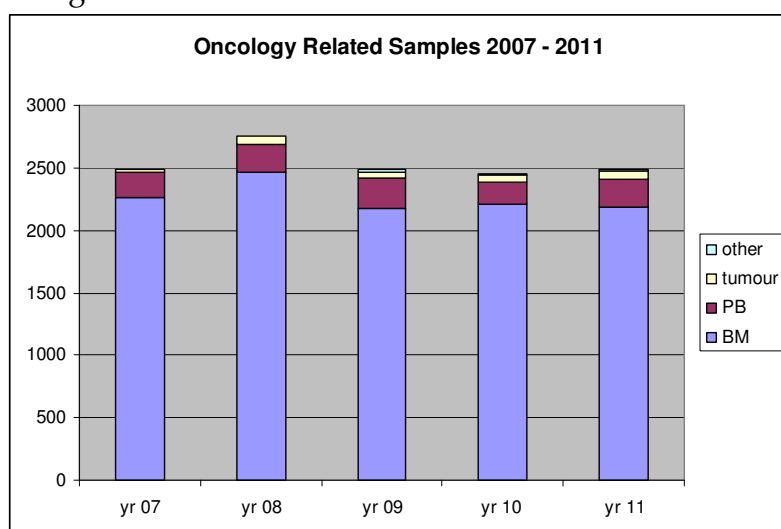
**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt

**Fig. 4:** The combined number of amniotic fluid and chorionic villus samples received in the Division of Cytogenetics during the years 2007 – 2011

The number of neoplastic related samples contrasts starkly with the other main sample types, with the exception of a small spike in 2008, there has been remarkably very little variation with approximately 2,500 samples being received every year (see fig. 5). The majority of samples are bone marrow (BM) aspirates, although more recently bone marrow smears have been received for some testing (see service changes for more details). Peripheral blood (PB) samples are also received, but in this instance the aim is to investigate for acquired genetic changes rather than constitutional.



**Fig. 5:** The combined number of neoplastic samples received in the Division of Cytogenetics during the years 2007 – 2011.

### 4.3 Service Changes

As already indicated in the previous sections the predominant service changes have been in the form of restrictions. The first restrictions were introduced at the start of 2008 when only tissues from live borns were accepted, until this point all tissue from post 26 week gestation were analysed. The major change occurred mid 2008, when in conjunction with the Division of Molecular Genetics, major restrictions were imposed due the significant backlogs that had arisen. Peripheral blood samples were most affected and initially only samples from children <1yr old were accepted for G-band analysis. This was subsequently revised to <5yrs early in 2010.

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



**Table 5:** Acceptance policy for constitutional samples as per end 2011

• Children (<5 yr old) for karyotype analysis
• Microdeletion syndromes for FISH-only analysis
• On-going family studies
• Tissue from live borns with documented abnormal phenotypic features

At the same time as the initial peripheral blood restrictions, an attempt was made to try and reduce the number of bone marrow samples that were not required by referring centres advising when non-urgent samples were being sent. This unfortunately proved unpopular with users and had to be abandoned. However, the issue of bone marrow samples that do not require cytogenetic analysis remains a major problem.

There have been changes to the service offered for some oncology samples with the introduction of a multiple myeloma FISH service in 2008 using bone marrow smears with documented evidence >15% plasma cell content and an increase in the number of paediatric tumours that are processed.

The Division has sort to encourage the use of buccal smears for FISH testing in situations where mosaicism is considered possible. The collection of cells is non invasive but gives the opportunity of testing fibroblast lineage cells for the presence or absence of markers, without the patient having to undergo a skin biopsy. The method is rapid and has proved particularly effective in situations where mosaicism has been shown in peripheral blood but the clinical phenotype is atypical.

Other changes can be said to represent an evolution of the service. New or different FISH probes are frequently employed for both constitutional and oncological disorders to ensure that the laboratory remains up to date with current best practice guidelines and scientific evidence.

#### 4.4 Accreditation

The Division of Cytogenetics applied for CPA accreditation in 2009 and was inspected in 2010. To help with the process a principal scientist took over the role as 50% quality manager, requiring the distribution of some of his previous duties to other staff members. Despite the large workload associated with the implementation throughout 2009, this was done without any compromise to the diagnostic service.

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

Following the initial full inspection, as expected, a small number of non-conformances (NCs) were raised and the Division obtained Conditional Accreditation. All NCs were cleared within the required time frame so that the Division received full Accreditation status early 2011.

The final CPA surveillance visit prior to the Division having to transfer to INAB is scheduled for early 2012.

### 4.5 Quality Assurance

The Division fully participates in the UKNEQAS quality assurance scheme for all test types that are performed at the centre.

Since 2008 the Division has provided an assessor for at least one UKNEQAS assessment each year.

The chief scientist was actively involved in the revision of ACC (Association of Clinical Cytogenetics) best practice guidelines for a number of neoplastic diseases and contributed to the revised European Cytogeneticist Association (ECA) Guidelines that were published in 2011.

A principal scientist was appointed as an advisor for the Clinical Laboratory Standards Institute (USA) to the subcommittee on Fluorescence *In Situ* Hybridisation (FISH) Methods for Medical Genetics. These guidelines are due to be published in 2012.

### 4.6 Teaching and Education

Staff from the Division have actively participated in the teaching and education of a wide range of students and other health professions. This has included students from DIT, TCD and UCD, and transition students. Staff have given lectures at a number of institutes to both Haematology and Pathology registrars.

Due to both funding and the need to ensure adequate cover within the laboratory to provide the diagnostic service the number staff attending external conferences has decreased since 2007. However, the Division has been more active in ensuring that abstract for posters or talks are submitted to those conferences that are attended.

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

### 4.7 Collaborations

The Division does not have any funded research but has participated in or offered active assistance to funded project groups including those from the CMRC and UCD.

### 4.8 Future Outlook

The Division will continue to face challenges due to unlikelihood of any dramatic changes to the economic climate in the near future. It must therefore, continue to strive to seek greater efficiencies and the most effective way of providing a diagnostic service for its users.

One major change and chance for the Division was the agreement by the CMRF to finance the purchase of array CGH equipment. This will be installed in the Division during 2012 with the view to also start offer this service during the year. Initially it is planned that the service will just be offered with OLCHC, thus establishing workflows etc, before offering the service to outside users.

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

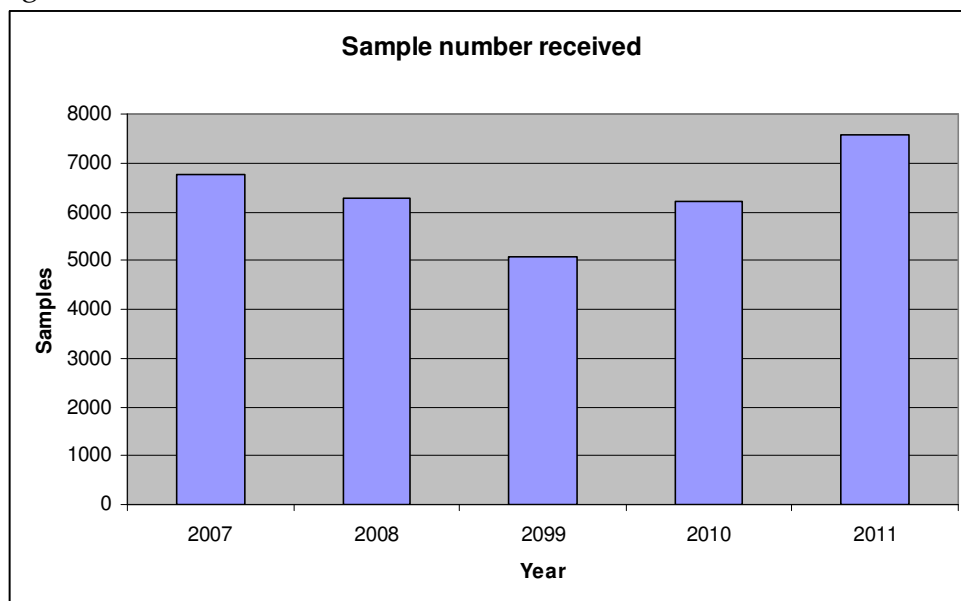
**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt

## 5 Division of Molecular Genetics

### 5.1 Sample Numbers, Reports & Staff numbers

The number of samples received in Molecular Genetics from 2007 – 2011 are shown below in figure 6.



**Figure 6:** Samples received each year. The drop in 2008-2009 is due to the service restrictions imposed in July 2008, lifted in February 2010.

Faced with staff cuts and a recruitment freeze in June of 2008, a decision was taken to curtail the services offered in order to ensure patient safety. The Hereditary Haemochromatosis (HH) (which has never received specific funding) was discontinued, while Fragile X testing was restricted to known Fragile X families. These restrictions resulted in a sharp drop in sample numbers in 2009. Restrictions on the Fragile X service were removed in February 2010. Sample numbers were up 15% in 2011 compared to 2010. Adding in CF newborn screening, numbers were up 21% to 7500. FRAX was the main mover, with 329 additional samples, a 55% increase. Across all the other in-house diseases, smallish sample number increases and decreases cancelled out exactly. Removing the anomalies caused by the service restrictions and the introduction of CF newborn screening, it is clear that there is an underlying trend for an annual increase of approximately 15% in requests for molecular genetic testing. With budgets and staff numbers declining each year, this provides a challenging environment in which to maintain a high-quality service which meets the demands of service users.

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

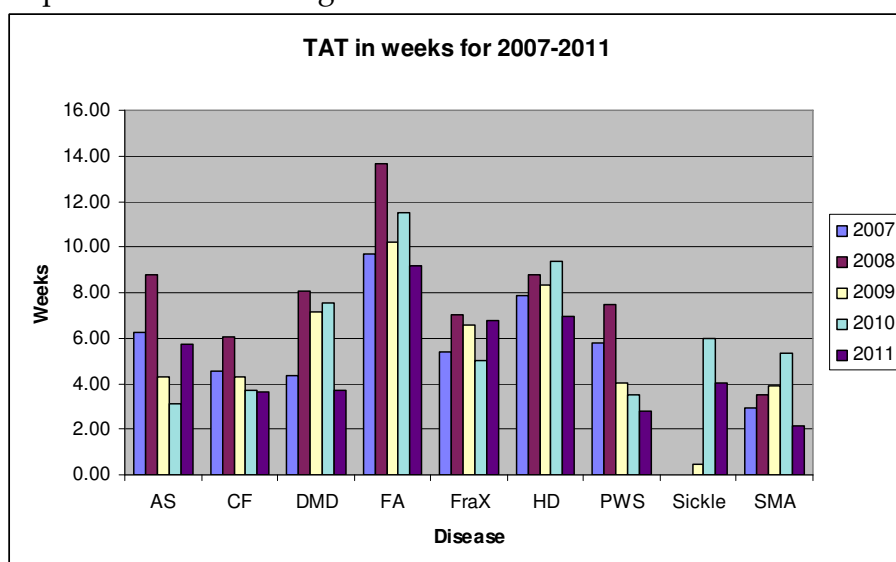
**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics Dublin, Ireland

Despite the increasing sample numbers, improving the time taken to issue reports (also known as turn-around time or TAT) has been an ongoing objective for all tests and was an issue identified in our user survey in 2009. Significant improvements in reporting (turn-around) times have been made in 2009; it was not possible in most cases to improve on these times further in 2010 & 2011. Notable exceptions were the two highest-volume requests, CF & FraX, where significant additional improvements were made. For the smaller-volume tests, changes in case mix (urgent vs. routine requests) can cause anomalies when comparing average reporting times. The scope for further improvements without additional resources is limited. Figure 7 shows that TATs improved across the board. This was achieved despite the staff shortages and the large amount of staff time devoted to preparation for accreditation inspections in 2009 & again in 2011.



**Figure 7:** TAT in weeks for 2007-2011

In addition to the in house testing, the division prepares DNA & acts as a send-out service for genetic testing to other laboratories worldwide. There has been a steady rise in these sample numbers has highlighted in Figure 8. In 2011 the number of samples sent away rose 23% in parallel to overall numbers, largely driven by a 51% increase in microarray requests. The number of arrays for sending away should drop significantly in 2012 & 2013 once the in-house array service begins.

These samples being sent out has lead to a loss of hard-won expertise from the Laboratory and making us very much less of a National Centre. It is certain that these tests could be performed more cheaply in-house, if the money was used to hire staff instead of paying for testing abroad.

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

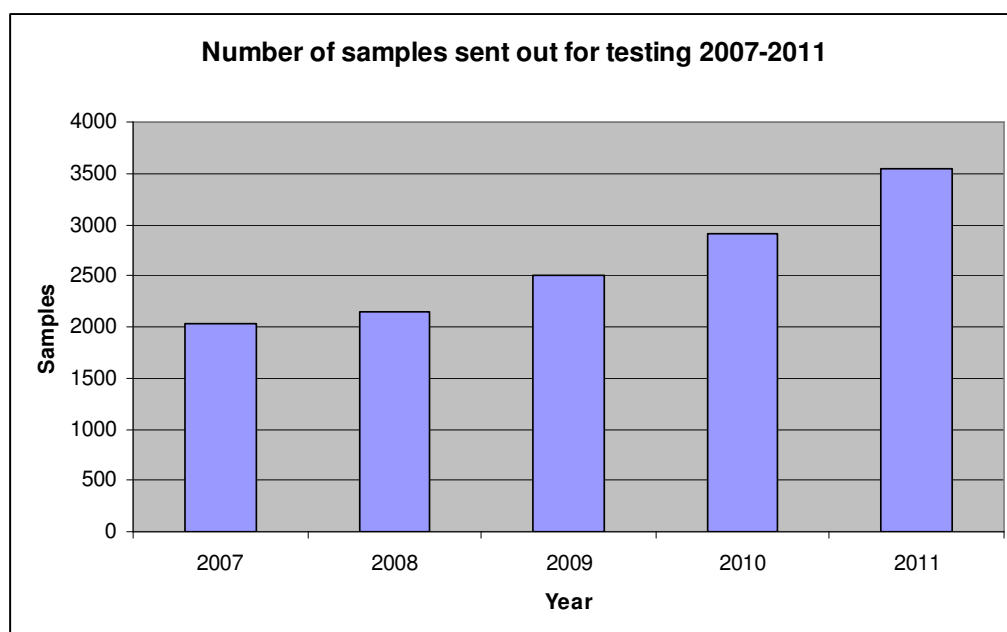
**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt





**Figure 8:** Number of samples sent out for testing from 2007-2011.

Due to the sustained tight financial position of OLCCH and the moratorium on recruitment and/or replacement of staff, 2007-2011 continued to present challenges for the management and organisation of staff resources. The introduction of CF newborn screening in 2010 led to the recruitment of 1 additional Clinical Scientist, 1 additional Genetic Technologist and an additional Grade 4 Administrator post shared 50/50 with Clinical Genetics. While CF NBS also brings with it an additional workload of 800+ samples per year, this boost to staff numbers has been very welcome. There is little prospect of any additional staff in the foreseeable future, unless the HSE takes up some of our business case proposals. At the end of 2011 the laboratory has an establishment of 25 staff (24.1 WTEs) across a range of skill mix. However, maternity leave, parental leave and long-term sick leave have reduced the available staff to 18.6 WTE.

An innovation in 2010 was the introduction of a graduate intern program. Biology graduates are given 2-4 month's unpaid work experience in the Division, providing the interns with a valuable enhancement to their CV and the Division with valuable clerical and technical assistance. However, these placements are necessarily short-term and therefore impose a heavy training burden on existing staff. The laboratory continues to rely on the help of graduate interns and students on work experience to carry out basic laboratory and office tasks. MGM and all Molecular Genetics staff have worked hard together with great team spirit to deal with these changes, to minimise the impact on services and maximise output

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

with decreased numbers of staff. It is a tribute to all staff that so much has been achieved despite the ongoing reduction of staff numbers.

The Irish Government, the Health Service Executive, Our Lady's Children's Hospital and the NCMG operate in a financial environment where resources are increasingly scarce, and the medium-term outlook is for this environment to get worse, not better. Much of the time of the Division's Management Group is taken up with juggling staff resources to maintain the service during maternity leave and long-term illness. The HSE's 2012 Service Plan, which envisages a further 7% cut in staff numbers across the HSE, does not indicate that there is any change in this outlook. The effects of HSE moratorium on recruitment include:

- massive pressure on lab office because staff reduced
- knock-on effect on laboratory staff doing admin work
- No replacement for Clinical Scientist on maternity leave – all other CS have to spend more time on rotas, training, reporting duties
- Delay in introduction of new tests
- Hiring of locums/replacements for staff leaving cannot commence, meaning inevitable delays in replacement staff starting, so effects of moratorium will be felt well into 2012.

Demand for molecular genetic testing continues to rise rapidly across all test types and sample numbers continue to increase. Such increases place the laboratory's staff and quality systems under great strain.

### 5.2 CPA Accreditation

A Senior Clinical Scientist (acting, half-time) voluntarily took up the role of Quality Manager in September 2008 & continued in this role throughout 2009, devising and implementing a quality management system and preparing the laboratory for accreditation. An observation raised at the CPA assessment in 2009 was that the current quality manager was fulfilling the role on a locum senior scientist basis, and there was the potential for the Division to lose the quality manager position when the post ceased in April 2010. A permanent senior part-time quality manager position was obtained in May 2010 and this was filled by the locum senior scientist acting as quality manager. This appointment was not on the full time as basis that had been hoped for, but the appointment was significant given the severe economic climate and recruitment moratorium. It was recognition by OLCHC of the importance of this senior permanent position and the crucial work of the quality manager to allow the Division of Molecular Genetics to continue meet the quality standards of Clinical Pathology Accreditation UK Ltd. In September 2011 the quality manager part time position became a permanent full time senior post.

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics Dublin, Ireland

In 2009 & 2010 a substantial investment of every staff member's time and laboratory resources and the first Clinical Pathology Accreditation UK Ltd (CPA) assessment was carried out in 2<sup>nd</sup> & 3<sup>rd</sup> February 2010. Accreditation was granted in June 2010 following closure of all NCs raised during the inspection held in February 2010. It was noted in the 2010 CPA report that 'the quality management system is well embedded within the department'. All members of the team play a part in managing and implementing quality and this has led to the evolution of a strong quality culture. The outcome of the assessment is evidence of the amount of preparation and work that has gone into the development of the quality management system. This is a huge achievement for the division and the NCMG and is testament to the hard work and dedication from all the staff in Molecular Genetics. The first surveillance visit was scheduled for February 14<sup>th</sup> 2012 and accreditation was confirmed in June 2012 for CPA UK. To comply with European legislation, CPA has been forced to withdraw from the Republic of Ireland. CPA will continue to support the NCMG until December 2013 but there will be no full accreditation inspection during 2013 and the NCMG will liaise with the Irish National Accreditation Board (INAB) with the prospect of being assessed under ISO 15189 during 2013.

### 5.3 Audits

In 2009 a program of internal audit was set up to audit the quality management system & examination processes within the division of Molecular Genetics. Training was provided both in house by members of the audit team and by an external trainer & a team of eight molecular staff was set up from different grades. Figure 9 shows the number of audits done by the number of auditors per year since 2009. The number of audits has been reduced over the last 3 years due to auditors stepping down due to workloads, maternity leave & extended sick leave.

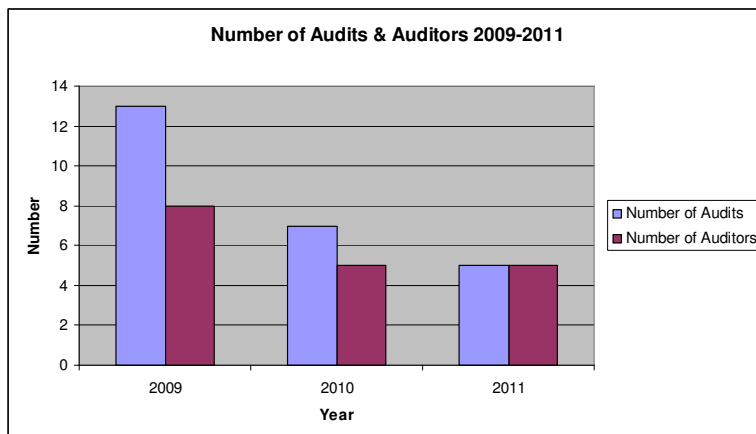


Figure 9: 13 audits were done by 8 auditors in 2009, 7 by 5 auditors in 2010 & 5 by 5 auditors in 2011.

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

### 5.4 User Survey

As part of our commitment to improving services at the Molecular Genetics Laboratory, we carried out our first user survey in 2009. The purpose was to seek the views on the service from our users. The survey was sent to 131 users and 57 completed surveys were received which is a response rate of 43.5%. A summary of the user survey report can be found on the NCMG website (<http://www.genetics.ie/documents/user-survey-aug-2009.pdf>). A second user survey is planned for 2012.

### 5.5 External quality assessment (EQA) reports

Participation in External Quality Assessment (EQA) is an essential part of the quality management system of the Division of Molecular Genetics. It is also a crucial element in informing both providers and users of the quality of the service provided. EQA schemes have a major educational component and go towards proving competency. They include assessment of the analytical service of the laboratory and the interpretations provided by members of staff. The Division of Molecular Genetics participates in the following EQA schemes:

- United Kingdom National External Quality Assessment Scheme (UK NEQAS) for Molecular Genetics
- European Molecular Genetics Quality Network (EMQN)
- Cystic Fibrosis (CF) European Network

In 2007 the Division of Molecular Genetics participated successfully in five UK NEQAS, seven EMQN and one CF Network (total 13 schemes, ~39 genotypes/reports) external quality assessment exercises, achieving perfect scores for genotyping and very satisfactory for interpretation.

For 2008-2009 the Division participated in six UKNEQAS, seven EMQN and one CF Network (total 14 schemes, ~42 genotypes/reports) disease or technique based EQA schemes. EQA performance was excellent for UKNEQAS and very satisfactory for EMQN (including the CF Network).

In 2009-2010 the Division of Molecular Genetics participated in five UKNEQAS, seven EMQN and one CF Network (total 13 schemes, ~39 genotypes/reports) EQA schemes. These schemes covered almost all aspects (domains) of the services offered by the laboratory. EQA performance was excellent for both UKNEQAS and EMQN (including the CF Network). The Laboratory performs extremely well in these UK and European EQA schemes, consistently ranking in the top 10% of laboratories with similar test repertoires. As the EQA feedback meetings are an excellent format to see 'at one go' the diversity of reports issued by the

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

laboratory, the necessity of a consistent 'new look' report format was recognised and was logged as an improvement idea.

For 2010-2011 the Division participated in nine UKNEQAS, seven EMQN, one CF Network and one new SPIDIA-DNA Ring Trial. This was a total of 18 schemes, 61 genotypes and 45 fully interpreted reports. EQA performance was perfect for EMQN (including the CF Network), excellent for UKNEQAS and very good for the new SPIDIA-DNA scheme.

The SPIDIA-DNA Ring Trial is a new European Project ([www.spidia.eu](http://www.spidia.eu)) aiming to address the standardisation and improvement of pre-analytical procedures for in-vitro diagnostics. One specific work package is dedicated to the pre-analytical procedures for blood samples, where the purity, concentration and quality of provided blood DNAs and DNA prepared from provided blood was assessed. The laboratory performed very well in this scheme, and it helped to address for the first time system improvements related to the pre-analytical phase (i.e. DNA preparation and concentration) that could have an impact on test results.

As the EQA schemes are an excellent way to see the diversity of reports issued by the laboratory, the need for a consistent generic reporting format was further explored. This resulted in the generation of a new agreed (colour coded) reporting template, which will be controlled in Q-Pulse and phased into use in 2012. These excellent EQA results are testament to the very hard work, skilled expertise and commitment to quality that is shown by the staff of the Division of Molecular Genetics, and is particularly commendable in the current challenging environment.

### 5.6 Training & Education in Molecular Genetics

The training budget for 2010 and 2011 was reduced €2000 for Molecular Genetics. In the face of such budgetary restrictions, the Division of Molecular Genetics continues to try and maximise dissemination of information from attendance at courses and conferences. The division also continues to source and access as many free resources as possible to advance CPD, including desktop conference facilities. The Division has introduced its own CPD points system which will be fully implemented in 2012. This system will help evaluate the amount and content of individual CPD activity and highlight any deficits that may be contributed to by lack of funding. Training relating to service provision (i.e. staff skills etc) is overseen in the Division by a Training Officer and MGM. Formal training programmes were devised for each staff grade and implemented for new trainees in 2011. Competence assessment requirements and procedures were devised for process and disease portfolios and will continue to be implemented in 2012. Both the training and competence assessment programmes were commented on in the most recent CPA inspection as being one of the best seen. The CPD

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

points acquisition and ongoing training needs are incorporated into the Joint Annual Review process and followed up by MGM. Wherever possible, in-house training is planned and provided by staff that have previous external training on a skill. It remains to be seen if these efforts are sufficient to achieve and maintain the international standards required in the continuously evolving and changing field of medical molecular genetic diagnosis.

### 5.7 *Molecular Genetics changes in service 2007-2011*

#### 5.7.1 **Suspension & temporary cessation of services**

Faced with staff cuts and a recruitment freeze in June of 2008, a decision was taken to curtail the services offered in order to ensure patient safety. The Hereditary Haemochromatosis (HH) (which has never received specific funding) was discontinued, while Fragile X testing was restricted to known Fragile X families.

In 2009 a decision was made to stop in-house pre-screening testing of the two Irish common BRCA mutations prior to sending out for full mutation BRCA screening. Due to in-house batching of this testing for economic and efficiency reasons, this had the net effect of slowing the overall turn around time of samples for mutation screen down and it was considered that the pick-up rate of the Irish mutations did not warrant this delay. A decision was also (reluctantly) made to out-source breast cancer predictive testing until the resources were available to continue this work in house. It is planned to re-introduce this service in 2012 if resources permit.

Since the re-introduction of microsatellite instability (MSI) testing for the investigation of Lynch syndrome (previously known as HNPCC) in 2008, the Histopathology laboratories of Our Lady's Children's hospital provided IHC testing for the MMR proteins involved in Lynch syndrome. Part of this process was also to cut and prepare slide sections from patient tumours for subsequent DNA preparation and MSI analysis. Unfortunately, the Histopathology lab had to cease the provision of this service in early 2011, and an adult hospital in Dublin was approached late in 2011 to provide this service. A response is awaited. Meanwhile, MSI testing has been temporarily suspended, pending a reply. Users of the service (primarily the Clinical Division of the NCMG) are fully apprised of the situation and the Director is actively engaged in both approaching an alternate provider and procuring a response. It is hoped to resume MSI testing very early in 2012 once this is resolved.

Due to the concurrent maternity leaves of three very experienced clinical scientists (including one Principal) in 2011, two of which were the lead reporting / checking scientists for

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

Duchenne muscular dystrophy (DMD) and spinal muscular atrophy (SMA), a decision was made to temporarily cease in-house testing for DMD and SMA. A major contributory factor was the imminent implementation of the CF NBS service also in 2011, as the third scientist was a lead reporting / checking CF scientist. It was decided that there simply wasn't sufficient clinical scientist resources to sustain DMD/SMA testing and introduce the CF NBS scheme. It is hoped to resume DMA and SMA testing in-house in 2012.

### 5.7.2 New services

2007 saw the introduction of a new diagnostic service for a rare disease present in the Irish Traveller Community, Byler disease (progressive familial intrahepatic cholestasis). In 2009 two new services were introduced. A prenatal service for sickle cell anaemia and a diagnostic service for osteogenesis perfecta type VIII. Whilst the sample numbers for all these new services are small, the clinical impact is significant. The new sickle service will avoid having to send-out sickle PNDs to external laboratories which have been extremely challenging and difficult in the past. The new Byler and OI services offer previously unavailable genetic tests for Irish Traveller families with unique mutations in the ATP8B1 and P3H1 genes, respectively. The introduction of the prenatal sickle service also saw the validation of the EZ1 DNA preparation robot for direct amnio samples, a change in process that will be introduced to all prenatal samples (including CVS) in 2010.

Also in 2009, a new analytical method for Prader-Willi and Angelman syndrome testing, based on MLPA, was validated and introduced into service. This new method brings benefits in sensitivity, specificity and robustness over the previous MS-PCR method. As the method can distinguish PWS or AS caused by a parental deletion from that caused by uniparental disomy, parental testing is required much less frequently, and karyotyping or FISH are rarely required. We have written to our service users to advise them not to send requests for karyotyping for PWS and AS diagnosis, just to send EDTA samples for MLPA testing. This reduction in FISH and karyotyping will result in significant savings.

There were no totally new services introduced in 2010, but restrictions in the fragile X service were lifted in April 2010 to allow a full fragile X service to resume. This was in conjunction with a substantial softening of restrictions in the Division of Cytogenetics for routine constitutional cytogenetic samples, which often request fragile X testing in tandem with a routine karyotype for childhood developmental delay. To facilitate the lifting of restrictions in 2010 PCR-based assays were investigated. In 2011, the validation of the Amplidex FMR1 kit (Asuragen Inc.) was completed and incorporated into the existing NCMG Fragile X testing protocol. The CE marked assay is based on gene-specific FMR1 PCR, CGG Repeat Primed PCR and ABI Prism 3130xl Genetic Analyzer protocols and allows the detection of all classes

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

of FMR1 alleles, including full mutations. Service users were informed of the lifting of restrictions, coupled with a comprehensive synopsis of the current service now being offered, for clarity and ease of use. The introduction of the Amplidex assay has resulted in the cessation of Southern blotting with radioactive DNA probes and this change-over, in conjunction with Fragile X requests being processed by the robotic DNA preparation method (EZ1 system), has substantially reduced laboratory workload.

### 5.7.3 Cystic Fibrosis Service – New Born Screening (NBS) and a new assay

Planning for a National Cystic Fibrosis (CF) newborn screening programme (proposed implementation July 2010), commissioned by the Department of Health & Children (DoHC) began in June 2009. Funding was received at the end of 2009 to purchase equipment to support this implementation. This was run in conjunction with the National Newborn Screening Programme for inherited metabolic and genetic disorders, based at the Children's University Hospital, Temple Street, Dublin. Detailed literature reviews led to an NCMG proposal of a 99<sup>th</sup> centile IRT threshold to trigger DNA testing, which was accepted by the Steering Committee. The program will result in an estimated 1,200 additional CF tests each year and has created four new posts at the NCMG. The Luminex platform for newborn screening was also implemented in-house for routine CF testing.

CF Newborn Screening, which is carried out in conjunction with the national newborn screening programme for inherited metabolic and genetic disorders, based at the Children's University Hospital, Temple Street, Dublin, began on 1<sup>st</sup> of July 2011. The NCMG receives a dried blood spot sample on the top 1% of newborns found to have an elevated IRT result.

As of 31<sup>st</sup> December 2011 (6 months), 391 newborns have been tested for CF mutations as part of this programme for early CF diagnosis. Of these 391 patients, thus far 15 patients have been found to have 2 mutations following our analysis. A diagnosis of CF for these patients is confirmed following a sweat chloride result of >60mmol/L. A further 34 patients have been found to have 1 CF mutation following initial analysis. These 34 patients will then proceed to have a sweat test to establish if they are at risk of having CF or simply a carrier of a CF mutation.

The assay used to analyse all the CF NBS samples, as well as all routine CF samples received to the NCMG, is the Luminex xTAG CF39 assay which tests for 39 CF mutations and 4 variants. The 39 mutations include the 23 mutations that are currently recommended by the American College of Medical Genetics and American College of Obstetricians and Gynaecologists (ACMG/ACOG) and 16 of the worlds most common CFTR mutations. The use of this assay allows for the detection of ~93.5% of CF mutations seen in the Irish population.

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt

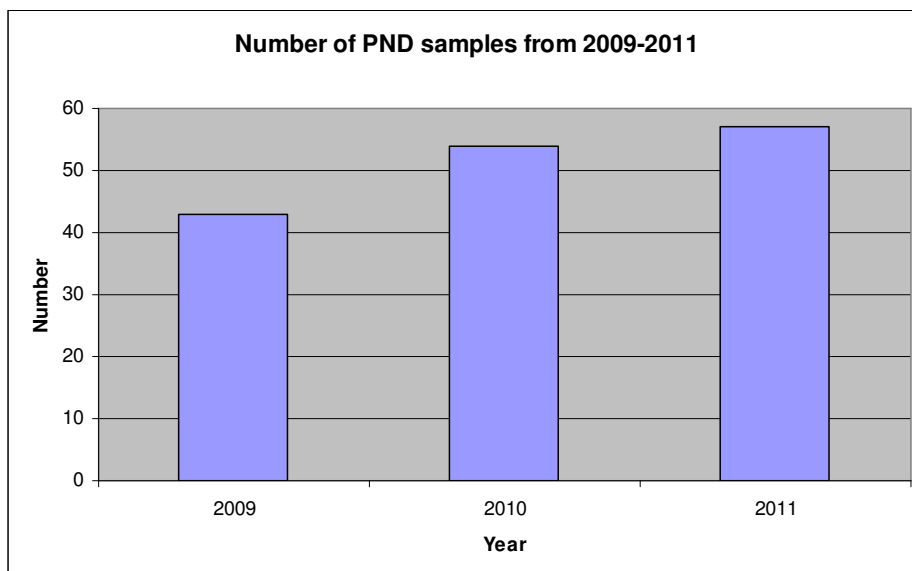




**5.7.4 Prenatal diagnostic service**

The PND programme continues to present challenges to the service. Some of these challenges include samples getting to NCMG on time, increasing numbers of PND samples and the complexity of each sample along with continued staff reductions in all divisions. Interdivisional PND meetings are held each year to ensure continued ongoing improvements to policies, procedures & communication between the NCMG divisions and with the external testing laboratories.

The number of PND samples are on the increase and Figure 10 shows the number of samples from 2009-2011. These figures don't include those PND samples that were planned but not taken. The number of samples going for foetal sexing are on the increase for X-linked disorders which reduces the need for PND in those families.



**Figure 10:** Number of PND samples from 2009-2011

The sickle cell anaemia PND service was introduced in late 2009 & was fully implemented in 2010 and has greatly improved the accessibility and convenience of this service to our users (primarily the Division of Clinical Genetics) and eliminated previous problems accessing and liaising with external test providers.

Future plans include the implementation of EZ1 preparation system for direct CVS's and Maternal Cell Contamination (MCC) on cultured CVS/amnios. This will reduce hands on time of technical staff and will make preparations more efficient. However future

<b>Clinical Authors:</b> Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. <b>Cytogenetics Authors:</b> David Betts.	
<b>Molecular Authors:</b> Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.	
<b>Admin Authors:</b> Lisa Malone, Sally Ann Lynch, Damien Moyles.	
<b>Collated by:</b> Christine Brady, Sally Ann Lynch, Alana Ward	<b>Authorised by:</b> NCMG Mgt
<b>Page 33 of 90</b>	



developmental plans for the PND service will depend on staffing resources and budgetary constraints.

### 5.7.5 DNA Preparation

The new Qiagen EZ1 'Advanced' DNA preparation robot was successfully validated for the xTAG CF39 kit and dried blood spots on the Luminex platform as part of the implementation of the CF NBS programme, which occurred 1st July 2011. The older EZ1 DSP Biorobot was also validated to provide backup.

An ongoing project to validate the 'Advanced' EZ1 robot for the preparation of DNA from chorionic villus prenatal samples resumed in 2011. This introduction will reduce the need for the use of the hazardous chemical phenol and to substantially decrease the process time for these time sensitive samples. Work progressed well throughout the year, with the introduction of the EZ1 robot for all specified CVS DNA preparations late 2011/early 2012. External laboratories providing PND testing will also be asked as to whether they can accept EZ1 purified CVS DNA for their analysis, increasing the number of samples that can be prepared in this more automatic fashion.

In 2011 a total of nine patient tissue samples were received, which is over double those received in 2009. DNA was prepared using the manual Qiagen DNeasy column kit from a number of tissue types (placenta, spleen, adrenal tissue, liver, tumour, brain and muscle). It is intended to also validate these tissue preparations on the EZ1 platform in 2012.

Preparations from fibroblast cultures also increased during the year, on average one per two weeks. Following a query from the Division of Cytogenetics as to whether culturing was always necessary, an audit was performed. The outcome was that culturing is necessary, to provide sufficient DNA for subsequent analysis. Consequently, all fibroblasts are to be cultured and the processing (clinician/external lab liaison/preparation) is to be co-ordinated via the PND pipeline in Molecular.

There is an ongoing requirement for a higher-throughput DNA preparation instrument; it is unlikely that the laboratory can expand its services or deal with the year on year sample increases and complexity while relying on the current mix of small-scale EZ1 preparations and labour intensive manual protocols.

### 5.7.6 Genetic & Rare Disorders Organisation (GRDO)

The NCMG, represented by Prof David Barton, continued its close interactions with an alliance of stakeholders representing patients and others affected by rare diseases. A

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

National Rare Diseases Conference was held in January 2011. The alliance and the conference are targeted at the development of a national rare diseases plan, as required of the Irish government under the European Council Recommendation on European Action in the field of Rare Diseases of June 9, 2009. A steering group has been set up for this purpose at the Department of Health. NCMG staff are actively involved in the broader Rare Diseases.

### 5.8 *Molecular Genetics plans for 2012 & onwards*

#### 5.8.1 **Service planning & implementation of copy-number variation analysis**

Copy-number variation analysis identifies genomic imbalance at a level of resolution higher than that achievable by G-band karyotyping, and is currently employed in many diagnostic laboratories to investigate selected patients with learning disabilities and dysmorphism/congenital abnormalities. The higher resolution achievable by arrays has also allowed more detailed evaluation of breakpoint locations and gene content. For these reasons, the use of copy-number variation analysis in genetic diagnostic testing is increasing rapidly. The Division of Molecular Genetics has in association with the Divisions of Cytogenetics and Clinical Genetics through NCMG management recognised the absolute need for the implementation of copy-number variation analysis into the service repertoire of the NCMG. To this end both Molecular Genetics and Cytogenetics staff have attended UK based meetings. Criteria for the selection of external service providers for copy-number variation analysis have been defined. In the medium term, an NCMG planning group has been set up to identify sources of funding and/or service agreements, and to ascertain an appropriate microarray platform and the bioinformatics personnel necessary to introduce this service.

The NCMG planning group with responsibility for the implementation of copy-number variation 'array' analysis was successful in sourcing funding from the Children's Medical Research Foundation in mid 2010. All Divisions of NCMG will liaise to develop new sample pathways for the diagnosis of children with intellectual disability in 2012.

#### 5.8.2 **Breast Cancer (BRCA) service**

BRCA predictive samples and the BRCA full screening samples are sent to Birmingham for analysis. Patients are currently seen in cancer genetics clinics held in NCMG with Prof Andrew Green and NCMG genetic counsellors; and in St James's Hospital with Dr David Gallagher and SJH genetic counsellors. The number of clinics are due to increase in 2012 due to additional clinics being held in the Mater Misericordiae (May) and NCMG (April) by Dr David Gallagher. This is expected to result in an increase in BRCA sample numbers during

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

2012. It is planned that BRCA predictive testing will be set up in the laboratory in NCMG during the second half of 2012. In the first instance, analysis will be by sequencing analysis with primers provided by Birmingham and using Mutation Surveyor to analyse the data. Once the sequence-based tests have been established, work-up of MLPA-based tests will proceed. Patients with MLPA-detectable mutations comprise approximately 2-3% of the total number of patients and these will continue to be sent to Birmingham in the interim.

### 5.8.3 Service planning & implantation of Next Generation Sequencing

New genetic technologies are revolutionising medicine. Recent advances in next generation sequencing (NGS) technologies have brought about a paradigm change in how medical researchers investigate human disease. These transforming technologies are now bringing a major shift in clinical practice in terms of the diagnosis and understanding of genetic disorders. NGS is set to change medical genetics and the diagnosis of genetic disease in the same way that mobile phones and the internet have revolutionised global communication and information systems.

NGS permits the study of mutations and their role in disease in a systematic genome wide (global) manner, in comparison to previous sequencing methods that could only look at one very small part of one gene at a time. It is now being used in clinical diagnostics for the accurate, rapid and cost effective identification of changes in targeted genes e.g. CF & BRCA1/2. It is also being applied to target 'gene packages' (e.g. cardiomyopathies, sensory disorders, neuropathies and muscular dystrophies) and 'whole exome sequencing' – such as for children with learning disabilities or mental retardation, where the entire coding DNA of all known genes was sequenced and *de novo* mutations identified.

The Division of Molecular Genetics recognises the need to acquire and introduce this technology into the service, and has incorporated this into the Business plan submitted to the HSE in 2011. This initial business strategy is to use this high through put, massively parallel sequencing technology to test more cheaply in-house for the diseases that are currently sent out (at a very significant cost ~€475,000 in 2010). NCMG management also supports this approach, and MGM have actively worked to put a proposal to the Hospital's Medical Equipment Procurement Committee to acquire a NGS platform and set up costs which will be submitted in 2012.

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## 6 Administration

The administrative team at NCMG provides essential support to all three divisions and are an integral part of the centre as a whole. As of the end of 2011 there were 7.17 WTE administrative staff in NCMG – this was divided between the Clinical, Molecular and Cytogenetics divisions. In terms of administration, the NCMG operates as a standalone service within our Lady’s Children’s Hospital, Crumlin. We do not use the hospital clinical or laboratory booking systems. Rather all clinical appointments are booked and sent directly from NCMG, and all laboratory referrals are booked and processed on the respective Molecular Genetics and Cytogenetics databases. Clinical administrative staff assist with triage, set up patients on our specialised database system, create family medical records before booking appointments, and then type and send out clinical letters. Administrative staff are the first point of phone contact for both families and clinicians. As a national centre they also deal with a high volume of general enquires. They oversee the administration section in the laboratory from booking in samples on two laboratory databases (total number accounting for approximately 13,000 per annum) to the issuing and posting of reports. They deal with telephone enquiries regarding results of tests and the payment of invoices for tests sent abroad (approximately 3,000 per year).

Ms Lisa Malone performed an audit on the Clinical appointments Failure to Attend rate (currently 8%). Recommendations following the audit included: reviewing the appointment letter sent to patients, making it more administrative friendly, contacting families by telephone who do not confirm their appointment to ensure optimum attendance and texting patients as a reminder to attend their clinic appointment. NCMG plan to implement a new texting reminder to patients in the near future.

The administrative staff undertook a Time Management & Change Management training day on 8th December 2008, which was very beneficial due to the complexity and ever-changing role the administrative team provide.

The introduction of iGene, a new specialised database system for both the Clinical and Cytogenetic divisions in November 2010 had a major beneficial impact on administrative staff.

New cancer clinical referrals require a high volume of administrative support as questionnaires are sent to approximately 85% of families requesting them to complete the form to enable NCMG provide patients with a more accurate assessment of potential cancer in the family and whether there may be a hereditary component.

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



# National Centre for Medical Genetics

Dublin, Ireland

The NCMG store all our patient records for the clinical division on site and currently have over 20,000 patient records. Our records are family based as opposed to individual files, and as such are stored separately in NCMG and not in the main OLCHC filing room.

The Government and HSE public sector staff embargo has impacted greatly on our Administrative staffing numbers.

We welcomed Ms Audrey Lewis to the NCMG in January 2011 as Secretary to Prof Green. In December 2011 Audrey was offered the Administration post which was secured by the advent of CF new-born screening.

Tragically in May 2011, one of our valued staff members, Ms Catherine McKenna, passed away suddenly whilst at work. Catherine had worked with NCMG for 6 years having previously worked within OLCHC with the Department of Psychiatry. Catherine was a popular member of our team and her loss was a great shock to us all at NCMG.

## 7 IT Systems

### 7.1 *iGene Database*

Due to the unique nature of genetic testing and the need to link family members, NCMG requires specialised laboratory and clinical databases. Since 1994 the Division of Molecular Genetics have used an in-house designed MS-Access database (Crumbase). From 1998-2010 the Divisions of Clinical and Cytogenetics used an Access 97-based Shire database.

From mid-2009 the Shire database was no longer supported, resulting in a significant clinical risk. Funding was granted from the Children's Research & Medical Foundation (CMRF) in April 2009, with approval obtained from the Information Communication and Technology department in the HSE in June 2009, for a new web based Genetics Database called 'iGene'. Following months of detailed discussions with Genial Genetics Solutions the iGene database was modified to allow it to meet the needs of both the Clinical and Cytogenetic Divisions. We went live in November 2010. The implementation and transfer of data of 75,000 patients and test results from the Shire database was project managed by Damien Moyles, NCMG manager.

iGene allows the management of patient waiting lists, appointments, and outcomes so that clinical activity can be more easily tracked than previously. It also facilitates the embedding

<b>Clinical Authors:</b> Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. <b>Cytogenetics Authors:</b> David Betts.
---

<b>Molecular Authors:</b> Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.
--

<b>Admin Authors:</b> Lisa Malone, Sally Ann Lynch, Damien Moyles.
--

<b>Collated by:</b> Christine Brady, Sally Ann Lynch, Alana Ward
--

<b>Authorised by:</b> NCMG Mgt
--------------------------------



## National Centre for Medical Genetics

Dublin, Ireland

of patient letters, clinical photographs and scanned images into the database. As would be expected from a modern database it allows the Division of Cytogenetics to log in samples and generate reports as a pdf. It has proved to be to be a much-improved management tool compared to Shire with the ease that data can be extracted to generate statistics.

The system is embedded into the hospital IT network allowing for regular data backup. It is protected to prevent external access and password protected for all users, with varying levels of data access depending on staff grade and Division.

Whilst this represents a system upgrade from the old database 'Shire' for the Divisions of Cytogenetic and Clinical Genetics, it is a major change for the Division of Molecular Genetics and will affect every aspect of every process. There was no functional iGene Molecular Genetics module ready to allow its implementation during 2010. We continue to liaise with the software providers 'Genial' in 2011 to introduce this web-based system to Molecular Genetics and the entire NCMG. Work has started on the implementation of the new system and will continue with increased impetus in 2012 & 2013. This will no doubt bring challenges, but also very welcomed efficiencies for all the processes in the laboratory.

### 7.2 *Electronic Data transfer*

Due to the many outreach clinics offered by NCMG issues with the transfer of confidential patient data remain a challenge. It is critical to secure a safe IT link that allows direct data transfer electronically between NCMG and the hospitals where NCMG clinics take place. A meeting held in 2006 involving IT staff from OLGHC & the Children's University Hospital, Temple St, as well as IT staff from St James Hospital did not result in any new developments. This issue was re-visited in 2010 and unfortunately all issues from 2006 remained unresolved. We met with the data protection office proactively to explain our problems.

### Meeting with IT from CUH

Date	Present	Agenda
06/03/10	David Wall Head of IT CUH Lucy Nugent CUH Clinical and Patient Services manager Andrew Green NCMG Sally Ann Lynch NCMG Debby Lambert NCMG Damien Moyles NCMG	Issues relating to trying to provide a safe service to the Children's University Hospital at Temple Street & minimise risks relating to data protection by improving secure IT .

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



**Meeting with the Data protection office**

Date	Present	Agenda
08/07/10	Deputy Data Commissioner Gary Davis Senior Compliance Officer Ciara O'Sullivan Andrew Green NCMG Sally Ann Lynch NCMG Debby Lambert NCMG Damien Moyles NCMG	Issues relating to trying to provide a safe service to the Children's University Hospital at Temple Street (& outreach clinics in Cork, Galway & Limerick) & minimise risks relating to data protection.

## 8 Engagement with HSE & DoH

NCMG Management has been actively pursuing interaction with the HSE and the NHO to address service difficulties and deliver a 'vision' for the provision and organisation of Medical Genetic Services in Ireland. A meeting with the HSE in early 2011 resulted in the creation of a 'business plan' to underpin this vision. This plan outlined the cost savings that could be achieved by the HSE in undertaking genetic tests within the NCMG instead of sending these tests abroad, plus the cost savings achievable by upgrading and implementing efficient automation and laboratory management systems. The proposal requires a capital investment to maximise efficiency and use of automation and an additional staff requirement. This business plan was submitted to the HSE for consideration. A meeting was held with HSE officials in November 2011 to discuss the possible staged implementation of this plan. Unfortunately, the proposals are not included in the HSE's Service Plan for 2012 and the prospects for funding are slim.

The NCMG has concerns about HSE-funded units directly outsourcing genetic tests abroad, both with respect to the quality of the tests provided and the lack of appropriate oversight of such testing in Ireland.

The NCMG has submitted a series of documents to the HSE outlining proposals for the development of genetic services and a framework in which these services can be delivered. The NCMG also met with the HSE to clarify the role of the NCMG in the future proposed National Paediatric Hospital. A list of those meetings, and of the documents submitted, is outlined below.

### Meetings with HSE Management

<b>Clinical Authors:</b> Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. <b>Cytogenetics Authors:</b> David Betts.	
<b>Molecular Authors:</b> Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.	
<b>Admin Authors:</b> Lisa Malone, Sally Ann Lynch, Damien Moyles.	
<b>Collated by:</b> Christine Brady, Sally Ann Lynch, Alana Ward	<b>Authorised by:</b> NCMG Mgt
<b>Page 40 of 90</b>	





## National Centre for Medical Genetics Dublin, Ireland

Date	Present	Agenda
30/07/08	Ann Doherty (NHO) John Bulfin (HSE) Fionnuala Duffy Lorcan Birthistle	Future of NCMG in light of recruitment/resource restrictions Capital for ICT and lab automation Genetics tests going abroad
26/01/09	Ann Doherty John Bulfin Fionnuala Duffy Paul Kavanagh	Future of NCMG Capital for ICT and lab automation Quality concerns re genetics tests going abroad
11/03/09	Ann Doherty John Bulfin Fionnuala Duffy Paul Kavanagh	Future of NCMG Capital for ICT and lab automation Quality concerns re genetics tests going abroad
24/04/09	Ann Doherty John Bulfin Fionnuala Duffy Paul Kavanagh	Organisation/governance of Medical Genetics Services Needs assessment for Medical Genetics Quality concerns re genetics tests going abroad
15/03/10	Brian Gilroy Eilish Hardiman Emma Curtis Colm Costigan David Vaughan	Inclusion of NCMG in NPH
22/09/10	Brian Gilroy Eilish Hardiman Emma Curtis	How to integrate NCMG into NPH
17/10/11	Brian Gilroy	Provision for NCMG in context of new NPH
13/10/11	Gerry McKiernan	NCMG business plan 2011
21/10/11	Philip Crowley Gerry McKiernan	Clinical Risk Assessment document discussion

### Meetings with Minister for Health & Children Mary Harney

Date	Present	Agenda
21/07/09	Minister for Health John Devlin Genetic & Rare Diseases Association representatives	Provision of services for rare diseases; NCMG role in rare disease services
17/09/10	Minister for Health John Devlin Fergal Lynch	Official opening of new labs at NCMG Inclusion of NCMG in NPH The future of Medical Genetics services in Ireland

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



**National Centre for Medical Genetics**  
Dublin, Ireland

OLCHC Board	CF newborn screening Staff shortages/clinical risk Medical Genetics training programme Designated contact persons in HSE and DoH
-------------	---

**Meeting with Chief Medical Officer Dr Tony Holohan**

Date	Present	Agenda
21/09/09	John Devlin	Funding crisis in NCMG Governance of NCMG

**Reports and Documents submitted by NCMG to the HSE regarding the future of Medical Genetics services in Ireland**

Document	Report type	Date submitted
Capital Proposal to the HSE National Hospitals Office	Business plan	Nov 2008
The National Centre for Medical Genetics at the National Paediatric Hospital (attached as Appendix 2)	Planning document	Jan 2010
Policy and Framework for the Delivery of a National Medical Genetics Service-	Full Needs assessment	Mar 2010
Short term needs for NCMG Service delivery	Short needs assessment	Mar 2010
Request for a workforce planning assessment to MetB unit HSE	Letter	Mar 2010
Clinical Risk Assessment of the practice of genetic test samples being sent by hospitals directly to commercial laboratories abroad	Risk assessment document	May 2010
Repeat Request for a workforce planning assessment to MetB unit HSE	Letter	May 2010
NCMG Report	Business plan	Mar 2011
Rethinking Genetic Testing Services for Ireland Executive summary	Business plan	Oct 2011

## 9 Premises and Environment

The clinical, laboratory, office, and staff facilities, occupied by the NCMG have been greatly improved since the Phase 1, 2, & 3 extension and renovations were completed during three project stages during 2007 and 2008. The NCMG now occupies a floor are of 1,352 square metres (14,553 square foot) and has the building facilities necessary for a national genetic service. The Minister for Health and Children, Ms Mary Harney TD, the CEO and members of the Board of OLCHC, HSE representatives and hospital/NCMG staff attended an official opening of the extension in September 2010.

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

Since October 2009 and throughout 2010 OLCHC continued its engagement with the planning process for the new National Paediatric Hospital (NPH). Early in 2010, the NPH Development Board expressed doubts as to whether the NCMG would be physically located within the NPH. A document entitled “The National Centre for Medical Genetics at the National Paediatric Hospital” was submitted by the NCMG Management team to the NPH, giving a clear and unequivocal justification for the full integration of the NCMG in the NPH. This resulted in the affirmation of the need for a genetic service within the NPH, but the exact location and size of the NCMG clinical and laboratory space is still to be defined. The NCMG will continue to liaise with the NPH Development Board to further engage with the design brief for the new hospital and plans for NCMG clinical and laboratory space.

Below is a schedule of meetings between 2009 and 2011 which took place between NCMG staff and the NPH, or health Partnership acting on behalf of the NPH.

### Meetings with NPH Planning & Design Team

Date	Meeting with	Agenda
23/01/09	Health Partnership	Initial meeting, scope
12/02/09	Health Partnership	Space planning
08/04/10	Health Partnership	Planning: OPD, interactions with other specialities, laboratory, ICT requirements
15/06/10	O’Connell Mahon Architects, & NPH Development board Health Partnership	OPD workshop
28/06/11	Healthcare Planning NPH Executive NPH Design Team	Planning OPD: Metabolics, Homecare and Genetics
7/9/11	Healthcare Planning NPH Executive NPH Design Team	Planning OPD: Metabolics, Homecare and Genetics

## 10 Procurement & management of equipment

As part of revenue-saving measures, all support contracts for equipment were renewed in 2009 on a “preventative maintenance only” basis. Very substantial savings were achieved. Contracts were scrutinised to ensure that no increase in agreed response times resulted from this change. The Hospital has acknowledged that it has now taken on the risk that a major piece of equipment will fail and that parts may need to be replaced at the Hospital’s cost to ensure that the laboratory service can continue.

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



The CPA assessment in 2009 identified a deficiency in the archiving of reports issued by the laboratories. This poses a risk that reports could be lost in a fire or other disaster. This issue was brought to the NCMG Management Committee, where it was agreed that a document scanning system should be sought through the Hospital's equipment procurement process. Such a system would allow all reports to be archived electronically and backed up on the Hospital's secure backup system. A plan to submit a proposal for a scanning system for the medical equipment procurement committee OLCHC will be formulated in 2012 for the NCMG.

## **11 NCMG Specimen Reception Committee**

A new joint laboratory (Molecular Genetics & Cytogenetics) Specimen Reception area was brought into service late 2008 and work to integrate, formulate and improve Specimen Reception policies and procedures has successfully progressed throughout 2009-2011.

## **12 NCMG Sample Identification Policy**

As a result of a number of non-conformances raised, changes requested on Q-Pulse, general concerns and the publication in May 2010 of the Clinical & Laboratory Standards Institute (CLSI) Guidelines GP33-A, 'Accuracy in Patient and Sample Identification; Approved Guideline,' a review of the Sample Acceptance policy was performed. It was found that the existing policy complied with the CLSI guidelines but that the policy failed to be implemented in many instances and control measures were not adequate. As a result, a clinical risk assessment was initiated via the hospital's Clinical Risk Department with results of the risk assessment available in early 2011. As a number of changes in policy implementation and practice were required, a Sample ID Working Group was set up comprising of senior staff members. An amended policy and improved procedures are to be implemented in 2012.

## **13 Continuing Professional Development**

As Clinical Genetics is such a rapidly evolving field Continuing Professional Development (CPD) by scientific and clinical staff is essential to ensure a high standard of clinical practice. The majority of staff are members of the Irish, British and/or European Societies of Human Genetics.

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

The NCMG's Education committee oversees continuous professional development opportunities for all staff. Suggestions for CPD can be made by any member of staff via a Division's Education representative(s), and these are assessed at Division level or by the NCMG management team. Since its inception, the NCMG had authority to sanction travel to conferences for its own staff, but this authority was curtailed by OLCHC in 2009 as part of budgetary constraints. Thus the Training budget for 2010 and 2011 was reduced to €6000 for the whole centre i.e. €2000 for each division. While this decision was appealed on several grounds, NCMG Management and the Education committee were confined in what could be achieved with such limited funds. Funding for "self-study" initiatives has also been discontinued. This has had a negative impact on NCMG scientists wishing to sit FRCPath examinations.

However, certain staff are obliged to show evidence of CPD activity every year - Clinicians (50 hours) through the The Royal College of Physicians UK and Genetic Counsellors (30 hours) through the AGNC registration system. There is a requirement for a significant proportion of these CPD hours to be attained via external sources which presents an on-going challenge with current funding.

In an attempt to encourage research and development within the centre a series of clinical laboratory liaison meetings involving staff from each division was initiated in 2007 and regular meetings have been held as outlined below.

Date	Presentation	Presenter
2007	Genetic counselling for prenatal diagnosis Prenatal diagnosis & maternal cell contamination Eurogentest Journal Access update	Marie Meany Aiveen Carey Christine Brady David Barton
2008	Cytogenetics in Neuroblastoma Continuing Professional Development Genetics & Irish Travelling families Incidence of additional abnormalities found in conjunction with trisomies: an Irish perspective Haemochromatosis molecular & clinical perspective CF Uptake Screening Male infertility Powerplex system & maternal cell contamination in PND	David Betts Caitriona King Andrew Green Lisa Preston  Catriona King & Andrew Green Debbie Lambert Zephra Adamson Bronagh O'hIci

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitriona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



**National Centre for Medical Genetics**  
Dublin, Ireland

	HD clinical aspects Clinical and genetic study of a XX (SRY negative) Male Does Noggin cause twinning: part I Does Noggin cause twinning: part II	Rose Kelly Helen O'Shea Miriam Russell Sally Ann Lynch
2009	Chronic lymphocytic Leukaemia Telomeres Skin Chromosomes CPA Accreditation and the NCMG New tests introduced by Molecular Genetics	Paula Carty Karen Meaney Patricia Foley Adam Dunlop & Christine Brady Shirley McQuaid & Bronagh Oh'Ici
2010	A 46,XX/46,XY CVS – what are the possibilities?  Non-parental alleles present in 1/3 cultures from a CVS Atypical 22q11 deletion detected by MLPA in two patients referred for Prader-Willi Syndrome testing Xq24 deletion Cystic Fibrosis New born screening Association of Monosomy 3 with del(5q) in myeloid neoplasms	Debby Lambert, Linda McArdle & Solvig Roring Solvig Roring Karen Meaney & Sally Ann Lynch  Andrew Green David Barton Gillian Clarke, Johanna Kelly, Claire Bermingham, Lynn Barton, Natasha Coen, Paula Carty, Sinead Ryan, David R Betts
2011	Inherited Cardiac Arrhythmias	Nicola Harper

Despite severe constraints considerable levels of CPD activity have been attained. The remainder of this document catalogues the very significant contribution made by NCMG staff members to the local, national and international Scientific and Clinical Genetics Community.

## 14 Teaching

NCMG staff participate in a wide range of teaching activities throughout each year. Teaching is provided for undergraduate & postgraduate students (medical, science and nursing), allied health professionals, nurses & clinicians associated with various organisations including Dublin Institute of Technology (DIT), Trinity College Dublin (TCD), Royal College of Surgeons in Ireland (RCSI) & University College Dublin (UCD) by members of all three divisions.

The clinical team participate in Grand Rounds in both OLCHC & Children's University Hospital, Temple Street.

Professor Andrew Green has regular teaching commitments:

### Undergraduate Teaching

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

Runs annual 1<sup>st</sup> year 30 lecture module in UCD on medical genetics, 16 lectures  
4 lectures annually on the UCD paediatric medical undergraduate course  
4 lectures annually on the RCSI paediatric medical undergraduate course  
4 lectures annually on the TCD paediatric medical undergraduate course  
Teaches & examines annually - UCD undergraduate law & ethics module

### Graduate Teaching

Annual symposium on genetics - RCSI Graduate Medicine biochemistry course  
Annual symposium on ethics and genetics- RCSI MSc in Medical Ethics course

Dr Sally Ann Lynch gives regular teaching sessions to Paediatric trainees – TSH  
Dr David Barton gives regular lectures to MSc courses in TCD and UCD and a biannual commitment to lectures and tutorials for UCD Medical students.

Clinical Scientists from both Molecular and Cytogenetics are regular contributors to biannual tutorials for 3<sup>rd</sup> year Medical students in UCD

The Genetic Counsellors have given lectures and ad hoc educational talks:

Neonatal Nurses – MSc in Women’s Health  
Midwifery courses – National Maternity Hospital, Holles St  
Short courses in Metabolics and Neurology for Graduate Nurses – TSH  
Metabolic lecture series for Neonatal Nurses – DCU  
Breast Care Nurses – Mater Hospital  
MSc programme in Obstetrics & Gynaecology – Cork University Maternity Hospital  
Diploma Child with a life-limiting condition – OLCHC  
Physio / OT – Limerick University  
Sims Fertility Clinic  
Postgraduate Diploma in Oncology Nursing – St Vincent’s University Hospital  
Higher Diploma in Oncology with Breast care – UCD  
ICU Nurses – OLCHC  
Professional Certificate in Advanced Breast care– UCD  
Family cancer risk assessment GP meeting – Cork

### Support groups

Members of NCMG have given a range of talks to patient support groups as detailed in the Platform Presentations section. Unfortunately, with current staffing levels it is becoming increasingly difficult to fulfil all such requests.

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## 15 NCMG Committee Representation

Members of the NCMG serve on a range of Local, National, European and International committees, councils and working groups as out-lined below.

Name	Committee	Dates served
David Barton	Management Committee, European Molecular Genetics Quality Network	1998 - present Chair 2011
David Barton	Steering Committee EuroGentest Network	2011
David Barton	Genetics Services Quality Committee, European Society of Human Genetics	2010 - present
David Barton	World Health Organisation, Expert Advisor to Committee on Biological Standardization	2009 - 2011
David Barton	Organization for Economic Cooperation and Development (OECD) Member, Advisory Group on Genetic Testing	2001 - 2008
David Barton	HSE Steering Group, Newborn Screening for Cystic Fibrosis	2009 - 2011
Caitriona King	Irish Society for Human Genetics (ISHG) Council	2007 - present
Shirley McQuaid	Expert Advisory Group on Inherited Cancer Risk, National Cancer Screening Service	2009 - 2010
Sally A Lynch	Irish Society for Human Genetics (ISHG) Council	2007 - 2010
Sally A Lynch	Research sub-group of Rare disease taskforce	2010 - 2011
Sally A Lynch	Republic of Ireland on Specialist advisory Committee UK	2009 - present
Andrew Green	Irish Council for Bioethics	2006 - 2010
Andrew Green	Medical Council Ethics committee working group	2009
Andrew Green	Chair of the research ethics committee & research forum OLCHC	2006-present
Andrew Green	Health Service Executive research ethics advisory group	2011
Andrew Green	UCD research ethics committee	2004-present
Andrew Green	UCC review committee on embryonic stem cell research [chair of group since 2010]	2006-present
Andrew Green	Chair of the Department of Health Advisory Committee on Bioethics	2011
Andrew Green	Advisory Council for EUROCAT – European congenital anomaly register	2002-present
Andrew Green	National Cancer Screening Service – committee on hereditary predisposition to cancer	2010-2011
Debby Lambert	Health and Social Care Professionals on the Ethics Committee Temple Street	2007-present
Debby Lambert	Irish representative on the European Network of Genetic Nurses and Counsellors	2008-2009
Nicola Harper	Sudden Cardiac Death Resource committee.	2011-present
Marie Meany	AGNC representative for NCMG	2007-present

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt





## National Centre for Medical Genetics Dublin, Ireland

Jackie Turner	Centres for Expertise sub-group of Rare disease working group	2011
Rosemarie Kelly	Rare disease taskforce	2011
Harinder Gill	Centres for Expertise sub-group of Rare disease working group	2011

## 16 Research

NCMG encourages its staff to be involved with research. As the field of genetics is constantly evolving, it is essential to keep abreast of new testing technologies and treatment options to ensure our services are up to date. We have a number of research projects ongoing.

### *16.1 The Genetics of Vesicoureteric Reflux*

#### **The disorder**

Primary vesicoureteric reflux (VUR), the retrograde flow of urine from the bladder towards the kidneys, is the commonest urological anomaly in childhood and occurs in 30-40 % of children who present with urinary tract infections. Some of these children have congenital renal dysplasia, and renal damage may also develop due to reflux of infected urine. These problems are jointly known as reflux nephropathy, which is a major cause of childhood hypertension and end stage renal failure. The incidence of VUR is unknown because it is often asymptomatic and often resolves as the child grows, and screening is not ethical or practical because diagnosis requires invasive investigation. Estimates vary between about 1 & 10 %.

#### **The genetic problem**

VUR is frequently familial and is often associated with other congenital anomalies of the kidney and urinary tract (CAKUT) in the same individual or in other members of the same family. Screening is offered for siblings of diagnosed children, and often reveals asymptomatic children, but screening may be refused if the children are symptomless, and even if screened, reflux may already have resolved though a mutation may have been inherited. Because the phenotype is not obvious, collecting large pedigrees is difficult. Added to these problems, it has become increasingly evident during the course of this project that VUR is highly genetically heterogeneous. This means not only that many different families in the same study are likely to have mutations in different genes, but also, because VUR is common, in large pedigrees, different affected cases may not have the same mutation. Furthermore, it has emerged recently that some mutations may require a second mutation in the same or a different gene to produce the phenotype.

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

### The project

The aim is to discover the genes and mutations responsible for VUR. Recruitment of VUR families and collection of samples for DNA has been ongoing here since 1998. There are at least 12 other centres worldwide working on the problem, and this is enlarged if one includes groups concentrating on obstructive uropathy, on renal dysplasia, or on CAKUT in general, all of which have overlapping aetiologies. We are working largely on our own, but attend meetings of investigators in the field, and have arranged collaborations on specific investigations with workers in Paris, Manchester and Melbourne, as well as having data and sample sharing agreements with groups in the UK (Newcastle & London), New York and Montreal. We had collected 250 families by the end of 2011, and are grateful for the use of 592 Irish blood-donor control DNA samples from the TCD-Trinity BioBank, and Affymetrix 6.0 SNP array genotyping data from around 850 of the BioBank samples. Technology is advancing so rapidly that it tends to become obsolete soon after it is introduced, and this has played a considerable part in moulding the course of our own investigations.

### Personnel

John Darlow since before 2007

Mark Dobson since mid-December 2009

Numerous students and interns from home and abroad since February 2008

### Summary of work in 2007-2011

1. Reanalysis of data, and preparation for publication, of a genome-wide linkage scan performed in 2003-4: The work had been done by a PhD student Helena Kelly, who left in 2005, and was taken up again in 2006. The work had involved genotyping of just over 600 members of 133 VUR families for about 4,700 SNPs. The results were published online in July 2007 and in print in November 2007<sup>1</sup>.
2. Search for mutations in candidate genes in linkage regions defined by the genome scan: The second half of 2007 and early 2008 saw intensive study of the genome and literature to determine likely candidate genes and conserved non-coding elements within our linkage regions. Mutation searching began in early 2008 by in-house PCR and high-resolution melting-curve analysis (HRM), followed by in-house Sanger sequencing to investigate individuals with deviant results. This method was replaced by commercial Sanger sequencing of candidate targets in index case DNA, followed by sifting of variants for likely pathogenic variants, and then by investigating families of index cases with likely mutations by PCR, HRM and in-house Sanger sequencing. A database 'VURbase' was constructed to aid in these processes. Over 700 variants

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

have been found in three rounds of commercial sequencing, and investigations are continuing.

- Investigation of the RET pGly691Ser variant: This variant was found to be present in a high proportion of primary VUR patients in Quebec. We genotyped 221 VUR families and 592 controls by restriction endonuclease digestion and found no linkage or association either with VUR or other phenotypic features. This was published online in early 2009<sup>2</sup>.
- A new genome-wide linkage, association and copy-number scan: With the award of a new grant in late 2009, we were obliged to perform a new genome scan: This was carried out by genotyping an enlarged number of VUR families (244) for a vastly enlarged number of SNPs, 900,000, on an array, which also carried an additional 900,000 invariant markers for copy-number analysis. Preparation of DNA samples and clinical information, genotyping and data analysis of this scan took the whole of 2010 and 2011, and precluded any further research publications during this time. It considerably reduced but did not halt the mutation search (2) above, but had the following benefits: (a) discovery of eight extended families linking independently recruited nuclear families within our cohort; (b) a much more detailed linkage landscape of the VUR genome, causing redirection of our mutation searches and engendering several new investigations.
- Whole-genome 'next-generation' sequencing of (a) members of one of the extended families discovered by (4) above, and (b) a case of inherited renal cell carcinoma with a germline balanced t(2;3) translocation in the same chromosomal band as our largest VUR linkage peak, 2q37.3: DNA was sent away for these investigations on 1<sup>st</sup> November 2011 and data analysis by the company (Knome) was still in progress at the end of the report period.

Several publications are in preparation from 2, 4 and 5 above.

### Publications during 2007-2011

- Kelly, H., Molony, C.M., Darlow, J.M., Pirker, M.E., Yoneda, A., Green, A.J., Puri, P., and Barton, D.E. (2007). A genome-wide scan for genes involved in primary vesicoureteric reflux. *Journal of medical genetics* 44, 710-717.
- Darlow, J.M., Molloy, N.H.N., Green, A.J., Puri, P., and Barton, D.E. (2009). The increased incidence of the RET p.Gly691Ser variant in French-Canadian vesicoureteric reflux patients is not replicated by a larger study in Ireland. *Human mutation* 30, E612-E617.
- Kelly, H., Barton, D., Molony, C., and Puri, P. (2009). Linkage analysis of candidate genes in families with vesicoureteral reflux. *The Journal of urology* 182, 1669-1672. (This reported work done in 2005)

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

4. Puri, P., Gosemann, J.H., Darlow, J., and Barton, D.E. (2011). Genetics of vesicoureteral reflux. *Nat Rev Urol* 8, 539-552.

### 16.2 SNI<sub>P</sub>2CHIP

Project start /end dates: Feb 2006 - April 2009

NCMG participants: Dr. Mark Dobson, Prof. David Barton

#### Project summary:

SNI<sub>P</sub>2CHIP was an EU 6th Framework project, involving participants from seven institutions around Europe that was developing a lab-on-a-chip microarray system for point-of-care genetic diagnosis. The project was focused on the development of an integrated SNP detection platform to include modules for DNA extraction and purification from biological samples, DNA amplification, genetic characterisation (including SNP detection), signal transduction, interpretation and data analysis. The clinical challenge addressed by the project, was the need to be able to provide clinicians with immediately actionable data based on near-patient diagnosis of infectious diseases or pharmacogenetic testing.

The NCMG was involved in an advisory role in the project; work involved the evaluation of competing point-of-care genetic testing systems, the development of strategies to ensure regulatory compliance, an evaluation of diagnostic kits that are currently available for CF testing and an analysis of the competitive environment in which SNI<sub>P</sub>2CHIP needed to compete.

#### Project output - Publications:

- Dobson M.G., Galvin P., Barton D.E. Testing Diagnostic tests; electronics meets point-of-care applications. *Bioworld Europe* (2007) (3) p6-9
- Dobson M.G., Galvin P., Barton D.E. Emerging technologies for point-of-care genetic testing. (2007) *Expert Review of Molecular Diagnostics* 7(4) p359-370.

#### Project output - Presentations:

- Dobson M.G., Point-of-care systems for genetic analysis. (Invited seminar) Biomedical Diagnostics Institute, Dublin City University 17th October 2008
- Clarke, L.A., Dobson, M., Galvin, P., Amaral, M.D., 'Development of an OLA-based Microarray Platform for Rapid Simultaneous Detection of Multiple CFTR Mutations'. (poster presentation) '22nd Annual North American Cystic Fibrosis Conference', Orlando FL, October 23-25, 2008

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

- Dobson M.G., Galvin P., Barton D.E. 'SNiP2CHIP' a point-of-care system for 'sample-in, answer-out' DNA analysis. (poster presentation) 'Enabling point-of-care diagnostics', Washington D.C., August 19-20, 2008

### 16.3 Group of Dr Sean Ennis

The medical genomics research group have been heavily involved in the international Autism Genome Project (AGP) consortium. The group acted as a major genotyping centre for the AGP phase II copy number variation (CNV) and genome wide association study (GWAS). This work has resulted in 3 major publications to date with a 4<sup>th</sup> to follow shortly. In addition the group pioneered a new type of analysis of GWAS datasets of homozygous haplotype sharing and applied this to identify candidate genes in autism spectrum disorder.

Because of the scale of acting as a major genotyping centre this research work moved from the NCMG to new premises in the Health Sciences Centre UCD in mid 2007. Two new postdoctoral fellows Dr. Regina Regan and Dr. Judith Conroy joined the group to spearhead this work. Jillian Casey and Naisha Shah also joined the group as PhD. Students and both successfully completed their theses in 2011. (Genetics of Autism Spectrum Disorder: A Bioinformatics Perspective, Naisha Shah. Identification of candidate disease genes for Mendelian and Complex disorders, Jillian Casey).

Involvement in a large scale project such as the AGP gave us access to the latest technological advances in genomics and as a group of clinicians and scientists we were early to recognise and apply these developments to the field of rare genetic diseases with unprecedented success.

In Ireland there are about 280,000 individuals with a rare disease and 60 recessive disorders in the Traveller population. In a pilot study we have completed data analysis on 6 of 10 rare disorders of unknown genetic basis affecting 25 small Irish families. Of the 6 studies, the disease mutation has been successfully identified for 5 families, of which 3 studies have been published to date and 4 translated back into the clinical setting, demonstrating our ability to identify rare disease genes in small families.

During this period we have fostered collaborative links with many groups both nationally and internationally. We developed strong links with the group of Dr. Astrid Vincente of Lisbon, Dr. Tiago Magalhães for the Lisbon group has spent several short term visits in Dublin and together with the group has developed new bioinformatic approaches to looking at large datasets.

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



### 16.4 Group of Dr Sally Ann Lynch

Dr Jillian Casey PhD secured a two year post-Doctorate position with Dr Sally Ann Lynch (as Principal Investigator) and Dr Amanda McCann as co-investigator in October 2011. The grant proposal came through the Medical Research Charities group (MRCG) with joint funding from NCRC & HRB. Jillian's project includes identifying the genetic basis of three disorders: Primary Ciliary Dyskinesia, microcephaly & cardiomyopathy & retinopathy

Dr Judith Conroy PhD, secured research funding in December 2011 in collaboration with Dr Lynch & Prof Mary King. This money came through the fundraising office at Temple Street Children's Hospital. Dr Conroy will be working on the genetic basis of Landau-Kleffner syndrome.

## 17 Papers

1. Casey JP, Magalhaes T, Conroy JM, Regan R, Shah N, Anney R, Shields DC, Abrahams BS, Almeida J, Bacchelli E, Bailey AJ, Baird G, Battaglia A, Berney T, Bolshakova N, Bolton PF, Bourgeron T, Brennan S, Cali P, Correia C, Corsello C, Coutanche M, Dawson G, de Jonge M, Delorme R, Duketis E, Duque F, Estes A, Farrar P, Fernandez BA, Folstein SE, Foley S, Fombonne E, Freitag CM, Gilbert J, Gillberg C, Glessner JT, Green J, Guter SJ, Hakonarson H, Holt R, Hughes G, Hus V, Iglizzi R, Kim C, Klauck SM, Kolevzon A, Lamb JA, Leboyer M, Le Couteur A, Leventhal BL, Lord C, Lund SC, Maestrini E, Mantoulan C, Marshall CR, McConachie H, McDougle CJ, McGrath J, McMahon WM, Merikangas A, Miller J, Minopoli F, Mirza GK, Munson J, Nelson SF, Nygren G, Oliveira G, Pagnamenta AT, Papanikolaou K, Parr JR, Parrini B, Pickles A, Pinto D, Piven J, Posey DJ, Poustka A, Poustka F, Ragoussis J, Roge B, Rutter ML, Sequeira AF, Soorya L, Sousa I, Sykes N, Stoppioni V, Tancredi R, Tauber M, Thompson AP, Thomson S, Tsiantis J, Van Engeland H, Vincent JB, Volkmar F, Vorstman JA, Wallace S, Wang K, Wassink TH, White K, Wing K, Wittemeyer K, Yaspan BL, Zwaigenbaum L, Betancur C, Buxbaum JD, Cantor RM, Cook EH, Coon H, Cuccaro ML, Geschwind DH, Haines JL, Hallmayer J, Monaco AP, Nurnberger JI Jr, Pericak-Vance MA, Schellenberg GD, Scherer SW, Sutcliffe JS, Szatmari P, Vieland VJ, Wijsman EM, Green A, Gill M, Gallagher L, Vicente A, Ennis S. A novel approach of homozygous haplotype sharing identifies candidate genes in autism spectrum disorder. **Hum Genet.** 2011 Oct 14. [Epub ahead of print]
2. Casey J, Kawaguchi R, Morrissey M, Sun H, McGettigan P, Nielsen JE, Conroy J, Regan R, Kenny E, Cormican P, Morris DW, Tormey P, Ní Chróinín M, Kennedy BN,

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



- Lynch S, Green A, Ennis S. First implication of STRA6 mutations in isolated anophthalmia, microphthalmia, and coloboma: A new dimension to the STRA6 phenotype. **Hum Mutat.** 2011 Sep 7. doi: 10.1002/humu.21590. [Epub ahead of print]
- Veronica J. Vieland & Joachim Hallmayer & Yungui Huang & Alistair T. Pagnamenta & Dalila Pinto & Hameed Khan & Anthony P. Monaco & Andrew D. Paterson & Stephen W. Scherer & James S. Sutcliffe & Peter Szatmari & The Autism Genome Project (AGP). Novel method for combined linkage and genome-wide association analysis finds evidence of distinct genetic architecture for two subtypes of autism. **Journal of Neurodevelopmental Disorders:** Volume 3, Issue 2 (2011), Page 113-123.
  - Anney RJ, Kenny EM, O'Dushlaine C, Yaspan BL, Parkhomenka E; The Autism Genome Project, Buxbaum JD, Sutcliffe J, Gill M, Gallagher L; The AGP Members, Bailey AJ, Fernandez BA, Szatmari P, Scherer SW, Patterson A, Marshall CR, Pinto D, Vincent JB, Fombonne E, Betancur C, Delorme R, Leboyer M, Bourgeron T, Mantoulan C, Roge B, Tauber M, Freitag CM, Poustka F, Duketis E, Klauck SM, Poustka A, Papanikolaou K, Tsiantis J, Gallagher L, Gill M, Anney R, Bolshakova N, Brennan S, Hughes G, McGrath J, Merikangas A, Ennis S, Green A, Casey JP, Conroy JM, Regan R, Shah N, Maestrini E, Bacchelli E, Minopoli F, Stoppioni V, Battaglia A, Iglizzo R, Parrini B, Tancredi R, Oliveira G, Almeida J, Duque F, Vicente A, Correia C, Magalhaes TR, Gillberg C, Nygren G, Jonge MD, Van Engeland H, Vorstman JA, Wittemeyer K, Baird G, Bolton PF, Rutter ML, Green J, Lamb JA, Pickles A, Parr JR, Couteur AL, Berney T, McConachie H, Wallace S, Coutanche M, Foley S, White K, Monaco AP, Holt R, Farrar P, Pagnamenta AT, Mirza GK, Ragoussis J, Sousa I, Sykes N, Wing K, Hallmayer J, Cantor RM, Nelson SF, Geschwind DH, Abrahams BS, Volkmar F, Pericak-Vance MA, Cuccaro ML, Gilbert J, Cook EH, Guter SJ, Jacob S, Nurnberger Jr JJ, McDougle CJ, Posey DJ, Lord C, Corsello C, Hus V, Buxbaum JD, Klevzon A, Soorya L, Parkhomenko E, Leventhal BL, Dawson G, Vieland VJ, Hakonarson H, Glessner JT, Kim C, Wang K, Schellenberg GD, Devlin B, Klei L, Minshew N, Sutcliffe JS, Haines JL, Lund SC, Thomson S, Yaspan BL, Coon H, Miller J, McMahon WM, Munson J, Estes A, Wijsman EM. Gene-ontology enrichment analysis in two independent family-based samples highlights biologically plausible processes for autism spectrum disorders. **Eur J Hum Genet.** 2011 Oct;19(10):1082-1089. doi: 10.1038/ejhg.2011.75. Epub 2011 Apr 27.
  - Abdul Noor, Annabel Whibley, Christian R. Marshall, Peter J. Gianakopoulos, Amelie Piton, Andrew R. Carson, Marija Orlic-Milacic, Anath C. Lionel, Daisuke Sato, Dalila Pinto, Irene Drmic, Carolyn Noakes, Lili Senman, Xiaoyun Zhang, Rong Mo, Julie Gauthier, Jennifer Crosbie, Alistair T. Pagnamenta, Jeffrey Munson, Annette M. Estes, Andreas Fiebig, Andre Franke, Stefan Schreiber, Alexandre F. R. Stewart, Robert Roberts, Ruth McPherson, Stephen J. Guter, Edwin H. Cook, Jr., Geraldine Dawson,

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

- Gerard D. Schellenberg, Agatino Battaglia, Elena Maestrini, Autism Genome Project Consortium, Linda Jeng, Terry Hutchison, Evica Rajcan-Separovic, Albert E. Chudley, Suzanne M. E. Lewis, Xudong Liu, Jeanette J. Holden, Bridget Fernandez, Lonnie Zwaigenbaum, Susan E. Bryson, Wendy Roberts, Peter Szatmari, Louise Gallagher, Michael R. Stratton, Jozef Gecz, Angela F. Brady, Charles E. Schwartz, Russell J. Schachar, Anthony P. Monaco, Guy A. Rouleau, Chi-chung Hui, F. Lucy Raymond, Stephen W. Scherer, and John B. Vincent. Disruption at the PTCHD1 Locus on Xp22.11 in Autism Spectrum Disorder and Intellectual Disability. **Sci Transl Med.** 15 September 2010: Vol. 2, Issue 49, p. 49ra68 DOI: 10.1126/scitranslmed.3001267
6. SA Lynch, N Foulds, AC Thuresson, AL Collins, G Annerén, BO Hedberg, CA Delaney, J Iremonger, CM Murray, JA Crolla, C Costigan, W Lam, DR FitzPatrick, R Regan, S Ennis & FH Sharkey. The 12q14 microdeletion syndrome; 6 new cases confirming the role of HMGA2 in growth. **Eur J Hum Genet.** 2011 19, 534-539.
  7. Agenesis of the corpus callosum with midline lipoma associated with an Xp22.31-Xp22.12 deletion. Baker LB, Conroy J, Donoghue V, Mullarkey M, Shah N, Murphy N, Murphy J, Ennis S, Lynch SA. **Clin Dysmorphol.** 2011 Jan;20(1):21-5
  8. Genome-wide SNP association-based localization of a dwarfism gene in Friesian dwarf horses. Orr N, Back W, Gu J, Leegwater P, Govindarajan P, Conroy J, Ducro B, Van Arendonk JA, MacHugh DE, Ennis S, Hill EW, Brama PA. **Anim Genet.** 2010 Dec;41 Suppl 2:2-7.
  9. C. T. Correia, A. M. Coutinho, A. F. Sequeira, I. G. Sousa, L. Lourenco Venda, J. P. Almeida, R. L. Abreu, C. Lobo, T. S. Miguel, J. Conroy, L. Cochrane, L. Gallagher, M. Gill, S. Ennis, G. G. Oliveira and A. M. Vicente. Increased BDNF levels and NTRK2 gene association suggest a disruption of BDNF/TrkB signaling in autism. **Genes, Brain and Behavior** (2010) 9: 841–848.
  10. Anney R, Klei L, Pinto D, Regan R, Conroy J, Magalhaes TR, Correia C, Abrahams BS, Sykes N, Pagnamenta AT, Almeida J, Bacchelli E, Bailey AJ, Baird G, Battaglia A, Berney T, Bolshakova N, Bölte S, Bolton PF, Bourgeron T, Brennan S, Brian J, Carson AR, Casallo G, Casey J, Chu SH, Cochrane L, Corsello C, Crawford EL, Crossett A, Dawson G, de Jonge M, Delorme R, Drmic I, Duketis E, Duque F, Estes A, Farrar P, Fernandez BA, Folstein SE, Fombonne E, Freitag CM, Gilbert J, Gillberg C, Glessner JT, Goldberg J, Green J, Guter SJ, Hakonarson H, Heron EA, Hill M, Holt R, Howe JL, Hughes G, Hus V, Iglizzi R, Kim C, Klauck SM, Kolevzon A, Korvatska O, Kustanovich V, Lajonchere CM, Lamb JA, Laskawiec M, Leboyer M, Le Couteur A, Leventhal BL, Lionel AC, Liu XQ, Lord C, Lotspeich L, Lund SC, Maestrini E, Mahoney W, Mantoulan C, Marshall CR, McConachie H, McDougle CJ, McGrath J, McMahon WM, Melhem NM, Merikangas A, Migita O, Minshew NJ, Mirza GK, Munson J, Nelson SF, Noakes C, Noor A, Nygren G, Oliveira G, Papanikolaou K, Parr

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt





## National Centre for Medical Genetics

Dublin, Ireland

- JR, Parrini B, Paton T, Pickles A, Piven J, Posey DJ, Poustka A, Poustka F, Prasad A, Ragoussis J, Renshaw K, Rickaby J, Roberts W, Roeder K, Roge B, Rutter ML, Bierut LJ, Rice JP, Salt J, Sansom K, Sato D, Segurado R, Senman L, Shah N, Sheffield VC, Soorya L, Sousa I, Stoppioni V, Strawbridge C, Tancredi R, Tansey K, Thiruvahindrapduram B, Thompson AP, Thomson S, Tryfon A, Tsiantis J, Van Engeland H, Vincent JB, Volkmar F, Wallace S, Wang K, Wang Z, Wassink TH, Wing K, Wittemeyer K, Wood S, Yaspan BL, Zurawiecki D, Zwaigenbaum L, Betancur C, Buxbaum JD, Cantor RM, Cook EH, Coon H, Cuccaro ML, Gallagher L, Geschwind DH, Gill M, Haines JL, Miller J, Monaco AP, Nurnberger JI Jr, Paterson AD, Pericak-Vance MA, Schellenberg GD, Scherer SW, Sutcliffe JS, Szatmari P, Vicente AM, Vieland VJ, Wijsman EM, Devlin B, Ennis S, Hallmayer J. A genome-wide scan for common alleles affecting risk for autism. **Hum Mol Genet.** 2010 Oct 15;19(20):4072-82. Epub 2010 Jul 27.
11. Pinto D, Pagnamenta AT, Klei L, Anney R, Merico D, Regan R, Conroy J, Magalhaes TR, Correia C, Abrahams BS, Almeida J, Bacchelli E, Bader GD, Bailey AJ, Baird G, Battaglia A, Berney T, Bolshakova N, Bölte S, Bolton PF, Bourgeron T, Brennan S, Brian J, Bryson SE, Carson AR, Casallo G, Casey J, Chung BH, Cochrane L, Corsello C, Crawford EL, Crossett A, Cytrynbaum C, Dawson G, de Jonge M, Delorme R, Drmic I, Duketis E, Duque F, Estes A, Farrar P, Fernandez BA, Folstein SE, Fombonne E, Freitag CM, Gilbert J, Gillberg C, Glessner JT, Goldberg J, Green A, Green J, Guter SJ, Hakonarson H, Heron EA, Hill M, Holt R, Howe JL, Hughes G, Hus V, Iglizoi R, Kim C, Klauck SM, Kolevzon A, Korvatska O, Kustanovich V, Lajonchere CM, Lamb JA, Laskawiec M, Leboyer M, Le Couteur A, Leventhal BL, Lionel AC, Liu XQ, Lord C, Lotspeich L, Lund SC, Maestrini E, Mahoney W, Mantoulan C, Marshall CR, McConachie H, McDougle CJ, McGrath J, McMahan WM, Merikangas A, Migita O, Minshew NJ, Mirza GK, Munson J, Nelson SF, Noakes C, Noor A, Nygren G, Oliveira G, Papanikolaou K, Parr JR, Parrini B, Paton T, Pickles A, Pilorge M, Piven J, Ponting CP, Posey DJ, Poustka A, Poustka F, Prasad A, Ragoussis J, Renshaw K, Rickaby J, Roberts W, Roeder K, Roge B, Rutter ML, Bierut LJ, Rice JP, Salt J, Sansom K, Sato D, Segurado R, Sequeira AF, Senman L, Shah N, Sheffield VC, Soorya L, Sousa I, Stein O, Sykes N, Stoppioni V, Strawbridge C, Tancredi R, Tansey K, Thiruvahindrapduram B, Thompson AP, Thomson S, Tryfon A, Tsiantis J, Van Engeland H, Vincent JB, Volkmar F, Wallace S, Wang K, Wang Z, Wassink TH, Webber C, Weksberg R, Wing K, Wittemeyer K, Wood S, Wu J, Yaspan BL, Zurawiecki D, Zwaigenbaum L, Buxbaum JD, Cantor RM, Cook EH, Coon H, Cuccaro ML, Devlin B, Ennis S, Gallagher L, Geschwind DH, Gill M, Haines JL, Hallmayer J, Miller J, Monaco AP, Nurnberger Jr JI, Paterson AD, Pericak-Vance MA, Schellenberg GD, Szatmari P, Vicente AM, Vieland VJ, Wijsman EM, Scherer SW, Sutcliffe JS, Betancur C.

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



- Functional impact of global rare copy number variation in autism spectrum disorders. **Nature**. 2010 Jun 9.
12. Weiss LA, Arking DE; Gene Discovery Project of Johns Hopkins & the Autism Consortium, Daly MJ, Chakravarti A. A genome-wide linkage and association scan reveals novel loci for autism. **Nature**. 2009 Oct 8;461(7265):802-8.PMID: 19812673
  13. Conroy J, Cochrane L, Anney RJ, Sutcliffe JS, Carthy P, Dunlop A, Mullarkey M, O'hici B, Green AJ, Ennis S, Gill M, Gallagher L. Fine mapping and association studies in a candidate region for autism on chromosome 2q31-q32. **Am J Med Genet B Neuropsychiatr Genet**. 2009 Jun 5;150B(4):535-44.PMID: 18846500
  14. Meisler MH, Russ C, Montgomery KT, Greenway M, Ennis S, Hardiman O, Figlewicz DA, Quenneville NR, Conibear E, Brown RH Jr. Evaluation of the Golgi trafficking protein VPS54 (wobbler) as a candidate for ALS. **Amyotroph Lateral Scler**. 2008 Jun;9(3):141-8.PMID: 18574757
  15. Doherty LS, Kiely JL, Deegan PC, Nolan G, McCabe S, Green AJ, Ennis S, McNicholas WT. Late-onset central hypoventilation syndrome: a family genetic study. **Eur Respir J**. 2007 Feb;29(2):312-6.

## 18 Publications

### 2007

1. McGovern MM, Elles R, Beretta I, Somerville MJ, Hoefler G, Keinanen M, Barton D, Carson N, Dequeker E, Brdicka R, Blazkova A, Aymé S, Schnieders B, Muller CR, Dalen V, Martinez AA, Kristoffersson U, Ozguc M, Mueller H, Boone J, Lubin IM, Sequeiros J, Taruscio D, Williamson B, Mainland L, Yoshikura H, Ronchi E (2007). Report of an international survey of molecular genetic testing laboratories. *Community Genet* **10**(3):123-131.
2. Barton DE, Kalman L (2007). Reliable genetic tests and testings - Diagnostic biomarkers, reference materials, and beyond. *Bioworld Europe* **1**:18-21.
3. Wilson JA, Barton DE (2007). Targeted versus whole-genome array comparative genome hybridization: The Atlantic Divide. *J Mol Diagn* **9**(2):278.
4. Dobson MG, Galvin P, Barton DE (2007). Testing diagnostic tests - Electronics meets point-of-care applications. *Bioworld Europe* **3**, September:6-9.
5. Dobson MG, Galvin P, Barton DE (2007). Emerging technologies for point-of-care genetic testing. *Expert Review of Molecular Diagnostics* **7**(4):359-370.

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

6. Kelly H, Molony C, Darlow J, Pirker M, Yoneda A, Green AJ, Puri P, Barton DE (2007). A genome-wide scan for genes involved in primary vesicoureteral reflux in 133 families. *J Med Genet* **44**(11):710-717.
7. Schaub R, Burger A, Bausch D, Niggli FK, Schäfer BW, Betts DR (2007). Array comparative genomic hybridization reveals unbalanced gain of the MYCN region in Wilms tumors. *Cancer Genet Cytogenet* **172**(1):61-65.
8. Stanchesu R, Betts DR, Yekutieli D, Ambros P, Cohen N, Rechavi G, Amariglio N, Trakhtenbrot L (2007). SKY analysis of childhood neural tumors and cell lines demonstrates a susceptibility of aberrant chromosomes to further rearrangements. *Cancer Lett* **250**(1):47-52.
9. Hertzberg L, Betts DR, Raimondi SC, Schäfer BW, Notterman DA, Domany E, Izraeli S (2007). Prediction of chromosomal aneuploidy from gene expression data. *Genes Chromosomes Cancer* **46**(1):75-86.
10. Brown A, Niggli F, Hengartner H, Caflisch U, Nobile L, Kuhne T, Angst R, Bourquin JP, Betts D (2007). Characterization of high-hyperdiploidy in childhood acute lymphoblastic leukemia with gain of a single chromosome 21. *Leuk Lymphoma* **48**(12):2457-2460.
11. Seppa L, Hengartner H, Leibundgut K, Kuhne T, Niggli FK, Betts DR (2007). Loss of i(8)(q10) at relapse in two cases of childhood acute myeloid leukaemia. *Leuk Lymphoma* **48**(5):1045-1047.
12. Betts DR, Ammann RA, Hirt A, Hengartner H, Beck-Popovic M, Kuhne T, Nobile L, Caflisch U, Wacker P, Niggli FK (2007). The prognostic significance of cytogenetic aberrations in childhood acute myeloid leukaemia. A study of the Swiss Paediatric Oncology Group (SPOG). *Eur J Haematol* **78**(6):468-476.
13. Henderson A, Lynch SA, Wilkinson S, Hunter M (2007). Adults with Down's syndrome: the prevalence of complications and health care in the community. *Br J Gen Pract* **57**(534):50-55.
14. Henderson RA, Williamson K, Cumming S, Clarke MP, Lynch SA, IM Hanson IM, D Fitzpatrick D, S Sisodiya S, van Heyningen V (2007). Inherited PAX6, NF1 and OTX2 mutations in a child with microphthalmia and aniridia. *Eur J Hum Genet* **15**(8):898-901.
15. Murphy AM, Flanagan O, Dunne K and Lynch SA (2007). High Prevalence of Cohen Syndrome amongst Irish Travellers. *Clin Dysmorphol* **16**(4):257-259.
16. Rice G, Patrick T, Parmar R, Taylor CF, Aeby A, Aicardi J, Artuch R, Montalto SA, Bacino CA, Barroso B, Baxter P, Benko WS, Bergmann C, Bertini E, Biancheri R, Blair EM, Blau N, Bonthron DT, Briggs T, Brueton LA, Brunner HG, Burke CJ, Carr IM, Carvalho DR, Chandler KE, Christen HJ, Corry PC, Cowan FM, Cox H, D'Arrigo S, Dean J, De Laet C, De Praeter C, Dery C, Ferrie CD, Flintoff K, Frints SG, Garcia-Cazorla A, Gener B, Goizet C, Goutieres F, Green AJ, Guet A, Hamel BC, Hayward

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

- BE, Heiberg A, Hennekam RC, Husson M, Jackson AP, Jayatunga R, Jiang YH, Kant SG, Kao A, King MD, Kingston HM, Klepper J, van der Knaap MS, Kornberg AJ, Kotzot D, Kratzer W, Lacombe D, Lagae L, Landrieu PG, Lanzi G, Leitch A, Lim MJ, Livingston JH, Lourenco CM, Lyall EG, Lynch SA, et al (2007). Clinical & molecular phenotype of Aicardi-Goutieres syndrome. *Am J Hum Genet* **81**(4):713-725.
17. Lynch SA (2007). Currarino Syndrome. *Atlas Genet Cytogenet Oncol Haematol* URL : <http://AtlasGeneticsOncology.org/Kprones/CurrarinoID10082.html>
18. Brashear A, Dobyns WB, de Carvalho Aguiar P, Borg M, Frijns CJ, Gollamudi S, Green A, Guimaraes J, Haake BC, Klein C, Linazasoro G, Munchau A, Raymond D, Riley D, Saunders-Pullman R, Tijssen MA, Webb D, Zaremba J, Bressman SB, Ozelius LJ (2007). The phenotypic spectrum of rapid-onset dystonia-parkinsonism (RDP) and mutations in the ATP1A3 gene. *Brain* **130**(Pt 3):828-835.
19. Doherty LS, Kiely JL, Deegan PC, Nolan G, McCabe S, Green AJ, Ennis S, McNicholas WT (2007). Late-onset central hypoventilation syndrome: a family genetic study. *Eur Respir J* **29**(2):312-316.
20. King C (2007). Diagnostic Techniques in Genetics. *Am J Hum Biol* **19**:892-893.

### 2008

1. Jaeger E, Webb E, Howarth K, Carvajal-Carmona L, Rowan A, Broderick P, Walther A, Spain S, Pittman A, Kemp Z, Sullivan K, Heinemann K, Lubbe S, Domingo E, Barclay E, Martin L, Gorman M, Chandler I, Vijayakrishnan J, Wood W, Papaemmanuil E, Penegar S, Qureshi M; CORGI Consortium, Farrington S, Tenesa A, Cazier JB, Kerr D, Gray R, Peto J, Dunlop M, Campbell H, Thomas H, Houlston R, Tomlinson I (2008). Common genetic variants at the CRAC1 (HMPS) locus on chromosome 15q13.3 influence colorectal cancer risk. *Nat Genet* **40**(1):26-28.
2. O'Shea J, Lynch SA, Macken S (2008). A case of persistent pulmonary hypertension in a newborn with Costello syndrome. *Clin Dysmorphol* **17**:287-288.
3. Zweier C, Sticht H, Bijlsma E, Clayton-Smith J, Boonen SE, Fryer A, Grealley MT, Hoffmann L, den Hollander NS, Jongmans M, Kant SG, King MD, Lynch SA, McKee S, Midro AT, Park SM, Ricotti V, Tarantino E, Wessels M, Peippo M, Rauch A (2008). Further delineation of Pitt-Hopkins syndrome: phenotypic and genotypic description of sixteen novel patients. *J Med Genet* **45**(11):738-744.
4. Cody N, Green A, McDevitt T, Lynch SA (2008). Cascade screening in BRCA1/2 mutation carriers. *Ir Med J* **101**(5):140-142.
5. McBrien J, Crolla JA, Huang S, Kelleher J, Gleeson J, Lynch SA (2008). Further case of microdeletion of 8q24 with phenotype overlapping Langer-Giedion without TRPS1 deletion. *Am J Med Genet* **146A**(12):1587-1592.

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

6. O'Riordan SM, Lynch SA, Hindmarsh PC, Chan LF, Clark AJ, Costigan C (2008). A novel variant of familial glucocorticoid deficiency prevalent among the Irish Traveller population. *J Clin Endocrinol Metab* **93**(7):2896-2899.
7. Bergmann C, Fliegau M, Bröchle NO, Frank V, Olbrich H, Kirschner J, Schermer B, Schmedding I, Kispert A, Kränzlin B, Nürnberg G, Becker C, Grimm T, Girschick G, Lynch SA, Kelehan P, Senderek J, Neuhaus TJ, Stallmach T, Zentgraf H, Nürnberg P, Gretz N, Lo C, Lienkamp S, Schäfer T, Walz G, Benzing T, Zerres K, Omran H (2008). Loss of nephrocystin-3 function can cause embryonic lethality, Meckel-Gruber-like syndrome, situs inversus, and renal-hepatic-pancreatic dysplasia. *Am J Hum Genet* **82**(4):959-970.
8. Shahdadpuri R, Lynch SA, Murchan H, McMahon CJ (2008). A novel constellation of cardiac findings for Kabuki syndrome: hypoplastic left heart syndrome and partial anomalous pulmonary venous drainage. *Pediatr Cardiol* **29**(4):820-822.
9. Barber JC, Maloney VK, Huang S, Bunyan DJ, Cresswell L, Kinning E, Benson A, Cheetham T, Wyllie J, Lynch SA, Zwolinski S, Prescott L, Crow Y, Morgan R, Hobson E (2008). 8p23.1 duplication syndrome; a novel genomic condition with unexpected complexity revealed by array CGH. *Eur J Hum Genet* **16**(1):18-27.
10. Gumy-Pause F, Ozsahin H, Khoshbeen-Boudal M, Betts DR, Maillet P, Sappino AP (2008). Detection of ATM gene deletion/duplication by multiplex ligation-dependant probe amplification in childhood lymphoid malignancies: a report from the Children's Oncology Group. *Leuk Res* **32**(8):1207-1213.
11. Muntean A, Bergsträsser E, Diepold M, Niggli FK, Betts DR (2008). Karyotypic characterization of infant embryonal rhabdomyosarcoma. *Cancer Genet Cytogenet* **180**(2):145-148.
12. De Melo V, Vetter M, Mazzullo H, Howard JD, Betts DR, Nacheva EP, Apperley JF, Reid AG (2008). A simple FISH assay for the detection of 3q26 rearrangements in myeloid malignancy. *Leukemia* **22**(2):434-437.
13. Betts DR, Stanchesu R, Niggli FK, Cohen N, Rechavi G, Amariglio N, Trakhtenbrot L (2008). SKY reveals a high frequency of unbalanced translocations involving chromosome 6 in t(12;21)-positive acute lymphoblastic leukemia. *Leukemia Res* **32**(1):39-43.
14. Berwouts S, Gordon JT, Rundell CA, Barton DE, Dequeker E (2008). Evaluation and use of a synthetic quality control material, included in the European EQA scheme for cystic fibrosis. *Hum Mutat* **29**(8):1063-1070.
15. Murphy AM, Sheridan M, O'Neill MB, Green A (2008). The walker-warburg phenotype and genotype among Irish travellers. *Clin Dysmorphol* **17**(2):119-120.
16. Baldridge D, Schwarze U, Morello R, Lenington J, Bertin TK, Pace JM, Pepin MG, Weis M, Eyre DR, Walsh J, Lambert D, Green A, Robinson H, Michelson M, Houge G,

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

- Lindman C, Martin J, Ward J, Lemyre E, Mitchell JJ, Krakow D, Rimoin DL, Cohn DH, Byers PH, Lee B (2008). CRTAP and LEPRE1 mutations in recessive osteogenesis imperfecta. *Hum Mutat* **29**(12):1435-1442.
17. Papaemmanuil E, Carvajal-Carmona L, Sellick GS, Kemp Z, Webb E, Spain S, Sullivan K, Barclay E, Lubbe S, Jaeger E, Vijayakrishnan J, Broderick P, Gorman M, Martin L, Lucassen A, Bishop DT, Evans DG, Maher ER, Steinke V, Rahner N, Schackert HK, Goecke TO, Holinski-Feder E, Propping P, Van Wezel T, Wijnen J, Cazier JB, Thomas H, Houlston RS, Tomlinson I, CORGI Consortium (2008). Deciphering the genetics of hereditary non-syndromic colorectal cancer. *Eur J Hum Genet* **16**(12):1477-1486.
  18. Liu XQ, Paterson AD, Szamari P, Autism Genome Project Consortium (2008). Genome-wide linkage analyses of quantitative and categorical autism subphenotypes. *Biol Psychiat* **64**(7):561-770.
  19. NiAinle F, Hamnvik OPR, Gulmann C, Bermingham C, Kelly J, Mc Evoy P, Murphy P (2008). Diffuse large B-cell lymphoma with isolated bone marrow involvement presenting with secondary cold agglutinin disease. *Int J Lab Hematol* **30**:444-445.

### 2009

1. Lugtenberg D, Kleefstra T, Oudakker AR, Nillesen WM, Yntema HG, Tzschach A, Raynaud M, Rating D, Journal H, Chelly J, Goizet C, Lacombe D, Pedespan JM, Echenne B, Tariverdian G, O'Rourke D, King MD, Green A, van Kogelenberg M, Van Esch H, Gecz J, Hamel BC, van Bokhoven H, de Brouwer AP (2009). Structural variation in Xq28: MECP2 duplications in 1% of patients with unexplained XLMR and in 2% of male patients with severe encephalopathy. *Eur J Hum Genet* **17**(4):444-453.
2. Murphy AM, Lambert DM, Treacy EP, O'Meara A, Lynch SA (2009). Incidence and prevalence of Mucopolysaccharidosis Type 1 in the Irish Republic. *Arch Dis Child* **94**(1):52-54.
3. Conroy J, Cochrane L, Anney RJ, Sutcliffe JS, Carthy P, Dunlop A, Mullarkey M, O'hici B, Green AJ, Ennis S, Gill M, Gallagher L (2009). Fine mapping and association studies in a candidate region for autism on chromosome 2q31-q32. *Am J Med Genet B Neuropsychiatr Genet* **150B**(4):535-544.
4. Weiss LA, Arking DE; Gene Discovery Project of Johns Hopkins & the Autism Consortium (including Green A, Ennis S, Regan R, Conroy J), Daly MJ, Chakravarti A (2009). A genome-wide linkage and association scan reveals novel loci for autism. *Nature* **461**(7265):802-808.
5. Canney A, Sheahan K, Keegan D, Tolan M, Hyland J, Green A (2009). Synchronous lung tumours in a patient with metachronous colorectal carcinoma and a germline MSH2 mutation. *J Clin Pathol* **62**(5):471-473.

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

6. Darlow JM, Molloy NH, Green AJ, Puri P, Barton DE (2009). The increased incidence of the RET p.Gly691Ser variant in French-Canadian vesicoureteric reflux patients is not replicated by a larger study in Ireland. *Hum Mutat* **30**(5):E612-617.
7. Chan LF, Metherell LA, Krude H, Ball C, O'Riordan SM, Costigan C, Lynch SA, Savage MO, Cavarzere P, Clark AJ (2009). Homozygous nonsense and frameshift mutations of the ACTH receptor in children with Familial Glucocorticoid Deficiency are not associated with long-term mineralocorticoid deficiency. *Clin Endocrinol* **71**(2):171-175.
8. Lynch NE, Lynch SA, McMenamin J, Webb D (2009). Bannayan-Riley-Ruvalcaba Syndrome: a cause of extreme macrocephaly and neurodevelopmental delay. *Arch Dis Child* **94**(7):553-554.
9. Foley P, Bunyan D, Stratton J, Dillon M, Lynch SA (2009). Further case of Rubinstein-Taybi syndrome due to a deletion in EP300. *Am J Med Genet* **149A**(5):997-1000.
10. Ceppi F, Brown A, Betts DR, Niggli F, Popovic MB (2009). Cytogenetic characterization of childhood acute lymphoblastic leukemia in Nicaragua. *Pediatr Blood Cancer* **53**(7):1238-1241.
11. Canney A, Sheahan K, Keegan D, Tolan M, Hyland J, Green A (2009). Synchronous lung tumours in a patient with metachronous colorectal carcinoma and a germline MSH2 mutation. *J Clin Pathol* **62**(5):471-473.
12. Hughes J, Ryan S, Lambert D, Geoghegan O, Clark A, Rogers Y, Hendroff U, Monavari A, Twomey E, Treacy EP (2009). Outcomes of siblings with classical galactosemia. *J Pediatr* **154**(5):721-726.
13. Shahdadpuri R, Lambert D, Lynch SA (2009). Diagnostic outcome following routine genetics clinic attendance. *Ir Med J* 1-2.
14. Giorda R, Bonaglia MC, Beri S, Fichera M, Novara F, Magini P, Urquhart J, Sharkey FH, Zucca C, Grasso R, Marelli S, Castiglia L, Di Benedetto D, Musumeci SA, Vitello GA, Failla P, Reitano S, Avola E, Bisulli F, Tinuper P, Mastrangelo M, Fiocchi I, Spaccini L, Torniero C, Fontana E, Lynch SA, Clayton-Smith J, Black G, Jonveaux P, Leheup B, Seri M, Romano C, dalla Bernardina B, Zuffardi O (2009). Complex segmental duplications mediate a recurrent dup(X)(p11.22-p11.23) associated with mental retardation, speech delay & EEG anomalies in males & females. *Am J Hum Genet* **85**(3):394-400.
15. Greene N, Lynch SA, Doudney K, Whittaker J, Copp A, Grinham J, Stanier P (2009). Evaluation of folate metabolism gene polymorphisms as risk factors for open and closed neural tube defects. *Am J Med Genet A* **149A**(7):1585-1589.
16. McDevitt T, Barton D (2009). Cystic fibrosis diagnostic testing: When good CF tests go bad. *Eur J Hum Genet* **17**:403-405.

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

17. Wehrli LA, Braun J, Buetti LN, Hagleitner N, Hengartner H, Kühne T, Luer S, Ozsahin H, Popovic MB, Niggli FK, Betts DR, Bourquin JP (2009). Non-classical karyotypic features in relapsed childhood B-cell precursor acute lymphoblastic leukemia. *Cancer Genet Cytogenet* **189**(1):29-36.
18. Stanchesu R, Betts DR, Rechavi G, Amariglio N, Trakhtenbrot L (2009). Involvement of der(12)t(12;21)(p13;q22) and as well as additional rearrangements of chromosome 12 homolog in ETV6/RUNX1-positive acute lymphoblastic leukemia. *Cancer Genet Cytogenet* **190**(1):26-32.
19. Theissen J, Boensch M, Spitz R, Betts D, Stegmaier S, Christiansen H, Niggli F, Schilling F, Schwab M, Simon T, Westermann F, Berthold F, Hero B (2009). Heterogeneity of the MYCN oncogene in neuroblastoma. *Clin Cancer Res* **15**:2085-2090.
20. Watson CJ, McCrohan AM, Woodfine K, Tosetto M, McDaid J, Gallagher E, Betts D, Baugh J, O'Sullivan J, Murrell A, Watson RW, McCann A (2009). Generation of an epigenetic signature by chronic hypoxia in prostate cells. *Hum Mol Genet* **18**(19):3594-3604.
21. Kelly H, Barton D, Molony C, Puri P (2009). Linkage analysis of candidate genes in families with vesicoureteral reflux. *J Urol* **182**(4 Suppl):1669-1672.
22. Hughes J, Ryan S, Lambert D, Geoghegan O, Clark A, Rogers Y, Hendroff U, Monavari A, Twomey E, Treacy EP (2009). Outcomes of siblings with classical galactosemia. *J Pediatr* **154**(5):721-726.
23. Gumy-Pause, F Ozsahin H Khoshbeen-Boudal M, Pardo B, Betts D, Philippe Maillet P, Attiyeh EF, Sappino AP (2009). ATM deletion is a frequent event in neuroblastoma: a report from the COG. *J Clin Oncol* **27**:15(suppl; abstr 10058)

### 2010

24. Wormald R, Viani L, Lynch SA, Green AJ (2010). Sensorineural hearing loss in children. *Ir Med J* **103**(2):51-54.
25. Haslam K, Cahdwick N, Kelly J, Browne P, Vandenberghe E, Flynn C, Conneally E, Langabeer SE (2010). Incidence and significance of FLT3-ITD and NPM1 mutations in patients with normal karyotype acute myeloid leukaemia. *Ir J Med Sci* **179**(4): 507-510.
26. O'Riordan J, O'Donoghue D, Green A, Keegan D, Hawkes L, Payne S, Sheahan K, Winter D (2010). Hereditary mixed polyposis syndrome due to a BMPR1A mutation. *Colorectal Dis* **12**(6):570-573.
27. von Neuhoff C, Reinhardt D, Sander A, Zimmermann M, Bradtke J, Betts DR, Zemanova Z, Sary J, Bourquin JP, Haas OA, Dworzak MN, Creutzig U (2010). Prognostic impact of specific chromosomal aberrations in a large group of pediatric patients with acute myeloid leukemia treated uniformly according to trial AML-BFM 98. *J Clin Oncol* **28**(16):2682-2689.

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt





## National Centre for Medical Genetics

Dublin, Ireland

29. Göhring G, Michalova K, Beverloo HB, Betts D, Harbott J, Haas OA, Kerndrup G, Sainati L, Bergstraesser E, Hasle H, Stary J, Trebo M, van den Heuvel-Eibrink MM, Zecca M, van Wering ER, Fischer A, Noellke P, Strahm B, Locatelli F, Niemeyer CM, Schlegelberger B (2010). Complex karyotype newly defined: the strongest prognostic factor in advanced childhood myelodysplastic syndrome. *Blood* **116**(19):3766-3769.
30. Sunnotel O, Hiripi L, Lagan K, McDaid JR, De León JM, Miyagawa Y, Crowe H, Kaluskar S, Ward M, Scullion C, Campbell A, Downes CS, Hirst D, Barton D, Mocanu E, Tsujimura A, Cox MB, Robson T, Walsh CP (2010). Alterations in the steroid hormone receptor co-chaperone FKBP1 are associated with male infertility: a case-control study. *Reprod Biol Endocrin* **8**:22.
31. Mocanu E, Shattock R, Barton D, Rogers M, Conroy R, Sheils O, Collins C, Martin C, Harrison R, O'Leary J (2010). All azoospermic males should be screened for cystic fibrosis mutations before intracytoplasmic sperm injection. *Fertil Steril* **94**(6):2448-2450.
32. Johnston JJ, Sapp JC, Turner JT, Amor D, Aftimos S, Aleck KA, Bocian M, Bodurtha JN, Cox GF, Curry CJ, Day R, Donnai D, Field M, Fujiwara I, Gabbett M, Gal M, Graham Jr JM, Hedera P, Hennekam RC, Hersh JH, Hopkin RJ, Kayserili H, Kidd AM, Kimonis V, Lin AE, Lynch SA, Maisenbacher M, Mansour S, McGaughan J, Mehta L, Murphy H, Raygada M, Robin NH, Rope AF, Rosenbaum KN, Schaefer GB, Shealy A, Smith W, Soller M, Sommer A, Stalker HJ, Steiner B, Stephan MJ, Tilstra D, Tomkins S, Trapane P, Tsai AC, Van Allen MI, Vasudevan PC, Zabel B, Zunich J, Black GC, Biesecker LG (2010). Molecular analysis expands the spectrum of phenotypes associated with GLI3 mutations. *Hum Mutat* **31**(10):1142-1154.
33. Langabeer SE, Crampe M, Haslam K, Kelly J, Cahill MR (2010). Sustained clinical remission despite suboptimal molecular response to imatinib in e1a2 BCR-ABL chronic myeloid leukaemia. *Leuk Res* **34**(7);e176-177.
34. Langabeer SE, Crampe M, Kelly J, Fadalla K, Connaghan G, Conneally E (2010). Nilotinib and allogeneic stem cell transplantation in a chronic myeloid leukemia patient with e6a2 and e1a2 BCR-ABL transcripts. *Leuk Res* **34**(8):e204-205.
35. Haslam K, Chadwick N, Kelly J, Browne P, Vandenberghe E, Flynn C, Conneally E, Langabeer SE (2010). Incidence and significance of FLT3-ITD and NPM1 mutations in patients with normal karyotype acute myeloid leukaemia. *Ir J Med Sci.* **179**(4):507-510.
36. Wentzel C, Lynch SA, Stattin EL, Sharkey FH, Annerén G, Thuresson AC (2010). Interstitial deletions at 6q14.1–q15 associated with obesity, developmental delay and a distinct clinical phenotype. *Mol Syndromol* **1**(2):75-81.
37. Pawlikowska L, Strautnieks S, Jankowska I, Czubkowski P, Emerick K, Antoniou A, Wanty C, Fischler B, Jacquemin E, Wali S, Blanchard S, Nielsen IM, Bourke B, McQuaid S, Lacaille F, Byrne JA, van Eerde AM, Kolho KL, Klomp L, Houwen R,

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDéVitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

- Bacchetti P, Lobritto S, Hupertz V, McClean P, Mieli-Vergani G, Shneider B, Nemeth A, Sokal E, Freimer NB, Knisely AS, Rosenthal P, Whittington PF, Pawlowska J, Thompson RJ, Bull LN (2010). Differences in presentation and progression between severe FIC1 and BSEP deficiencies. *J Hepatol* 53(1):170-178.
38. Kagami M, O'Sullivan MJ, Green AJ, Watabe Y, Arisaka O, Masawa N, Matsuoka K, Fukami M, Matsubara K, Kato F, Ferguson-Smith AC, Ogata T (2010). The IG-DMR and the MEG3-DMR at Human Chromosome 14q32.2: Hierarchical interaction and distinct functional properties as imprinting control centers. *PLoS Genet* 6(6):e1000992.
39. Noor A, Whibley A, Marshall CR, Gianakopoulos PJ, Piton A, Carson AR, Orlic-Milacic M, Lionel A, Sato D, Pinto, Drmic D, Noakes C, Senman L, Zhang X, Mo R, Gauthier J, Crosbie J, Pagnamenta AT, Munson J, Estes AM, Fiebig A, Franke A, Stefan Schreiber S, Stewart AFR, Roberts, McPherson R, Guter SJ, Cook EH, Dawson G, Schellenberg GD, Battaglia A, Maestrini E; Autism Genome Project Consortium, Jeng L, Hutchison T, Rajcan-Separovic E, Chudley AE, Lewis SM, Liu X, Jeanette Holden, Bridget Fernandez, Lonnie Zwaigenbaum, Susan E. Bryson, Wendy Roberts, Peter Szatmari, Louise Gallagher, Michael R. Stratton, Jozef Gecz, Angela F. Brady, Schwartz CE, Schachar RJ, Monaco AP, Rouleau GA, Hui C, Raymond FL, Scherer S, Vincent JB (2010). Disruption at the PTCHD1 Locus on Xp22.11 in Autism spectrum disorder and intellectual disability. *Sci Transl Med* 2(49):49ra68.
40. Pinto D, Pagnamenta AT, Klei L, Anney R, Merico D, Regan R, Conroy J, Magalhaes TR, Correia C, Abrahams BS, Almeida J, Bacchelli E, Bader GD, Bailey AJ, Baird G, Battaglia A, Berney T, Bolshakova N, Bölte S, Bolton PF, Bourgeron T, Brennan S, Brian J, Bryson SE, Carson AR, Casallo G, Casey J, Chung BH, Cochrane L, Corsello C, Crawford EL, Crossett A, Cytrynbaum C, Dawson G, de Jonge M, Delorme R, Drmic I, Duketis E, Duque F, Estes A, Farrar P, Fernandez BA, Folstein SE, Fombonne E, Freitag CM, Gilbert J, Gillberg C, Glessner JT, Goldberg J, Green A, Green J, Guter SJ, Hakonarson H, Heron EA, Hill M, Holt R, Howe JL, Hughes G, Hus V, Iglizoi R, Kim C, Klauck SM, Kolevzon A, Korvatska O, Kustanovich V, Lajonchere CM, Lamb JA, Laskawiec M, Leboyer M, Le Couteur A, Leventhal BL, Lionel AC, Liu XQ, Lord C, Lotspeich L, Lund SC, Maestrini E, Mahoney W, Mantoulan C, Marshall CR, McConachie H, McDougle CJ, McGrath J, McMahon WM, Merikangas A, Migita O, Minshew NJ, Mirza GK, Munson J, Nelson SF, Noakes C, Noor A, Nygren G, Oliveira G, Papanikolaou K, Parr JR, Parrini B, Paton T, Pickles A, Pilorge M, Piven J, Ponting CP, Posey DJ, Poustka A, Poustka F, Prasad A, Ragoussis J, Renshaw K, Rickaby J, Roberts W, Roeder K, Roge B, Rutter ML, Bierut LJ, Rice JP, Salt J, Sansom K, Sato D, Segurado R, Sequeira AF, Senman L, Shah N, Sheffield VC, Soorya L, Sousa I, Stein O, Sykes N, Stoppioni V, Strawbridge C, Tancredi R, Tansey K, Thiruvahindrapduram B, Thompson AP, Thomson S, Tryfon A, Tsiantis J, Van Engeland H, Vincent JB,

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

- Volkmar F, Wallace S, Wang K, Wang Z, Wassink TH, Webber C, Weksberg R, Wing K, Wittmeyer K, Wood S, Wu J, Yaspan BL, Zurawiecki D, Zwaigenbaum L, Buxbaum JD, Cantor RM, Cook EH, Coon H, Cuccaro ML, Devlin B, Ennis S, Gallagher L, Geschwind DH, Gill M, Haines JL, Hallmayer J, Miller J, Monaco AP, Nurnberger JI Jr, Paterson AD, Pericak-Vance MA, Schellenberg GD, Szatmari P, Vicente AM, Vieland VJ, Wijsman EM, Scherer SW, Sutcliffe JS, Betancur C (2010). Functional impact of global rare copy number variation in autism spectrum disorders. *Nature* **466**:368-372.
41. van der Klift HM, Tops CM, Bik EC, Boogaard MW, Borgstein AM, Hansson KB, Ausems MG, Garcia EG, Green A, Hes FJ, Izatt L, van Hest LP, Alonso AM, Vriends AH, Wagner A, van Zelst-Stams WA, Vasen HF, Morreau H, Devilee P, Wijnen JT (2010). Quantification of sequence exchange events between PMS2 and PMS2CL provides a basis for improved mutation scanning of Lynch syndrome patients. *Hum Mutat* **31**(5):578-587.
42. Hoornaert KP, Vereecke I, Dewinter C, Rosenberg T, Beemer FA, Leroy JG, Bendix L, Björck E, Bonduelle M, Boute O, Cormier-Daire V, De Die-Smulders C, Dieux-Coeslier A, Dollfus H, Elting M, Green A, Guerci VI, Hennekam RC, Hilhorts-Hofstee Y, Holder M, Hoyng C, Jones KJ, Josifova D, Kaitila I, Kjaergaard S, Kroes YH, Lagerstedt K, Lees M, Lemerrer M, Magnani C, Marcelis C, Martorell L, Mathieu M, McEntagart M, Mendicino A, Morton J, Orazio G, Paquis V, Reish O, Simola KO, Smithson SF, Temple KI, Van Aken E, Van Bever Y, van den Ende J, Van Hagen JM, Zelante L, Zordania R, De Paepe A, Leroy BP, De Buyzere M, Coucke PJ, Mortier GR (2010). Stickler syndrome caused by COL2A1 mutations: genotype-phenotype correlation in a series of 100 patients. *Eur J Hum Genet* **18**(8):872-880.
43. Anney R, Klei L, Pinto D, Regan R, Conroy J, Magalhaes TR, Correia C, Abrahams BS, Sykes N, Pagnamenta AT, Almeida J, Bacchelli E, Bailey AJ, Baird G, Battaglia A, Berney T, Bolshakova N, Bölte S, Bolton PF, Bourgeron T, Brennan S, Brian J, Carson AR, Casallo G, Casey J, Chu S, Cochrane L, Corsello C, Crawford EL, Crossett A, Dawson G, de Jonge M, Delorme R, Drmic I, Duketis E, Duque F, Estes A, Farrar P, Fernandez BA, Folstein SE, Fombonne E, Freitag CM, Gilbert J, Gillberg C, Glessner JT, Goldberg J, Green A, Green J, Guter SJ, Hakonarson H, Heron EA, Hill M, Holt R, Howe JL, Hughes G, Hus V, Iglizzi R, Kim C, Klauck SM, Kolevzon A, Korvatska O, Kustanovich V, Lajonchere CM, Lamb JA, Laskawiec M, Leboyer M, Le Couteur A, Leventhal BL, Lionel AC, Liu XQ, Lord C, Lotspeich L, Lund SC, Maestrini E, Mahoney W, Mantoulan C, Marshall CR, McConachie H, McDougale CJ, McGrath J, McMahon WM, Melhem NM, Merikangas A, Migita O, Minshew NJ, Mirza GK, Munson J, Nelson SF, Noakes C, Noor A, Nygren G, Oliveira G, Papanikolaou K, Parr JR, Parrini B, Paton T, Pickles A, Piven J, Posey DJ, Poustka A, Poustka F, Prasad A,

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

- Ragoussis J, Renshaw K, Rickaby J, Roberts W, Roeder K, Roge B, Rutter ML, Bierut LJ, Rice JP, Salt J, Sansom K, Sato D, Segurado R, Senman L, Shah N, Sheffield VC, Soorya L, Sousa I, Stoppioni V, Strawbridge C, Tancredi R, Tansey K, Thiruvahindrapduram B, Thompson AP, Thomson S, Tryfon A, Tsiantis J, Van Engeland H, Vincent JB, Volkmar F, Wallace S, Wang K, Wang Z, Wassink TH, Wing K, Wittmeyer K, Wood S, Yaspan BL, Zurawiecki D, Zwaigenbaum L, Betancur C, Buxbaum JD, Cantor RM, Cook EH, Coon H, Cuccaro ML, Gallagher L, Geschwind DH, Gill M, Haines JL, Miller J, Monaco AP, Nurnberger JI Jr, Paterson AD, Pericak-Vance MA, Schellenberg GD, Scherer SW, Sutcliffe JS, Szatmari P, Vicente AM, Vieland VJ, Wijsman EM, Devlin B, Ennis S, Hallmayer J (2010). A genomewide scan for common alleles affecting risk for autism. *Hum Mol Genet* **19**(20):4072-4082.
44. de Leeuw N, Bulk S, Green A, Jaekle-Santos L, Baker LA, Zinn AR, Kleefstra T, van der Smagt JJ, Vianne Morgante AM, de Vries BB, van Bokhoven H, de Brouwer AP (2010). UBE2A deficiency syndrome: Mild to severe intellectual disability accompanied by seizures, absent speech, urogenital, and skin anomalies in male patients. *Am J Med Genet A* **152A**(12):3084-3090.

### 2011

1. Baker L, Conroy J, Donoghue V, Mullarkey M, Shah N, Murphy N, Murphy J, Ennis S, Lynch SA (2011). Lipomatous cortical dysplasia with lipoma of the corpus callosum associated with an Xp deletion. *Clin Dysmorphol* **20**(1):21-25.
2. Lynch SA, Foulds N, Thuresson AC, Collins AL, Annerén G, Hedberg BO, Delaney CA, Iremonger J, Murray CM, Crolla JA, Costigan C, Lam W, FitzPatrick DR, Regan R, Ennis S, Sharkey FH (2011). The 12q14 microdeletion syndrome; 6 new cases confirming the role of HMGA2 in growth. *Eur J Hum Genet* **19**(5):534-539.
3. O'Shea R, Murphy AM, Treacy E, Lynch SA, Thirlaway K, Lambert D (2011). Communication of genetic information by other health professionals: The role of the genetic counsellor in specialist clinics. *J Genet Couns* **20**(2):192-203.
4. 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 (2011). Molecular screening of ADAMTSL2 gene in 33 patients reveals the genetic heterogeneity of geleophysic dysplasia. *J Med Genet* **48**(6):417-421.
5. 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

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDévvitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

- S, Macdermot K, Mansour S, Megarbané A, Santos HG, Splitt M, Superti-Furga A, Unger S, Williams D, Munnich A, Cormier-Daire V (2011). Mutations in the TGF $\beta$  binding protein-like domain 5 of FBN1 are responsible for acromicric and geleophysic dysplasias. *Am J Hum Genet* **89**(1):7-14.
6. Palomares M, Delicado A, Mansilla E, de Torres ML, Vallespín E, Fernandez L, Martinez-Glez V, García-Miñaur S, Nevado J, Simarro FS, Ruiz-Perez VL, Lynch SA, Sharkey FH, Thuresson AC, Annerén G, Belligni EF, Martínez-Fernández ML, Bermejo E, Nowakowska B, Kutkowska-Kazmierczak A, Bocian E, Obersztyn E, Martínez-Frías ML, Hennekam RC, Lapunzina P (2011). Characterization of a 8q21.1 microdeletion syndrome associated with intellectual disability and a recognizable phenotype. *Am J Hum Genet* **89**(2):295-301.
  7. Fitzgerald K, Lynch SA, McKiernan E (2011). Case report: Unusual dental morphology in a child with ankyloblepharon-ectodermal defects-cleft lip/palate (AEC) syndrome. *Eur Arch Paediatr Dent* **12**(4):219-223.
  8. Casey J, Kawaguchi R, Morrissey M, Sun H, McGettigan P, Nielsen JE, Conroy J, Regan R, Kenny E, Cormican P, Morris DW, Tormey P, Ní Chroinin M, Kennedy BN, Lynch SA, Green A, and Ennis S (2011). First implication of STRA6 mutations in isolated anophthalmia, microphthalmia, and coloboma: A new dimension to the STRA6 phenotype. *Hum Mutat* **32**(12):1417-1426.
  9. Clayton-Smith J, O'Sullivan J, Daly S, Bhaskar S, Day R, Anderson B, Voss AK, Thomas T, Biesecker LG, Smith P, Fryer A, Chandler KE, Kerr B, Tassabehji M, Lynch SA, Krajewska-Walasek M, McKee S, Smith J, Sweeney E, Mansour S, Mohammed S, Donnai D, Black G (2011). Whole-exome-sequencing identifies mutations in histone acetyltransferase gene KAT6B in individuals with the Say-Barber-Biesecker variant of Ohdo Syndrome. *Am J Hum Genet* **89**(5):675-681.
  10. Lynch SA (2011). What price a diagnosis? *Dev Med Child Neurol* **53**(11):971.
  11. Puri P, Gosemann JH, Darlow J, Barton DE (2011). Genetics of vesicoureteral reflux. *Nat Rev Urol* **8**(10):539-552. Review.
  12. Dinis JM, Barton DE, Ghadiri J, Surendar D, Reddy K, Velasquez F, Chaffee CL, Lee MC, Gavrilova H, Ozuna H, Smits SA, Ouverney CC (2011). In search of an uncultured human-associated TM7 bacterium in the environment. *PLoS One* **6**(6):e21280.
  13. Boyle J, Hawkins M, Barton DE, Meaney K, Guitart M, O'Grady A, Tobi S, Ramsden SC, Elles R, Gray E, Metcalfe P, Hawkins JR (2011). Establishment of the first WHO international genetic reference panel for Prader Willi and Angelman syndromes. *Eur J Hum Genet* **19**(8):857-864.

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

14. Berwouts S, Christensen TM, Brandon J, Bejjani BA, Barton DE, Dequeker E (2011). Multiallelic synthetic quality control material: Lessons learned from the Cystic Fibrosis external quality assessment scheme. *Genet Test Mol Bioma* **15**(9):579-586.
15. Hawkins M, Boyle J, Wright KE, Elles R, Ramsden SC, O'Grady A, Sweeney M, Barton DE, Burgess T, Moore M, Burns C, Stacey G, Gray E, Metcalfe P, Hawkins JR (2011). Preparation and validation of the first WHO international genetic reference panel for Fragile X syndrome. *Eur J Hum Genet* **19**(1):10-17.
16. Anney RJ, Kenny EM, O'Dushlaine C, Yaspan BL, Parkhomenka E; The Autism Genome Project, Buxbaum JD, Sutcliffe J, Gill M, Gallagher L; The AGP Members, Bailey AJ, Fernandez BA, Szatmari P, Scherer SW, Patterson A, Marshall CR, Pinto D, Vincent JB, Fombonne E, Betancur C, Delorme R, Leboyer M, Bourgeron T, Mantoulan C, Roge B, Tauber M, Freitag CM, Poustka F, Duketis E, Klauck SM, Poustka A, Papanikolaou K, Tsiantis J, Gallagher L, Gill M, Anney R, Bolshakova N, Brennan S, Hughes G, McGrath J, Merikangas A, Ennis S, Green A, Casey JP, Conroy JM, Regan R, Shah N, Maestrini E, Bacchelli E, Minopoli F, Stoppioni V, Battaglia A, Iglizzo R, Parrini B, Tancredi R, Oliveira G, Almeida J, Duque F, Vicente A, Correia C, Magalhaes TR, Gillberg C, Nygren G, Jonge MD, Van Engeland H, Vorstman JA, Wittemeyer K, Baird G, Bolton PF, Rutter ML, Green J, Lamb JA, Pickles A, Parr JR, Couteur AL, Berney T, McConachie H, Wallace S, Coutanche M, Foley S, White K, Monaco AP, Holt R, Farrar P, Pagnamenta AT, Mirza GK, Ragoussis J, Sousa I, Sykes N, Wing K, Hallmayer J, Cantor RM, Nelson SF, Geschwind DH, Abrahams BS, Volkmar F, Pericak-Vance MA, Cuccaro ML, Gilbert J, Cook EH, Guter SJ, Jacob S, Nurnberger Jr JI, McDougle CJ, Posey DJ, Lord C, Corsello C, Hus V, Buxbaum JD, Kolevzon A, Soorya L, Parkhomenko E, Leventhal BL, Dawson G, Vieland VJ, Hakonarson H, Glessner JT, Kim C, Wang K, Schellenberg GD, Devlin B, Klei L, Minshew N, Sutcliffe JS, Haines JL, Lund SC, Thomson S, Yaspan BL, Coon H, Miller J, McMahon WM, Munson J, Estes A, Wijsman EM (2011). Gene-ontology enrichment analysis in two independent family-based samples highlights biologically plausible processes for autism spectrum disorders. *Eur J Hum Genet* **19**:1082-1089.
17. Vieland VJ, Hallmayer J, Huang Y, Pagnamenta AT, Pinto D, Khan H, Monaco AP, Paterson AD, Scherer SW, Sutcliffe JS, Szatmari P; Autism Genome Project (AGP). Novel method for combined linkage and genome-wide association analysis finds evidence of distinct genetic architecture for two subtypes of autism (2011). *J Neurodevel Disord* **3**:113-123.
18. Feenstra I, Hanemaaijer N, Sikkema-Raddatz B, Yntema H, Dijkhuizen T, Lugtenberg D, Verheij J, Green A, Hordijk R, Reardon W, Vries BD, Brunner H, Bongers E, Leeuw ND, van Ravenswaaij-Arts C (2011). Balanced into array: genome-wide array analysis

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

- in 54 patients with an apparently balanced de novo chromosome rearrangement and a meta-analysis. *Eur J Hum Genet* **19**(11):1152-1160.
19. Nowakowska BA, de Leeuw N, Ruivenkamp CA, Sikkema-Raddatz B, Crolla JA, Thoelen R, Koopmans M, den Hollander N, van Haeringen A, van der Kevie-Kersemaekers AM, Pfundt R, Mieloo H, van Essen T, de Vries BB, Green A, Reardon W, Fryns JP, Vermeesch JR. Parental insertional balanced translocations are an important cause of apparently de novo CNVs in patients with developmental anomalies. *Eur J Hum Genet* Epub 2011 Sep.
  20. Casey JP, Magalhaes T, Conroy JM, Regan R, Shah N, Anney R, Shields DC, Abrahams BS, Almeida J, Bacchelli E, Bailey AJ, Baird G, Battaglia A, Berney T, Bolshakova N, Bolton PF, Bourgeron T, Brennan S, Cali P, Correia C, Corsello C, Coutanche M, Dawson G, de Jonge M, Delorme R, Duketis E, Duque F, Estes A, Farrar P, Fernandez BA, Folstein SE, Foley S, Fombonne E, Freitag CM, Gilbert J, Gillberg C, Glessner JT, Green J, Guter SJ, Hakonarson H, Holt R, Hughes G, Hus V, Iglizzi R, Kim C, Klauck SM, Kolevzon A, Lamb JA, Leboyer M, Le Couteur A, Leventhal BL, Lord C, Lund SC, Maestrini E, Mantoulan C, Marshall CR, McConachie H, McDougle CJ, McGrath J, McMahon WM, Merikangas A, Miller J, Minopoli F, Mirza GK, Munson J, Nelson SF, Nygren G, Oliveira G, Pagnamenta AT, Papanikolaou K, Parr JR, Parrini B, Pickles A, Pinto D, Piven J, Posey DJ, Poustka A, Poustka F, Ragoussis J, Roge B, Rutter ML, Sequeira AF, Soorya L, Sousa I, Sykes N, Stoppioni V, Tancredi R, Tauber M, Thompson AP, Thomson S, Tsiantis J, Van Engeland H, Vincent JB, Volkmar F, Vorstman JA, Wallace S, Wang K, Wassink TH, White K, Wing K, Wittmeyer K, Yaspan BL, Zwaigenbaum L, Betancur C, Buxbaum JD, Cantor RM, Cook EH, Coon H, Cuccaro ML, Geschwind DH, Haines JL, Hallmayer J, Monaco AP, Nurnberger JI Jr, Pericak-Vance MA, Schellenberg GD, Scherer SW, Sutcliffe JS, Szatmari P, Vieland VJ, Wijsman EM, Green A, Gill M, Gallagher L, Vicente A, Ennis S. A novel approach of homozygous haplotype sharing identifies candidate genes in autism spectrum disorder. *Hum Genet* Epub 2011 Oct.
  21. Jenkinson EM, Clayton-Smith J, Mehta S, Bennett C, Reardon W, Green A, Pearce SH, De Michele G, Conway GS, Cilliers D, Moreton N, Davis JR, Trump D, Newman WG. Perrault syndrome: further evidence for genetic heterogeneity. *J Neurol* Epub 2011 Oct.
  22. Haslam K, Kelly J, Morris T, Connaghan G, Gilligan O, Browne P, Langabeer SE (2011). Screening for CRLF2 overexpression in adult acute lymphoblastic leukaemia. *Int J Lab Hematol* **33**:e17-e19.
  23. McCarron SL, Kelly J, Cown N, McCabe S, Fay M, O'Dwyer M, Hayden PJ, Langabeer SE (2011). A novel e8a2 BCR-ABL1 fusion with insertion of RALGPS1 exon 8 in a

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



- patient with relapsed Philadelphia chromosome-positive acute lymphoblastic leukaemia. *Leuk Lymphoma* **52**(5): 919-921.
24. Langabeer SE, McCarron SL, Carroll P, Kelly J, O'Dwyer M, Conneally E (2011). Molecular response to first line nilotinib in a patient with e19a2 BCR-ABL1 chronic myeloid leukaemia. *Leuk Res* **35**(9):e169-170.
  25. Langabeer SE, Haslam K, Kelly J, Leahy M, Vandenberghe E. Acute lymphoblastic leukaemia with an e1a3 BCR-ABL1 fusion. *Acta Haematol* **126**:214-215.
  26. Lockwood WW, Stack D, Morris T, Grehan D, O'Keane C, Stewart GL., Cumiskey J, Lam WL, Squire JA, Thomas DM, O'Sullivan MJ (2011). Cyclin E1 is amplified and overexpressed in osteosarcoma. *J Mol Diagn* **13**(3):289-296.
  27. Curry S, Ibrahim F, Grehan D, McDermott M, Capra M, Betts D, O'Sullivan M (2011). Rhabdomyosarcoma-associated renal cell carcinoma: a link with constitutional Tp53 mutation. *Pediatr Dev Pathol* **14**(3): 248-251.

## 19 Submitted Abstracts

1. S. Ennis Rare Disease Research developments and Research funding (Sept 2011). *THE 5TH ANNUAL GENERAL MEETING OF IPPOSI LTD*
2. A Green, J Casey, R Kawaguchi, M Morrissey, H Sun, P McGettigan, J Nielsen, J Conroy, R Regan, P Tormey, M Ni Chroinin, B Kennedy, SA Lynch, S Ennis. (2011) First implication of STRA6 mutations in isolated anophthalmia, microphthalmia and coloboma. *BSHG British Society for Human Genetics*
3. N. Shah, J. Casey, T. Magalhães, R. Regan, J. Conroy, E. Heron, R. Anney, A. Vicente, A. Green, M. Gill, L. Gallagher, S. Ennis, DC. Shields (2011) The Search of Maternal Genetic Effects in Autism: A Novel Approach *Human Variome Project Meeting*
4. Sally Ann Lynch, M Kram, N Goggin, M Earley, S Ennis, J Conroy. (2011) Ptosis, arched eyebrows, hypernasal speech, obesity & mild learning disability- a clinical & mapping study. *ISHG Irish Society for Human Genetics*
5. Judith Conroy, Murphy R, McDonagh C, Webb D, Casey J, Regan R, Ennis S, Lynch SA. (2011) A new locus for Episodic Ataxia *ISHG Irish Society for Human Genetics*
6. Jillian Casey, J Conroy, R Regan, E Crushell, SA Lynch, S Ennis. (2011) Identification of a novel disease gene for pediatric mitochondrial disorder. *ISHG Irish Society for Human Genetics*
7. J. Casey, E. Crushell, J. Conroy, R. Regan, B. Bourke, S.A. Lynch, S. Ennis. (July 2011) From research to genetic diagnosis: keeping up with the next-generation. *Temple Street Children's University Hospital Research Day, Dublin*

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt





## National Centre for Medical Genetics

Dublin, Ireland

8. Jillian Casey, J. Conroy, R. Regan, N. Shah, S. A. Lynch, **S. Ennis**. Homozygosity mapping and exome sequencing identifies a novel disease gene for pediatric mitochondrial disorder (June 2011) *2<sup>nd</sup> GATC Symposium on Next and Third Generation Sequencing*
9. J. Casey, R. Kawaguchi, M. Morrissey, H. Sun, P. McGettigan, J. Nielsen, J. Conroy, R. Regan, P. Tormey, M. Ní Chróinín, b. Kennedy, S. A. Lynch, A. Green, S. Ennis. (2011) First implication of *STRA6* mutations in isolated anophthalmia, microphthalmia and coloboma. *European Society of Human Genetics*
10. J. Casey, R. Kawaguchi, M. Morrissey, H. Sun, P. McGettigan, J. Nielsen, J. Conroy, R. Regan, P. Tormey, M. Ní Chróinín, b. Kennedy, S. A. Lynch, A. Green, **S. Ennis**. (May 2011). Adding a new dimension to the *STRA6* phenotype. *Our Lady's Children's Hospital Research Day, Dublin*
11. S. Ennis, R. Regan, J. Conroy, J. Casey, T. Magalhaes, N. Shah, R. Anney, E. Heron, L. Gallagher, M. Gill, A. Green, D. Shields, A. Vicente, Autism Genome Project (May 2011). The novel approach of homozygous haplotype sharing reveals candidate genes in autism spectrum disorder *Our Lady's Children's Hospital Research Day, Dublin*
12. Louise Gallagher and Sean Ennis Autism is an extremely variable disorder, Clinical and molecular genetics considerations. (March 2010) NCRC National Childrens Research Centre seminar series
13. S. Ennis Microarray & NGS Exome capture in Rare/Orphan Disease Research (Feb 2011). *Advances in Genomics Meeting*
14. J. Casey, J. Conroy, R. Regan, N. Shah, E. B. Crushell, S. A. Lynch, S. Ennis. (2010) The use of whole exome sequencing and linkage analysis to identify novel candidate loci for pediatric mitochondrial disorder. *American Society of Human Genetics*
15. R. Regan, L. Baker, J. Conroy, V. Donoghue, M. Mullarkey, N. Shah, N. Murphy, S. Ennis, S. A. Lynch. Lipomatous cortical dysplasia with lipoma of the corpus callosum associated with an Xp deletion. (2010) *American Society of Human Genetics*
16. J. Conroy, J. Casey, N. Shah, R. Regan, M. Morgan, K. Collins, B. Parry-Fielder, S. A. Lynch, M. King, S. Ennis. An investigation into the causes of Landau-Kleffner syndrome. (2010) *American Society of Human Genetics*
17. V. Vieland, J. Hallmayer, Y. Huang, A. Pagnamenta, D. Pinto, H. Khan, A. P. Monaco, A. D. Paterson, S. W. Scherer, J. S. Sutcliffe, P. Szatmari, Autism Genome Project. Novel statistical methods for combining genome-wide linkage and association analyses provide evidence of different genetic architecture for autism in the presence or absence of intellectual disability. (2010) *American Society of Human Genetics*
18. A. F. Sequeira, C. Correia, J. Almeida, S. Mouga, C. Cafe, F. Duque, D. Pinto, P. Szatmari, S. W. Scherer, G. Oliveira, A. M. Vicente, Autism Genome Project Consortium. Recurrent rearrangements of 16p13.11: Further evidence for a pathogenic

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

- role of deletions in autism spectrum disorders. (2010) *American Society of Human Genetics*
19. C. Correia, A.F. Sequeira, J. Almeida, C.Café, S. Mouga, F. Duque, T. Magalhaes, D. Pinto, W. Roberts, S.W. Scherrer, G. Oliveira, A.M. Vicente, Autism Genome Project Consortium. Rare copy number variants in the ANXA1 gene in patients with autism spectrum disorders. (2010) *American Society of Human Genetics*
  20. A. Noor, A. Whibley, C.R. Marshall, AGP. Autism Genome Project Consort., G.A. Rouleau, C.C. Hui, F.L. Raymond, S.W. Scherer, J.B. Vincent. Disruption at the PTCHD1 locus on Xp22.11 results in autism spectrum disorder and intellectual disability. (2010) *American Society of Human Genetics*
  21. J. Buxbaum for the Autism Genome Project Consortium (AGP). A two-stage genomewide scan for common alleles affecting risk for autism. (2010) *American Society of Human Genetics*
  22. D. Pinto, S.W. Scherer, Autism Genome Project Consortium (AGP). Functional impact of global rare copy number variation in autism spectrum disorders. (2010) *American Society of Human Genetics*
  23. N. Shah, R. Regan, J. Conroy, T. Magalhães, J. Casey, A. Green, M. Gill, A. Vicente, L. Gallagher, DC. Shields, S. Ennis (2010). Genetics of Autism Spectrum Disorder. Presented at Computational Biology and Innovation PhD Symposium
  24. S. Ennis Copy Number Variation & Structural Rearrangements. (June 2010) *Molecular Medicine Ireland– Human Disease Genomics*
  25. S. Ennis SNPs and Next-Generation Sequencing in the Study of Single Gene Disorders. Applications in Study of Sensory Phenotypes. (June 2010) *Molecular Medicine Ireland– Human Disease Genomics*
  26. J. P. Casey, J. Conroy, R. Regan, N. Shah, S. Lynch, A. Green, S.Ennis; (2010) Identification of a novel candidate disease locus for anophthalmia/microphthalmia by homozygosity mapping in an Irish traveller family. *ESHG European Society for Human Genetics*
  27. T. R. Magalhães , J. Casey , C. Correia , F. Sequeira , M. Espada , S. Ennis , A. M. Vicente , A. G. Project , Autism Genome Project. Genome-Wide Association Analysis of Susceptibility Genes in Autism Using with a Gene-Centric Approach. (2010) *IMFAR International Meeting for Autism Research*
  28. Autism Genome Project Consortium , AGP Institutions in, North America and Europe, Genome-Wide Analysis Identifies Global Rare Variation in Autism . (2010) *IMFAR International Meeting for Autism Research*
  29. Milewski MA, Leahy DT, Conroy J, Ennis S, Mulcahy H, Hyland J, O'Donoghue D, Sheahan K. (2010) LABORATORY INVESTIGATION 90: Suppl. 1, 156 Genome-wide DNA methylation profiling of sporadic and familial colorectal cancer

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

30. Milewski MA, Leahy DT, Conroy J, Ennis S, Mulcahy H, Hyland J, O'Donoghue D, Sheahan K. (2010) MODERN PATHOLOGY 23: Suppl. 1, 156 Genome-wide DNA methylation profiling of sporadic and familial colorectal cancer
31. J. Conroy, AT. Pagnamenta, N. Shah, R. Segurado, J. Casey, R. Regan, T. Magelhaes, K. Tansey, D. Pinto, JB. Cazier, A. Vicente, A. Green, M. Gill, L. Gallagher, AP. Monaco, S. Ennis, Autism Genome Project (2009) The Role of the Mitochondria in Autism ASHG *American Society for Human Genetics*
32. Richard Anney, On behalf of the Autism Genome Project (2009) The Autism Genome Project:Genome-wide Association Studies In Autism ISHG *Irish Society for Human Genetics*
33. N. Shah, R. Regan, J. Conroy, T. Magalhaes, J. Casey, R. Anney, A. Green, L. Gallagher, M. Gill, DC. Shields, A. Vicente, S. Ennis (2009) Parental Origin Bias in de novo CNVs Detected in Autism Probands ASHG *American Society for Human Genetics*
34. B. L. Yaspan, J. S. Sutcliffe, M. A. Pericak-Vance, J. L. Haines, and the Autism Genome Project (2009) Pathway analysis of multiple GWAS datasets implicates genes in the extracellular matrix - receptor interaction pathway with autism risk ASHG *American Society for Human Genetics*
35. A. T. Pagnamenta, D. Pinto, H. Khan, V. J. Vieland, A. S. Le-Couteur, S. W. Scherer, A. P. Monaco, The Autism Genome Project Consortium (2009) Copy Number Variation Discovery in Autism Spectrum Disorder ASHG *American Society for Human Genetics*
36. S. Ennis on behalf of the Autism Genome Project Consortium (AGP) (2009) The Autism Genome Project: Dissecting the genetic and genomic etiology of autism ASHG *American Society for Human Genetics*
37. Casey, T. Magelhaes, J. Conroy, R. Regan, N. Shah, R. Anney, E. Heron, A. Green, L. Gallagher, M. Gill, D. Shields, A. Vicente, S. Ennis. Autism Genome Project (2009) Genome-wide homozygous haplotype mapping to identify autism spectrum disorder candidate genes 2009 IRCSET Symposium 'Innovation fuelling the Smart Society'
38. R Anney on behalf of the PGC (2009) COMBINED GWAS OF AUTISM, THE PSYCHIATRIC GWAS CONSORTIUM PGC XVII *World Congress of Psychiatric Genetics*
39. R Anney on behalf of the AGP (2009) THE AUTISM GENOME PROJECT: GENOME-WIDE ASSOCIATION STUDIES IN AUTISM XVII *World Congress of Psychiatric Genetics*
40. S. Ennis on behalf of the Autism Genome Project Consortium (AGP) (2009) The Autism Genome Project:CNVs in Autism Spectrum Disorder *5th International Meeting on Cryptic Chromosomal Rearrangements in Mental Retardation and Autism*

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

41. S. Ennis on behalf of the Autism Genome Project Consortium (AGP) (2009) The Autism Genome Project: The Genetics of Autism Spectrum Disorder *9th Annual International Gene Forum 2009 'New Frontiers in Genomics'*
42. R. Regan, S.A. Lynch, C. Costigan, N. Foulds, A. Collins, A.C. Thureson, G. Annerén, B.O. Hederg, D.R. Fitzpatrick, S. Ennis, F.H. Sharkey (2009) The 12q14 microdeletion syndrome, 5 further cases ISHG *Irish Society for Human Genetics*
43. SA Lynch, M King, J Conroy and S Ennis (2009) Monozygous Twins discordant for Landau-Kleffner Syndrome ISHG *Irish Society for Human Genetics*
44. N. Shah, R. Regan, J. Conroy, T. Magalhaes, J. Casey, R. Anney, A. Green, L. Gallagher, M. Gill, DC. Shields, A. Vicente, S. Ennis (2009) Parental Origin Bias in de novo CNVs Detected in Autism Probands ISHG *Irish Society for Human Genetics*
45. Linda McArdle, Sally Ann Lynch, Sean Ennis, Thomas Morris, David R. Betts (2009) Tissue Specific Mosaicism of a der(18) in a Developmentally Delayed Boy ISHG *Irish Society for Human Genetics*
46. Naisha Shah, Judith Conroy, Regina Regan, Sean Ennis, Denis C. Shields (2009) Parental Origin Bias in de novo CNVs Detected in Autism Probands *Human Variome Project Meeting*
47. J. Casey, J. Conroy, R. Regan, N. Shah, T. Magalhaes, A. Green, S A Lynch, S. Ennis, (2009) The Use of SNP Homozygosity mapping to identify disease genes in Irish Families ISHG *Irish Society for Human Genetics*
48. Linkage Analysis by the Autism Genome Project (AGP) Reveals Strong Evidence of Linkage to Multiple Loci as well as Gene-Gene Interactions. J. Hallmayer, representing the Autism Genetics Cooperative (AGC) and the Autism Genome Project (AGP). (2009) IMFAR *International Meeting for Autism Research*
49. C. Correia, A. Coutinho, S. Silva, I. Sousa, L. Lourenço, J. Almeida, R. Lontro, C. Lobo, T. S. Miguel, L. Gallagher, M. Gill, S. Ennis, T. Magalhães, G. Oliveira, A. Vicente. BDNF/TRKB Signalling Pathway in Autism: Increased Plasma BDNF Levels and Association of NTRK2 Genetic Variants in an Autism Population Sample. (2009) IMFAR *International Meeting for Autism Research*
50. Catarina Correia, Ana Margarida Coutinho, Inês Sousa, Isabel Peixeiro, Lara Lourenço, Joana Almeida, Raquel Lontro, Louise Gallagher, Michael Gill, Sean Ennis, Guiomar Oliveira, Astrid M. Vicente (2008) Brain-derived Neurotrophic Factor (BDNF) in autism: plasma levels and analysis of candidate genes BDNF and NTRK2 *The XVIth World Congress on Psychiatric Genetics*
51. Correia C, Sousa I, Peixeiro I, Lourenço L, Almeida J, Lontro R, Gallagher L, Gill M, Ennis S, Oliveira G, Vicente AM (2008) The BDNF receptor gene NTRK2 is a susceptibility gene for autism *European Society for Human Genetics*

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

52. L. A. Weiss, D. E. Arking, T. Green, J. F. Gusella, S. L. Santangelo, R. E. Tanzi, P. Sklar, A. Chakravarti, M. J. Daly, Autism Consortium Gene-Finding Group & Autism Genome Project. (2008) Genome-wide Association Mapping in Multiplex Autism Families *ASHG American Society for Human Genetics*
53. O. Stein and the Autism Genome Project (2008) Data coordinating infrastructure for the Autism Genome Project *ASHG American Society for Human Genetics*
54. P. Szatmari, X.-Q. Liu, J. A.D. Paterson and The Autism Genome Project Consortium (2008) Sex differences in repetitive stereotyped behaviours in autism: implications for genetic liability *ASHG American Society for Human Genetics*
55. VJ Vieland for the AGC and AGP (2008) New linkage analysis by the Autism Genome Project (AGP) reveals strong evidence of linkage to multiple loci as well as gene-gene interactions *ASHG American Society for Human Genetics*
56. G.D. Schellenberg, for the Autism Genome (2008) Analysis of the EAAT2 glutamate transporter (SLC1A2) locus as an 11p13 positional candidate for autism *ASHG American Society for Human Genetics [Details]*
57. J.S. Sutcliffe, for the Autism Genome Project (2008) The Autism Genome Project: Dissecting the genetic and genomic etiology of autism *ASHG American Society for Human Genetics*
58. Naisha Shah, Judith Conroy, Regina Regan, Sean Ennis, Denis C Shields. (2008). Analyzing Illumina Human 1M SNP Data For CNVs Using Raw Bead-Level Data. *Ataxia ISHG Irish Society for Human Genetics*
59. S. Ennis Overview of the International Autism Genome Project (AGP) and the usefulness of SNP Arrays in Cytogenetics (Oct 2008). *Inaugural Joint Belfast/Dublin Cytogenetic Meeting*
60. Naisha Shah, Judith Conroy, Regina Regan, Sean Ennis, Denis C Shields. (2008). Evaluating Illumina's Infinium Human 1M SNP Data and Existing CNV Prediction Algorithms. *Human Variome Project Meeting*
61. P Szatmari, X-Q Liu, A Paterson and the Autism Genome Project (2007) Sex Differences in ASD Phenotypes *6th Annual International Meeting for Autism Research (IMFAR)*
62. Liu X-Q, Paterson AD, Szatmari P. The Autism Genome Project (AGP) Consortium. (2007) Genome-wide linkage analysis of ADI-R social and repetitive behaviour domain total scores *6th Annual International Meeting for Autism Research (IMFAR)*
63. Schellenberg, Gerard D., Devlin, Bernie, Scherer, Stephen W., The Autism Genome Project (AGP) Consortium. (2007) Copy Number Variation and linkage analysis of multiplex autism families *6th Annual International Meeting for Autism Research (IMFAR)*

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

64. Thomas Wassink, Kacie Meyer, Val Sheffield, The Autism Genome. (2007) A NRXN1 paternal germ-line mutation causing autism in two female siblings *6th Annual International Meeting for Autism Research (IMFAR)*
65. Janine Lamb for the Autism Genome Project (2007) Autism Genome Project: Genome Screen Linkage and Copy Number Variation analyses Autism Research in the UK - from diagnosis to intervention. *The Open University, UK*
66. The Autism Genome Project (2007) Integration of Phenotype, Genotype and Function to Identify Autism Genes *The XVth World Congress of Psychiatric Genetics*
67. Stephen O'Riordan, Sean Ennis, Andrew Green, Sherly. George, Hilary Hoey, Elaine Hand, Colm Costigan (2007) Genetics of cystic fibrosis related diabetes and non diabetes Hormone Research Proceedings of the Irish Paediatric Association meeting
68. K. J. Meyer, L. K. Davis, A. L. Librant, D. S. Rudd, E. M. Berg, C. M. Taylor, J. Piven, E. M. Stone, V. C. Sheffield, T. H. Wassink, Autism Genome Project Consortium. (2007) A Neurexin 1 deletion implicates a synaptic defect in the pathophysiology of autism *ASHG American Society for Human Genetics*

## 20 PLATFORM PRESENTATIONS

### 2007

1. Irish Society of Human Genetics: AM Murphy, C Halling, AA Monavari, S Harty, E Crushell, EP Treacy, SA Lynch. A prospective study of referrals from the Irish Traveller community to the National Centre for Inherited Metabolic Disorders
2. Irish Paediatric Association Spring meeting: J Walsh, D Lambert, DM Baldrige, R Morello, D Eyre, B Lee, AJ Green. The Genetic Basis of Autosomal Recessive Osteogenesis Imperfecta in the Irish Traveller Population.
3. Irish Perinatal Society Meeting Belfast: M Meany & A Dunlop. A 5 year audit of prenatal referrals to the National Centre for Medical Genetics Ireland 2001-2006.
4. Medical Grand Rounds Our Lady's Children's Hospital Crumlin. M Sweeney. How common is Fragile X Syndrome? - NCMG perspective.
5. Medical Grand Rounds Children's University Hospital, Temple St. M Sweeney. 'Fragile X Syndrome?'
6. British Society of Human Genetics - Invited presentation. A Green, SA Lynch, E Treacy, D Lambert, F Stewart. Autosomal Recessive Disorders in the Irish Travellers.
7. Haematology / Oncology Journal Club Our Lady's Children's Hospital Crumlin. 1. K Kelly, A O'Marcaigh, S Rooney, J Kelly. Acute promyelocytic leukaemia: A transitional research paradigm.
8. S Hassan, S Rooney, J Kelly, OP Smith. Burkitt Lymphoma / leukaemia.

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

9. R Desmond, S Rooney, J Kelly, OP Smith t(12;21)(p13;q22) [ETV6/RUNX1 fusion] positive ALL: What is the prognostic impact?
10. Belfast / Dublin Joint Clinical Genetics Meeting
  - C de Baroid. Prenatal cases
  - D Lambert. NCMG Translocation case
  - L Hodgkin. Familial Cancer Centre, The Royal Melbourne Hospital, Victoria
  - Genetic counseling in Australia
  - R O'Shea, AM Murphy & D Lambert. Knowledge and understanding of inheritance patterns amongst families affected by inherited metabolic disease who attend the metabolic centre in Temple Street Dublin
  - J McBrien. Pitt Hopkins syndrome

### 2008

11. Irish Society of Human Genetics: Paula Carty, Johanna Kelly, Sarah McCabe, Natasha Coen, Claire Bermingham, Thomas Morris, David Betts. Biallelic deletions of chromosome 13q are frequent at diagnosis in chronic lymphocytic leukaemia.
12. Rosie O'Shea, Eileen Treacy, Anne Marie Murphy, Sally Ann Lynch, Debby Lambert. Study of the Knowledge of Inherited of metabolic Disorders among patients and their families in the Irish population
13. *Irish Perinatal Society Fota, Cork*: D Lambert, M Morgan, SA Lynch. Uptake of prenatal services and cascade carrier testing for cystic fibrosis in Ireland.
14. *Irish Paediatric Association Spring Meeting Limerick*: R Shahdadpuri, D Lambert & S Lynch. Diagnostic outcome following Routine Clinical Genetics referral for the assessment of developmental delay. *Awarded Best Long Paper*
15. *Royal College of Physicians and Child Health Society Meeting, York*: R Shahdadpuri, D Lambert & S Lynch. Diagnostic outcome following Routine Clinical Genetics referral for the assessment of developmental delay.
16. *European Cystic Fibrosis Conference, Prague*: C King, D Lambert, M Rogers, T McDevitt, D Barton, SA Lynch. Genotypes and Borderline Sweat Tests in Irish CF Patients – An Update
17. Belfast / Dublin Joint Clinical Genetics Meeting
  - L Bradley. Pitfalls in the diagnosis of mitochondrial inheritance.
  - A Ward. Counselling issues when more that one genetic disorder occurs within the family.
  - A Ward. 47, XYY cases in the Irish Republic.
  - N Cody. Proposal for follow on study of cascade screening for BRCA1/2 in the Republic of Ireland.
18. Belfast / Dublin Joint Cytogenetic Meeting

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

- C Bermingham. Overview of karyotypic features in AML at diagnosis.
- G Clarke. Audit of clinical samples with developmental delay as clinical indication.
- J Mc Daid. Factors affecting success and abnormality rate in prenatal samples in Dublin

### 2009

#### 19. Irish Society of Human Genetics

- J Kelly, N Coen, L Barton, M O'Dwyer, P Browne, E Conneally, DR Betts. Cytogenetic Analysis in Donor Cell Neoplasms.
  - K Nolan, M Dobson, J Brady, C Brady, D Barton. Determination of the contribution of H63D/H63D genotype to iron overload, and validation of a dual hybridisation probe assay for detecting HFE genes.
  - P Foley, R Kelly, N de Leeuw, A Green. Study of the Knowledge of Inherited Metabolic Familial Learning Disability & dysmorphism due to a cryptic insertional translocation determined by CGH array.
  - J Casey, J Conroy, R Regan, A Green, SA Lynch, S Ennis. The use of SNP homozygosity mapping to identify disease genes in Irish families.
20. *6<sup>th</sup> International Neural Tube defect meeting Vermont, USA:* SA Lynch, J Casey, R Regan, J Conroy, A Green, S Ennis. Mapping disease genes in the Irish Traveller population
  21. *5<sup>th</sup> International DECIPHER Symposium Cambridge:* SA Lynch, N Foulds, AC Thuresson, C Costigan R Regan, S Ennis, & FH Sharkey. The 12q14 microdeletion syndrome, 4 further cases
  22. *Association of Genetic Counselors & Nurses (AGNC) Annual Meeting, Cardif.* R O'Shea. A study into the knowledge of inherited metabolic diseases among patients and their parents in Irish families.
  23. All Ireland Genetics Meeting. R O'Shea. Mosaicism - a review of Down Syndrome Cases.
  24. Neonatal Nursing Day Croke Park. S Lynch. Genetic issues in a neonatal unit
  25. Introductory talk on Genetic Counselling, given to ICU nurses OLCHC Jacqueline Turner 31<sup>st</sup> of March 2009
  26. Muscular Dystrophy Ireland (MDI) Annual Support Group Meeting. J Turner. Genetic Counselling for Myotonic Dystrophy.
  27. Irish Paediatric Association Spring Meeting. Baker, M Sweeney, D Barton & SA Lynch. Incidence of Fragile X syndrome in the Republic of Ireland.
  28. L Baker M Sweeney, SA Lynch. Clinical features and demographics of 18 positive Fragile X cases identified by NCMG from 2000-2008
  29. Belfast / Dublin Joint Clinical Genetics Meeting

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt





## National Centre for Medical Genetics

Dublin, Ireland

- J Turner. Reviewing the Website [www.geneticseducation.nhs.uk](http://www.geneticseducation.nhs.uk). Supporting genetics education for Health Professionals.
  - D Donnelly & P Foley. Skin chromosome mosaicism; a review of cases in Northern and Southern Ireland
  - L Baker & D Donnelly. Incidence and prevalence of Fragile X syndrome in Ireland and Northern Ireland
  - J Turner. Cascade screening for Hypertrophic Cardiomyopathy - economic cost of cascade screening.
  - R O'Shea. Recurrent trisomy 21.
  - M Meany. An unusual Sickle cell case.
30. Belfast / Dublin Joint Cytogenetic Meeting, Belfast.
- Z Adamson. Implications of Gain of 9p.
  - J Kelly. Cytogenetic Analysis in Donor Cell Neoplasms.
  - D Betts. Cytogenetics of Neuroblastoma.

### 2010

31. *American Society of Human Genetics, Washington DC.* J Casey, J Conroy, R Regan, N Shah, EB Crushell, SA Lynch, S Ennis. The use of whole exome sequencing & linkage analysis to identify novel candidate loci for pediatric mitochondrial disorder.
32. *Haematology Association of Ireland, Galway.* G Clarke, J Kelly, C Bermingham, L Barton, S Ryan, P Carty, D Betts. Association of monosomy 3 with del(5q) in myeloid neoplasms.
33. *Friedreich Ataxia Society Ireland.* D Lambert. Genetic counselling for Friedreich's and other recessive ataxias
34. Presentation in Rotunda. D Lambert. A 46,XX / 46,XY CVS – what are the possibilities?
35. Irish Society of Human Genetics. K Meaney, B O'hici, SA Lynch, DE Barton. Atypical 22q11 deletion detected by multiplex ligation-dependent probe amplification (MLPA) in patients referred for Prader-Willi Syndrome (PWS) testing.
36. Belfast / Dublin Joint Clinical Genetics Meeting.
- A Green, F Stewart, J Turner. CPVT in Ireland
  - SA Lynch. The genetic basis of Landau-Kleffner syndrome
  - D Lambert Vanishing twin or not - a difficult prenatal case.
  - A Ward. CF Newborn screening

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

2011

37. Irish Society of Human Genetics, Dublin.
- SA Lynch, M Kram, N Goggin, M Earley, S Ennis, J Conroy. Ptosis, arched eyebrows, hypernasal speech, obesity & mild learning disability- a clinical & mapping study.
  - L Ng, N Harper, A Green. Familial catecholaminergic polymorphic ventricular tachycardia in Ireland.
  - F McElligott, E Beatty, S O'Sullivan, J Hughes, D Lambert, A Cooper, E Crushell. Incidence of I-cell disease (mucopolidosis type II) in the Irish population.
  - J Casey, J Conroy, R Regan, E Crushell, SA Lynch, S Ennis. Identification of a novel disease gene for pediatric mitochondrial disorder.
  - J Conroy, R Murphy, C McDonagh, D Webb, J Casey, R Regan, S Ennis, SA Lynch. A new locus for Episodic Ataxia.
  - M Dobson, J Darlow. A new genome scan for vesicoureteric reflux.
38. Association of Genetic Counsellors & Nurses (AGNC), Belfast. J Turner. Genetic Counselling for the Irish Traveller Community Presented at the April 2011
39. NF Association AGM, Dublin. A Ward. Neurofibromatosis – Clinical Genetics Services for NF
40. Muscular Dystrophy Ireland (MDI) Annual Support Group Meeting. Genetic Counselling for Facioscapulo Humeral Muscular Dystrophy (FSHD):
41. GRDO (Genetic Rare disease organisation) meeting. NCMG - the future. J Turner, M Meany SA Lynch.
42. *PlanetxMap 2011, Vienna*. T McDevitt, M Rogers, S Roring, DE Barton. Validation of Luminex xTAG™ Cystic Fibrosis 39 Kit v2 for Diagnostic Testing & Newborn Screening using Dried Blood Spots.
43. Irish CF Conference, Killarney. T McDevitt. CF Newborn Screening
44. Temple Street Children's University Hospital Research Day, Dublin.
- 1. J Casey, E Crushell, J Conroy, R Regan, B Bourke, SA Lynch, S Ennis. From research to genetic diagnosis: keeping up with the next-generation.
  - 2. J Casey, D Slattery, J Conroy, R Regan, S Ennis, SA Lynch. Towards identification of a disease gene for primary ciliary dyskinesia.
  - 3. J Conroy M King, M Moran S Ennis & SA Lynch. An investigation into the genetic causes of Landau-Kleffner syndrome.
  - 4. L Bradley, C Murphy, D Murray, A McGillivray Dabir T & Sally Ann Lynch. Craniosynostosis in the Island of Ireland.

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

45. Our Lady's Children's Hospital Research Day, Dublin.
  - J Casey, R Kawaguchi, M Morrissey, H Sun, P McGettigan, J Nielsen, J Conroy, R Regan, P Tormey, M Ní Chróinín, B Kennedy, SA Lynch, A Green, S Ennis. Adding a new dimension to the STRA6 phenotype.
46. European Society of Human Genetics, Amsterdam. J Casey, R Kawaguchi, M Morrissey, H Sun, P McGettigan, J Nielsen, J Conroy, R Regan, P Tormey, M Ní Chróinín, b. Kennedy, SA Lynch, A Green, S Ennis. First implication of STRA6 mutations in isolated anophthalmia, microphthalmia and coloboma.
47. British Society of Human Genetics. Warwick. A Green, J Casey, R Kawaguchi, M Morrissey, H Sun, P McGettigan, J Nielsen, J Conroy, R Regan, P Tormey, M Ní Chróinín, b. Kennedy, SA Lynch, S Ennis. First implication of STRA6 mutations in isolated anophthalmia, microphthalmia and coloboma.
48. Haematology Association of Ireland. J Kelly, O Smith, A O'Marcaigh, D Betts. Incidence of cytogenetic aberrations in paediatric acute lymphoblastic leukaemia presenting in the period 2006-2010.
49. National Children's Research Centre Research Seminars. J Conroy, S Lynch & S Ennis. Next generation sequencing: A NCRC experience"

## 21 Abstract from Meetings

1. C. King BSHG Report on 31st European Cystic Fibrosis Conference, Prague, 11-14 June 2008.
2. NHS Technology Assessment Report. Fragile X analysis: A multi-centre assessment of the Abbott Molecular Fragile X analyte specific reagent (ASR) kit; January 2008. A Wallace, DE Barton, PA van Bunderen, J Duncan, J Dunlop, S Man, J MacPherson, G Monaghan, J McLuskey, G Norbury, Y Patel, H Powell, V Race, M Sweeney, E Thompson, R Treacy, MM Weiss, N Williams, HE White, B Wymer.
3. T McDevitt – Participation in draft EMQN Best Practice Guidelines for Molecular Genetic Analysis in Hereditary Breast/Ovarian Cancer 2008
4. Testing Guidelines for molecular diagnosis of Cystic Fibrosis. CMGS Guidelines Prepared by Schwarz M, Gardner A, Jenkins L, McQuaid S, Norbury G, Renwick P, Robinson D.

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## 22 Poster Presentations

### 2007

1. J Walsh, D Lambert, DM Baldrige, R Morello, D Eyre, B Lee, AJ Green. The genetic basis of autosomal recessive osteogenesis imperfecta in the Irish traveller population. Irish Society of Human Genetics
2. J Kelly, E Conneally, E Vandenberg, SA Lynch. Audit of MDS cases submitted for cytogenetic analysis over a two year period. Irish Society of Human Genetics
3. K Meaney, DE. Barton. Detection of subtelomeric rearrangements in children with unexplained mental retardation using Multiplex Ligation-dependent Probe Amplification. Irish Society of Human Genetics
4. A Butler & DE Barton. Estimating Carrier Risks by Linkage in a DMD Family with a Triple X Female, British Society of Human Genetics Conference
5. DE Barton & C Brady EuroGentest: Reference Materials for Genetic Testing
6. European Society for Human Genetics Conference.
7. A Butler & DE Barton Estimating Carrier Risks by Linkage in a DMD Family with a Triple X Female, British Human Genetics Conference
8. Z Adamson, AJ Green. How useful is parental karyotyping in finding the cause of miscarriage? Irish Paediatric Association

### 2008

9. C King, D Lambert, M Rogers, T McDevitt, D Barton, SA Lynch. Genotypes and Borderline Sweat Tests in Irish CF Patients – An Update. 31st European Cystic Fibrosis Conference, Prague.
10. R Shahdadpuri, D Lambert & SA Lynch. Diagnostic outcome following routine Genetics clinic attendance. Manchester Dysmorphology meeting
11. MP Farrell, MJ Kennedy, D Flannery, CL Stuart, BJ Mehigan, RB Stephens, SAWhite, CB Muldoon, AJ Green, ST Duke. Clinical & Molecular strategies to screen for Lynch Syndrome. All-Ireland Cancer Conference.
12. M Russell, S Ennis, DE Barton and SA Lynch. Does Noggin cause Twinning? Irish Society for Human Genetics.
13. L Bradley, AJ Green, SA Lynch. Four cases Of Mowat-Wilson syndrome. Irish Society for Human Genetics.
14. J Kelly, C Bermingham, P Carty, A O'Marcaigh, H Enright, D Betts. Uncommon presentation features Of the t(8;14) (q11.2;q32) translocation in acute lymphoblastic Leukaemia (All). Irish Society for Human Genetics.

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

15. A Dunlop, A Green, G Clarke, D Betts. A familial t(2;9)(q37.3;q12) translocation: an illustration of the potential limitations of Commercially available FISH probes. Irish Society for Human Genetics.
16. A Ward, C deBaroid, SA Lynch. Challenges in genetic counselling arising from the risk of multiple genetic conditions in a single Family. Irish Society for Human Genetics
17. N Molloy, JM Darlow, A J Green P Puri, DE Barton. RET variation in the aetiology of vesicoureteric reflux. Irish Society for Human Genetics.
18. N Molloy, JM Darlow, AJ Green P Puri, DE Barton. RET variation in the aetiology of vesicoureteric reflux. UCD Conway Institute Festival of Research.
19. W S Wong, C McGuinness, JM Darlow, A J Green, Prem Puri, David E Barton. The search for genes involved in vesicoureteric reflux. Irish Society for Human Genetics.
20. W S Wong, C McGuinness, J M Darlow, AJ Green, P Puri, DE Barton. The search for genes involved in vesicoureteric reflux. UCD Conway Institute Festival of Research.
21. T McDevitt, A Crowley, M Higgins, N Cody, M Adams, E Berkeley, C Nolan , R Clarke , M Farrell, P DalyA. AJ Green, DE Barton. Incidence of BRCA1 and BRCA2 Mutations in Irish Breast Cancer Families. Hereditary Cancer Conference CNIO.
22. Shahdarpuri R, Lambert D & Lynch SA. Diagnostic outcome following routine Genetics clinic attendance. Manchester Dysmorphology meeting
23. S A Lynch, Debby Lambert &. R Shahdarpuri, Diagnostic outcome following Routine Clinical Genetics referral for the assessment of developmental delay. ISHG
24. SA Lynch, S Finn & M Colreavy Does Noggin cause twinning? Irish Society of Human Genetics
25. S A Lynch, J. Casey, P. McGettigan, R. Regan, J. Conroy, J. Nielsen, K. Butler, A. Cant, J. Kelleher, S. Ennis Localisation of a gene for rare immuno-osteodysplasia syndrome British Society of Human Genetics
26. MC Nobbs, S Lynch, E Roberts, T Davies. Two Pedigrees with an unidentified disorder which include consistent equivocal Fanconi Anaemia results. British Society of Human Genetics
27. CJ Breen, B O'hici, M Mullarkey, A Carey, R O'Shea, A Green, DE Barton, F Malone and DR Betts. Maternal UPD 16 and Low Level Mosaic Trisomy 16 Observed in Amniotic Fluid Following Non-Mosaic Trisomy 16 in CVS. ISHG, Dublin. Ulster Med J 2010 79 (1); 33-42.
28. L Barton, J Kelly, C Flynn, S Langabeer, T Morris, DR. Betts. A Complex G-Band-Cryptic t(9;22) in a Case of Acute Lymphoblastic Leukaemia. HAI, Kilkenny, October 2009.
29. L McArdle, SA Lynch, S Ennis, T Morris, DR Betts. Tissue Specific Mosaicism of a der(18) in a Developmentally Delayed Boy. ISHG

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

### 2009

30. M Russell, SA Lynch, and DE Barton. Facio-audio Symphalangism and Monozygotic Twinning. Clinical Molecular Genetics Society.
31. SA Lynch, J Conroy, M Moran, M King, S Ennis. Monozygotic twins discordant for Landau-Kleffner syndrome Irish Society of Human Genetics
32. R Regan , C Costigan , N Foulds , A Collins , AC Thuresson , G Anneren, B-O Hedberg, DR Fitzpatrick, FH Sharkey, S Ennis, SA Lynch. The 12q14 microdeletion syndrome, 5 further studies Irish Society of Human Genetics.
33. M Sweeney, L Baker, CA Graham, DE Barton, Lynch SA. Incidence of Fragile X syndrome in the Republic of Ireland British Society of Human Genetics, Warwick August 2009
34. H O'Shea, S A Lynch, S Ennis, G Scherer, E Troppmann, D Betts. Cytogenetic and Clinical Study of a SRY-Negative 46,XX Male. ACC Spring Meeting, Edinburgh.
35. L McArdle, S A Lynch, S Ennis, T Morris, DR Betts. Tissue Specific Mosaicism of a der(18) in a Developmentally Delayed Boy. ISHG, Dublin. Ulster Med J 2010 79 (1); 33-42.
36. T McDevitt, M Higgins, A Crowley, N Cody, M Meany, C de Baroid, M Adams, C Nolan, M Farrell, E Berkley, R Clarke, P Daly, A Green, D Barton. Spectrum and Incidence of BRCA1 and BRCA2 mutations in the Republic of Ireland: ESHG
37. T McDevitt, M Higgins, A Crowley, N Cody, M Meany, C de Baroid, M Adams, C Nolan, M Farrell, E Berkley, R Clarke, P Daly, A Green, D Barton. Spectrum and Incidence of BRCA1 and BRCA2 mutations in the Republic of Ireland: BSHG
38. T McDevitt, M Higgins, A Crowley, N Cody, M Meany, C de Baroid, M Adams, C Nolan, M Farrell, E Berkley, R Clarke, P Daly, A Green, D Barton. Spectrum and Incidence of BRCA1 and BRCA2 mutations in the Republic of Ireland: ISHG
39. F Sánchez Jiménez, J Darlow J, P Puri, D Barton. Estudio de un protocolo de screening para detección de mutaciones en genes implicados en el reflujo vesicouretral. Clinical Laboratory National Congress, Valencia, Spain.

### 2010

40. R O'Shea, AM Murphy, E Treacy, K Thirlaway, DM Lambert. Communication of genetic information by other health professionals: the role of the genetic counsellor in specialist clinics. EMPAG
41. DM Lambert, L McArdle, S A Lynch, S Roring. Genetic counselling for ambiguity: 46,XX /46,XY on chorionic villus sampling, what are the possibilities? EMPAG

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

42. SA Lynch, M King, D Webb, O O'Mahoney, M Morgan, S Ennis & J Conroy. Towards identification of the genetic basis of Landau-Kleffner syndrome. Manchester Dysmorphology Conference
43. J Kelly, N Coen, L Barton, M O'Dwyer, P Browne, E Conneally, DR. Betts. Cytogenetic Analysis in Donor Cell Neoplasms. ISHG Ulster Med J 2010 79 (1); 33-42.
44. K Meaney, B Ó hCí, S A Lynch, DE. Barton. Atypical 22q11 deletion detected by MLPA in two patients referred for Prader-Willi Syndrome testing. British Society of Human Genetics.
45. Fabienne Gumy-Pause, Hulya Ozsahin, Mary Khoshbeen-Boudal, Bruno Pardo, David Betts, Philippe Maillet, Edward F. Attiyeh, André-Pascal Sappino ATM deletion is a frequent event in neuroblastoma: a report from the COG. Advances in Neuroblastoma Research, Stockholm

### 2011

46. L Bradley, C Murphy, D Murray, A McGillivray T Dabir & SA Lynch
47. Craniosynostosis in the Republic of Ireland Seventh Neural Tube Defect Meeting, Austin, Texas 2011
48. S A Lynch, M Ahmed, N Goggins, M Earley, S Ennis, J Conroy Ptosis, arched eyebrows, hypernasal speech, obesity & learning disability 7<sup>th</sup> International Neural Tube defect meeting 2011
49. M Rogers, S Roring, T McDevitt, DE. Barton. Validation of Luminex xTAG™ Cystic Fibrosis 39 Kit v2 for Diagnostic Testing & Newborn Screening using Dried Blood Spots. OLGHC Audit & Research Day, 2011
50. M Rogers, S Roring, T McDevitt, D E. Barton. Validation of Luminex xTAG™ Cystic Fibrosis 39 Kit v2 for Diagnostic Testing & Newborn Screening using Dried Blood Spots. Irish Society of Human Genetics, Dublin
51. L Ekstrom, SA Lynch, J Crolla, T Morris, DR Betts A familial ins(6;11)(p21.1;p12p14.3) with unexpected phenotypic consequences Irish Society of Human Genetics
52. E McMorrow, M Sheridan-Pereira, N Coen, H O'Shea, DR Betts. Jumping translocations involving chromosome 14q11 in a new born of a mother on methadone maintenance. ACC Spring meeting, Durham 2011
53. J McDaid, AJ Green, DR Betts An audit of amniocentesis: does gestational age affect the success rate and/or the report time? OLGHC Audit & Research Day, 2011
54. M Rogers, S Roring, T McDevitt, D E Barton. Validation of Luminex xTAG™ Cystic Fibrosis 39 Kit v2 for Diagnostic Testing & Newborn Screening using Dried Blood Spots. British Society of Human Genetics.

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.

**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.

**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt



## National Centre for Medical Genetics

Dublin, Ireland

55. M Sweeney, K Meaney, D Barton. 'Validation of the Asuragen Amplidex FMR1 kit for diagnostic Fragile X testing and further characterization of the WHO FRAX Reference Panel'. BSHG, Warwick.
56. JM Darlow, MG Dobson, M Hunziker, CM Molony, P Puri and DE Barton. A new genome scan for Vesicoureteric Reflux. British Human Genetics Conference, Warwick, September 2011 and joint 12<sup>th</sup> International Congress of Human Genetics with American Society of Human genetics annual meeting, Montreal, October 2011.
57. SA Lynch, J Casey, P McGettigan, R Regan, J Conroy, J Nielsen, K Butler, A Cant, J Kelleher, S Ennis. Localisation of a gene for rare immuno-osteodysplasia syndrome. European Society of Human Genetics Amsterdam.
58. J Kelly, O Smith, A O'Marcaigh, T Morris, D Betts. Incidence of cytogenetic aberrations in the paediatric acute lymphoblastic leukaemia presenting in the period 2006-2010. HAI, Wicklow

## 23 Research Grants awarded

Title	EuroGentest 2: Network for Quality Improvement & Harmonization of Genetic testing in Europe.
NCMG PI	David Barton
Collaborators	27 partners in 20 institutions across Europe
Funding Agency	EU 7th Framework Coordination Action HEALTH-F4-2010-261469
Total Funding	€2,000,000
NCMG Funding	€93,000
Duration	Jan 2011- Dec 2013
Title	The Genetics of Vesicoureteric Reflux
NCMG PI	David Barton
Collaborators	Profs Prem Puri, Andrew Green
Funding Agency	The Children's Research Centre
Total Funding	€888,300
NCMG Funding	€888,300
Duration	Jan 2010-Dec 2012
Title	The Autism Genome project
NCMG PI	Sean Ennis Andrew Green
Collaborators	Prof Michael Gill and Louise Gallagher
Funding Agency	HRB Programme grant
Total Funding	€5 million
Duration	2006-2011
Title	Identification of an autosomal recessive gene causing mitochondrial disease in 3
<b>Clinical Authors:</b> Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. <b>Cytogenetics Authors:</b> David Betts. <b>Molecular Authors:</b> Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt. <b>Admin Authors:</b> Lisa Malone, Sally Ann Lynch, Damien Moyles.	
<b>Collated by:</b> Christine Brady, Sally Ann Lynch, Alana Ward	<b>Authorised by:</b> NCMG Mgt
<b>Page 88 of 90</b>	





**National Centre for Medical Genetics**  
Dublin, Ireland

	related families attending the NCIMD
PI	Sally Ann Lynch & Dr Ellen Crushell (CUH)
Collaborators	Ms Jillian Casey & Dr Sean Ennis UCD
Funding Agency	Children's University Hospital, Temple Street
Total Funding	€27,760
Duration	Jan 2010-Dec 2010
Title	Identifying the genetic basis of Landau-Kleffner syndrome.
PI	Dr Sally Ann Lynch & Professor Mary King (CUH)
Collaborators	Dr Judith Conroy & Dr Sean Ennis, UCD
Funding Agency	Children's University Hospital, Temple Street
Total Funding	€35,580
Duration	Jan 2010-Dec 2010
Title	Isolation of disease genes in the Irish Traveller population
NCMG PI	Sally Ann Lynch
Collaborators	Dr Sean Ennis, UCD & Ms Jillian Casey UCD
Funding Agency	Health Research Board
Total Funding	€36,700
Duration	Oct 2010-Sept 2011
Title	Facio-Audio-Symphalangism- the genetic basis in two unrelated sets of triplets
PI	Dr Judith Conroy
Collaborators	Sally Ann Lynch & Sean Ennis
Funding Agency	2010 KnomeDISCOVERY Awards program
Total Funding	€24,000
Duration	Oct 2010-Sept 2011
Title	Identifying the genetic basis of three recessive disorders, PCD, microcephaly and cardiomyopathy and retinopathy.
PIs	Dr Sally Ann Lynch & Dr D Slattery (CUH)
Collaborators	Ms Jillian Casey & Dr Sean Ennis
Funding Agency	Children's University Hospital, Temple Street
Total Funding	39,580 euro
Duration	Jan 2011-Dec 2011
Title	Mapping an episodic ataxia gene in a large Irish family
PI	Judith Conroy UCD
Collaborators	SA Lynch & Drs Ray Murphy (AMNCH), D Webb (OLCHC) & S Ennis (UCD). 2011Ataxia Ireland Dr J Conroy [PI]
Funding Agency	Ataxia Ireland
Total funding	€13,300 (plus VAT)
Duration	1 year
Title	Identifying recessive genes for Primary Ciliary Dyskinesia, microcephaly & cardiomyopathy & retinopathy.
<b>Clinical Authors:</b> Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. <b>Cytogenetics Authors:</b> David Betts. <b>Molecular Authors:</b> Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt. <b>Admin Authors:</b> Lisa Malone, Sally Ann Lynch, Damien Moyles.	
<b>Collated by:</b> Christine Brady, Sally Ann Lynch, Alana Ward	
<b>Authorised by: NCMG Mgt</b>	
<b>Page 89 of 90</b>	



**National Centre for Medical Genetics**  
Dublin, Ireland

PI	Dr Sally Ann Lynch
Collaborators	Ms Jillian Casey & Dr Amanda McCann
Funding Agency	MRCG (HRB & NCRC)
Total funding	€95,580
Duration	Oct 2011-Sept 2013
Title	Investigation into the aetiology of Landau-Kleffner syndrome
PI	Dr Sally Ann Lynch & Professor Mary King:
Collaborators	Dr Judith Conroy & Dr Sean Ennis UCD
Funding Agency	Children's University Hospital, Temple Street 2011
Total funding	€50892
Duration	Dec 2011- 1 year

**Clinical Authors:** Sally Ann Lynch, Alana Ward, Rose Kelly, Andrew Green. **Cytogenetics Authors:** David Betts.  
**Molecular Authors:** Christine Brady, Shirley McQuaid, David Barton, Caitrona King, Trudi McDevitt.  
**Admin Authors:** Lisa Malone, Sally Ann Lynch, Damien Moyles.

**Collated by:** Christine Brady, Sally Ann Lynch, Alana Ward

**Authorised by:** NCMG Mgt