NHS South West
NHS Genomic Medicine Centre

100,000 Genomes Project
South West GMC
Rare Disease Recruitment

December, 2015 **Number 2**

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Highlights in this newsletter

- Leaflets are ready for distribution (see section 1, below)
- Recruiting children with learning difficulties or behavioural problems: any potential issues should be flagged with the project office in advance. Please see section 3 below
- New information about timeframe for feedback of results, please see section 5 below
- For recruitment team *__important__* Please see section 7 below for plans regarding implementation of new consent form and information sheet

1. Introductory leaflets

The introductory leaflets are now ready for circulation. We have a currently limited supply and will be distributing some of these. Please contact Steve Johnson (details opposite) if you would like some and they will be sent over.

2. Recruitment

a. Recruitment so far

We are close to target so far. Our target for the first year of the study is 304 samples. Our recruitment target in terms of numbers of samples to the end of November 2015 was 149, and we have collected 141 samples (95%) to that date- good news, and thanks to all for their efforts! But we need to increase monthly recruitment to reach the target of 304 samples by April so please keep referring potential recruits!

b. How to recruit a patient

We have tried to make this as simple as possible. An example, the version for paediatricians, is shown on the next page.

We feel that the process is about as straightforward as it could possibly be, and indeed clinicians from different specialties throughout the Peninsula have risen to the occasion and recruited dozens of families so far- see the recruitment figures above.

The easiest way to recruit a patient/family is from clinic, but phoning on receipt of a negative molecular test is also an effective option.

Ask for help if needed!

Timetable for 'onboarding' of Local Delivery Partners (LDPs)

The LDPs are the partner hospital Trusts in the Peninsula and Somerset:

Derriford Hospital, Plymouth

Royal Cornwall Hospital, Truro

North Devon District Hospital, Barnstaple

Torbay Hospital

Musgrove Park Hospital, Taunton

Yeovil District Hospital

LDPs are 'on board' when patients/families can be recruited, and the samples processed, locally in that hospital

Projected timetable for onboarding:

Derriford, RCH Truro, MPH Taunton by January 31st 2016

NDDH, Yeovil DH, Torbay Hospital by July 31st 2016

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100 000 Genomes Project recruitment for paediatricians

This is for a 'trio' family structure, with affected child and unaffected parents. If family structure differs, please contact for advice.

Step 1: Check eligibility

A comprehensive list of eligibility criteria is available via the link below:
http://www.genomicsengland.co.uk/library-and-resources/
(See under "Eligibility statements"/"Rare disease eligibility statements")

Some examples of eligible disorders:
Intellectual disability; Congenital Heart Disease; Congenital anaemias; Non-syndromic hearing loss; Craniosynostosis syndromes

Step 2: Discuss with the family in clinic or by telephone

1. Purpose of study is to try to obtain a molecular genetic diagnosis [NB there must be a diagnostic question]
2. Blood samples are needed from the affected individual and unaffected parent(s) or other affected family members
3. Family members will be offered opportunity to consent to 'secondary' findings
4. Data will be made available in anonymized form to research/commercial bodies (non-negotiable)

Step 3: Notify GMC office (Steve Johnson, Project Manager)

Please email the following information to: rde-tr.GMC@nhs.net

1. Name and NHS number of affected individual, or name and date of birth
2. Names and dates of birth of other individuals who would be recruited (typically the parents)
3. The diagnostic category (Intellectual disability etc)
4. An email address (preferred but not essential) or postal address for the family

The project office will then contact family re consent/sampling appointment

Step 4: Clinical data entry

Once the consent/sampling process has been completed, the recruiting consultant will be asked to complete an online phenotype data entry form. This will include growth parameters, systems examination and dysmorphology. (Help with this will be available)

Please contact us if you have any questions about any aspect of the project:

charles.shaw-smith@nhs.net	T: 5737
sian.ellard@nhs.net	T: 8259
rde-tr.GMC@nhs.net	T: 8177 (Project office)

c. Recruitment outside Exeter

See side panel for definitions of LDPs, onboarding, and projected onboarding timetable, which we are still hoping to meet. Currently, patients known to the Clinical Genetics service are being recruited in Exeter, Plymouth and Truro. It is a complex procedure because samples have to be brought back to Exeter for processing within the timeframe specified in the protocol (6 hours). We are getting help from Devon Freewheelers (https://bloodbikes.org/) with this- and are very grateful to them. These logistical complexities mean that specialties outside Clinical Genetics are currently recruiting only from Exeter (although we can probably help if you have someone you would like to recruit. We will keep you updated on progress with this.

Picture shows a few of the Devon Freewheelers-with one of their bikes! (Photo: https://bloodbikes.org/)

New disorders shortly to be open for recruitment

-already approved

Haematology/immunology
Aplastic anaemia +/- PNH
Inherited Complement Deficiency

Renal
Atypical haemolytic uraemic syndrome

Dermatology
Autosomal recessive congenital ichthyosis
Ectodermal dysplasia without a known gene mutation
Epidermolysis bullosa
Meige's disease (lymphoedema)
Palmoplantar keratoderma and erythrokeratodermas
Undiagnosed familial neurocutaneous syndromes
Generalised pustular psoriasis

Respiratory
Familial and multiple pulmonary AVMs
Familial pulmonary fibrosis
Hereditary haemorrhagic telangiectasia (HHT)

Paediataric neurology
Infantile nystagmus

Metabolic
Familial hypercholesterolaemia

-likely to be approved

Neurology
CADASIL

Dermatology
Alopecia- familial cicatricial with scarring

3.Children and the consent appointment

Last month, some members of the recruitment team encountered difficulties with a child with behavioural problems from whom it was extremely difficult to obtain a blood sample.

We have to recognize that obtaining blood samples from children can be very difficult; also, that having a child with learning or behavioural problems in the clinic room can be highly disruptive to the smooth running of the consent appointment

Following discussion, the following recommendations were made, which would apply in the case of recruitment of a minor to the study:

- The consultant clinician responsible for recruitment should specifically enquire about any behaviour problems
- Any foreseeable problems of this type should be notified to the Project Office at the time at which the child and family are proposed for recruitment to the study, so that additional resources can be put in place, if needed

These new requirements have been added to the 'Read_Me' documents. Updated versions of these documents are now available on the swgmc website (see below, section 6)

4.Entry of phenotype data

The SW GMC started using the Genomics England online tool, OpenClinica, but we found the lack of flexibility to be a limitation. The West Midlands GMC has developed an alternative version, named **Genie**, which we have purchased.

The Genie system is now live in the SW GMC and phenotype data entry has started. We have identified some enhancements that will be prioritized before taking forward data entry at scale. Detailed information on how to do this will be circulated.

We will advise of any updates regarding phenotype data entry as they become available.

5.Results

When the project started, we were asked to advise recruits that it would not be possible to give a precise timeframe for feedback of results especially in the initial phase, but to say that a minimum of six months should be allowed before any prospect of feedback.

Genomics England will release a newsletter for participants. We have seen a draft version which is currently going through ethical approval. This newsletter will be circulated to all recruits by Genomics England when it is ready.

Concerning timescale for feedback of results, the draft version of the

Recruitment team

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Paediatric Research Nurses, Truro
Nina Worrin

Genetic Counsellors, Exeter
Anne Searle

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Matilda Bradford
Nicol Lambord

Specialist Registrars
Lettie Rawlins (Clinical Genetics, Exeter)
Rhian Clissold (Renal Medicine, Exeter)
Harriet Aughey (Paediatrics, Truro)

newsletter contains the following information:

When will I get my results?

Not everyone will get a result, but if you do, it will be given to your clinical team.

We anticipate that the first results will be sent to clinical teams from **early Summer 2016**. The clinical team will then run some validation (quality) checks on the results before giving any results to you.

Results will be produced continuously, so **Summer 2016** is the earliest that you could expect to hear back. If you joined the project recently, it will be longer than that before we have finished analysing your genome and health data. The 100,000 Genomes Project is at the cutting edge of science. No-one has ever attempted whole genome sequencing at this scale before as part of everyday medical care in hospitals. Thank you for your patience while we set up and test all the processes and systems.

This is just the initial analysis as your data will also be entered into a research database. As our knowledge grows, our researchers will continue to look at and analyse your data. We will let your clinical team know anything that we find in the future which could be important for your health or for your family members.

6. Website

Please note that the 'Read_Me' documents providing a quick guide on how to recruit a patient are available to view via the SW GMC website: www.swgmc.org

7. Recruitment team

Joining the recruitment team

The team is open to new members, especially in Torquay and Barnstaple. Team members should be up to date on the following:

1. Good Clinical Practice training- usually offered as part of Trust mandatory training
2. Completion of online consent training provided by Health Education England- the module can be completed in around an hour
3. Face-to-face consent training specifically for 100 000 Genomes Project, provided to date by Charles Shaw-Smith, Rare Disease Lead.

New members this month:

Nina Worrin, Paediatric Research Nurse, Truro

Changes to consent form/information sheet *important*

There are no 'drastic' changes. Mostly the changes are subtle rewordings/changes in emphasis.

Information sheet

1. The phrase 'The person taking your consent will show you the list

Thanks to the following for commitment to the project:

All members of Peninsula Regional Clinical Genetics Service

Richard Tomlinson, Eleanor Thomas, and all members of the Community Paediatrics team, RDE, Exeter

Coralie Bingham, Rhian Clissold, Renal Medicine, RDE, Exeter

Claire Bethune, Lucy Leeman, Andrew Whyte, Immunology and Allergy, Derriford Hospital, Plymouth

Vijay Baidya and Andrew Hattersley, Diabetes and Endocrinology, RDE, Exeter

Nick Gutowski, Neurology, RDE, Exeter

Elizabeth Househam, Neurology, Derriford Hospital, Plymouth

Kayal Vijayakumar, Paediatric Neurology, Bristol Children's Hospital

Carolyn Charman, Naomi Goldstraw, Dermatology, RDE, Exeter

of these additional rare diseases, which will be fully explained to you along with the implications of a positive test' has been removed from the information sheet. We weren't doing this anyway but now it's official that we don't have to!

2. The PIS now includes the fact that participants can vary their own Additional Findings consent (or this can be done in respect of a child participant) at any time and as many times as needed, via the recently-approved Opt-In or Opt-Out forms.
3. The previous PIS had a focus (p10) on 'women-only' additional reproductive findings. This has been changed to include men as well. This is good news for gender equality but it is genetically complicated. I won't go into details here but happy to discuss.

Consent form

1. The new consent form is significantly shorter (5 pages instead of 6, 14 boxes instead of 19).
2. The term 'incidental findings' (box 17 on the old form, box 12 on the new form) has been changed to 'other findings' – less confusing.
3. A tick box has been added to state 'Carrier testing is not relevant to me'.

Plans for phasing in new consent form/information sheet

From Monday December 7th, potential recruits receiving information about the study will be sent the new consent form and information sheet.

Likewise from that date, patients who have previously been sent information about the study but who have not yet responded will receive prompts which contain the new consent form and information sheet.

Patients whose appointments have already been scheduled by Monday December 7th and who have already received copies of the old consent form/information sheet will be consented using the old material.

8. Thank you!

Thank you to all clinicians who have recruited to the project, and to all members of the recruitment team for their work.

From the SW GMC!