Genomics Education Programme

NHS
Health Education England

Clinician's guide for requesting whole genome sequencing: rare disease

Introduction

This guide has been developed to support clinicians who will be requesting whole genome sequencing (WGS) for patients with certain rare diseases. The guide covers the practicalities of requesting WGS and highlights key points to cover during conversation(s) with patients based on the statements in the record of discussion (RoD) in order to facilitate consent.

Further information to support the guides can be found at www.genomicseducation.hee.nhs.uk.

SEE PAGE 2...
... for a handy pre-appointment checklist

Key points to cover when discussing clinical WGS

Introduction and context of the test

- Test is diagnostic (to identify an underlying cause for the individual's presenting condition).
- Sequencing of the whole genome will take place, although diagnostic analysis will focus on gene panels (known genes associated with the clinical presentation).
- Samples from other family members may be required for whole genome sequencing, or after results.

Results

- Test may not yield any significant finding; this would not exclude a genetic diagnosis.
- Uncertainty of genomic information: interpretation and knowledge about results may change over time.
- Main findings: results in connection with the patient's existing condition. They may or may not affect current/future care, or provide insight to prognosis or other health conditions.
- Variant(s) of uncertain significance: uncertain findings that may require following up now or in the future.
- Incidental findings: unexpected results not related to reason for the test (including family relationships).
- Results will not inform all health conditions (currently no additional looked-for findings).
- Confirm approximate timeline for results and communication process (how any results are fed back, by whom, and with whom they would be shared).

Implications for the patient

- Onward referrals may be made for screening or management based on results.
- Potential psychosocial impact of receiving results and support available.
- Implications for family planning and reproductive choices.
- Association of British Insurers' code for disclosing genetic test results vs medical/family history.

Implications for family members

- Opportunities based on results or family history where relatives could have access to preventative screening, predictive testing, and/or information about reproductive choices.
- Discuss importance of sharing results with family members, as they may impact blood relatives, and strategies that may be used (such as 'To whom it may concern' letter).

Use of samples

- Samples: typically blood; may be saliva or tissue
- Samples are stored and accessed within the Genomic Laboratory Hub, other local labs (such as pathology) and other labs within the NHS Genomic Medicine Service.
- Stored samples may be used for further genomic tests in the future with appropriate consent.
- Sample can be used as a control for testing other individuals, including family members.
- De-identified samples may be used for lab test development or quality control procedures.

Use of data

- Data includes patient's health and genomic information, which can be securely accessed on an ongoing basis by NHS healthcare professionals.
- National (identifiable) and international (not identifiable) comparison of data for greater understanding of significance of results.
- Genetic variant(s) may be shared for relatives to access testing (limited identifiers to process test); medical information will not be shared with relatives.

Key points to cover when discussing the NGRL

Introduction and context

- National Genomic Research Library: a collection of data from patients that can be accessed by researchers.
- Aim and potential benefits of having a large dataset and access to research to improve diagnostic potential of genomic information.
- Patient can request to withdraw at any time, either partially (no future contact) or fully (no future data use) at any time.

Implications for the patient

- Increased chance of a diagnosis in the future, whereby new significant findings may be shared with the NHS to use in future clinical care.
- Wider benefits of learning more about rare diseases to guide management.
- Individuals may be re-contacted for further information, regarding new findings or other studies.

Use of samples

- Samples can be sent to approved organisations within and outside of the UK for research.
- Patient may be invited to donate additional samples for research.

Use of data

- Data and samples will have name, contact and other personal identifiers removed.
- Data includes genomic information as well as other health and social care records.
- Controlled, read-only access by approved researchers both in and outside of the UK including not-for-profit and commercial (for-profit) organisations.

PRE-APPOINTMENT CHECKLIST

- **Is your patient eligible for WGS?**
  Check the National Genomic Test Directory (www.bit.ly/NatGenTests), which specifies which patients may be offered a WGS test. Tests should be targeted primarily at situations where a genetic diagnosis will affect the healthcare of a patient or their family members.
- **Should other family members be included?**
  This will depend on the suspected inheritance pattern of the condition. In general, for childhood-onset conditions it is best to test the affected individual and both parents (where possible). For adult-onset conditions, it is usually best to test just the affected individual. If you need advice on testing family members, please contact your local GLH.
- **Do you have the forms you need?**
  A WGS order form must be completed with relevant clinical (HPO terms) and family history information. As well as an order form, patient choice forms are required to record each individual (patient and relative)'s choices to consent to WGS and the NGRL:

	Individuals aged 16+ years with capacity	Children (less than 16 years)	Patient representative /consultee (for adults without capacity)	Deceased
Clinical test	RoD signed by individual	RoD signed by parent/guardian	RoD signed by person acting in best interests of patient	RoD signed by appropriate relative
NGRL	Research choice captured within RoD; additional form to note choice about NGRL if not made at time of clinical test discussion			
	No additional forms	OPTIONAL Assent form signed by child	MANDATORY Consultee form signed by consultee	No additional forms

Note: The process of requesting WGS may be adapted for local needs, so please make sure you have checked with your Genomics Laboratory Hub, which can assist with queries about submitting patient clinical information, which family members to include, and ensuring you have the correct forms.

Additional points to consider

- The patient may decide to not proceed with the clinical test and/or research offer, or may wish to have more time to consider following the initial discussion.
- Consider referral for genetic counselling for further discussion about managing risk and/or a diagnosis, where there are complex social/communication issues or family communication barriers.
- If the patient is deemed to not have capacity to consent, a parent, guardian or other person representing the patient's interests should be available. Where possible, the patient should be involved to provide assent.
- If the sample being tested is from a deceased individual, consent must be discussed with a relative or other relevant individual.
- Additional materials and support may be required for patients who are non-English speaking, hearing impaired, visually impaired, or have learning disabilities.
- Further resources may be informative and/or supportive for patients (such as NHS Choices, Genetic Alliance).