Genomics england

NHS England

Introduction to the 100,000 Genomes Project

Cancer Programme

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Introduction

Sampling for molecular analysis is recognised as a part of standard care for cancer diagnosis. The future of cancer care will rely on whole genome sequencing to give a full diagnosis and a much more complete prognostic picture as well as to direct clinicians to which treatments will best benefit a patient and which will only cause harm.

The NHS is undergoing a service transformation to enable access to genomic technologies for all cancer patients for the future. The 100,000 Genomes Project is helping to establish the value of whole genome sequencing in these diagnostic pathways and to develop an extensive research database to provide a greater understanding of the disease and the development of new drugs and treatments. The cancer arm of the project will inform how the current standard of care needs to change to enable benefits for patients both now and in the future.

For example we already know that sometimes 100 patients may be treated with adjuvant chemotherapy in certain types of breast and colon cancer, for five patients to benefit.

It is important to have healthcare professionals from all specialties aware, enthused and involved with the project to ensure as many patients as possible benefit from the new diagnostic pathway and ensure that the whole cancer pathway is transformed from clinic to diagnostic biopsy, surgery all the way through to pathology. Any clinician who comes into contact with patients with cancer should be aware of this service transformation project.

Benefits of the project to today's patients

Information from the project can impact a patient in three ways:

1 | Information that can directly impact on the choice, timing and duration of treatment.

- a | Choice of treatment.
  - i | Identification of a gene mutation that can predict a good response to a treatment. The treatment may be licensed or off-license.
  - ii | Identification of currently un-actionable mutations. This will enable open and honest conversations with patients about interventions that may or may not be available.
- b | Timing of treatment.
  - i | Identification of a mutation that informs prognosis. This may influence recommendations on choice and duration of standard chemotherapy.
  - ii | Identification of a mutation that can be used to monitor early recurrence in order to decide when to start a further course of treatment.reference.

2 | Suggestions for other treatments (where there is no evidence in that tumour type).

- a | Information from sequencing can establish the patient's eligibility for taking part in a future clinical trial. If they are invited patients can freely decide whether or not to consent to joining such a trial.

3 | Information that we do not yet understand the relevance of This information may be useful in the future for that particular patient. It must be kept as part of their diagnostic record for future reference.

Benefits for tomorrow's patients

As part of the 100,000 Genomes Project, the whole genome sequence data is combined with the patient's entire electronic clinical record.

Together these are de-identified and then collated with data from all the participants. This will form an incredible resource for researching cancer. The impact of different treatment on outcome can be tracked and related back to the genome enabling differing approaches for patients in the future. The ability to track patients' progress alongside their genome sequence is thanks to the NHS and is unique to this project. This will lay the foundations for more personalised cancer treatment in the NHS.

Once this project has established the necessary pathways in the NHS we can look towards whole genome sequencing becoming an everyday part of healthcare – giving patients the best possible treatment options.

Identifying suitable patients

All invasive malignancies are eligible for submission except for a few rare conditions. Tissue can be collected either as a biopsy at diagnosis or at surgical resection. MDT coordinators have a crucial role in recording the patients who are eligible for the 100,000 Genomes Project and making sure they are flagged with colleagues.

Recruiting to the 100,000 Genomes Project requires every member of the multidisciplinary team to be involved.

Role of nurses in taking consent

Introducing the project to patients

Patients are first approached about the project at a particularly sensitive time when they have just been diagnosed with cancer. Patients are often overwhelmed with information and need plenty of time to absorb anything new. We need clinicians who can handle the situation sensitively and gently feed information to the patient about the project. Often nurses have succeeded by handing the patient an information leaflet on first encounter and then following this up by phone before consenting the patient face to face or via a phone conversation.

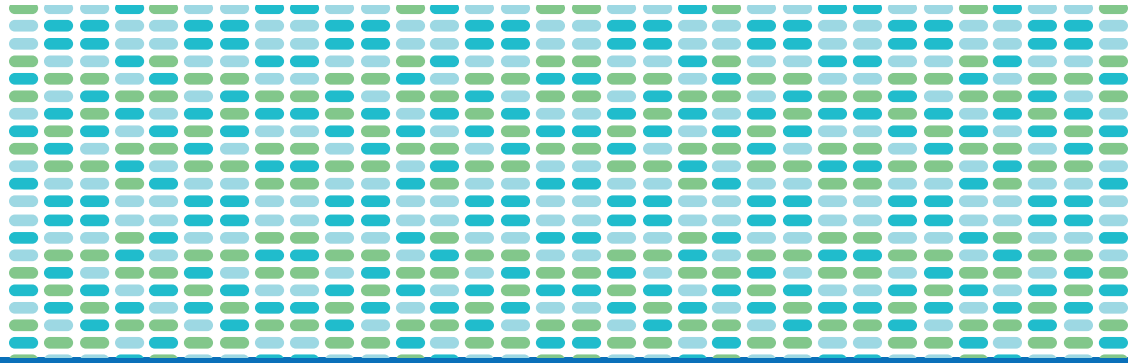
Information about the project for patients is available here:
https://www.genomicsengland.co.uk/taking-part information-for-participants/

Consenting patients

The aim of the project is to create an ethical and transparent programme based on consent and to keep the public supportive. To this end, even though there is an intention that the programme be embedded as part of routine care, we are particularly detailed when seeking consent to ensure patients fully understand the implications for them and their families.

The consent form takes a little while to become familiar with. Once you have read it through you can decide how to take a patient through each step and develop a script for the next time. For example, remember to emphasise that a patient can change their mind at any time about whether they want to have other, non-cancer mutations looked for in their DNA. There are additional resources for consenting patients available on the Genomics England website aimed at both staff and patients e.g. summary presentations and videos.

The same questions recur with most patients for example about the impact on life insurance and their immediate family and FAQs are answered on the Genomics England website.



Consent forms are available here:
https://www.genomicsengland.co.uk/information-for-gmc-staff/ recruitment-materials

Fresh Frozen tissue sampling

The Royal College of Pathologists, Human Tissue Authority, Health Research Authority, NHS England, Genomics England and the Clinical Directors at the 13 NHS Genomic Medicine Centres in England have all agreed a consensus statement that fresh tissue sampling for whole genome analysis is part of the diagnostic pathway[1]. This means that these samples do not fall under the remit of the Human Tissue Authority and that samples can be taken as part of a diagnostic pathway with consent sought afterwards once a diagnosis of cancer has been made.

For optimal analysis fresh frozen tissue is required. This means that tissue needs to be handled differently.
We know that formalin fixation causes damage to DNA. For nearly a third of cases that have been formalin fixed this means that there is inadequate DNA for sequencing. For the remaining cases using formalin fixed tissue increases the risk of false positive and false negative mutations in the sequence compared with fresh frozen tissue. We are working on quantifying the risk of false positives and false negatives but already know that it's worth avoiding if at all possible.
When patients who want to participate in the project have their surgery delayed until the end of the day or pushed to a weekend list then the problems of taking fresh tissue becomes more difficult as the laboratory is likely to be closed.

The options available to take tissue fresh are:

1 | Biopsy samples specifically for the project can be handled as fresh alongside those put into formalin for diagnosis.
Once the pathologist has ensured there is enough material in the fixed tissue for diagnosis then the fresh tissue can be released for DNA extraction.

[1]Find out more about the consensus statement:
https://www.genomicsengland.co.uk/information-for-gmc-staff/cancer-programme/

2 | The surgical team vacuum pack the sample and keep refrigerated until the laboratory is ready to sample the tissue.

3 | Surgeons, with the consent of their pathologist, take a post-operative core biopsy sample of the tumour and keep that sample refrigerated.

4 | Operative samples are taken to the laboratory for fresh tissue sampling by a pathologist on arrival. This option requires good communication with the laboratory.

Sampling small tumours

When a sample is small or close to surgical margins this presents challenges to the pathologist sampling the fresh tissue. There are a number of approaches to solve this problem.

1 | Taking a full face of tumour for a paraffin block and a mirror section for freezing.

2 | Sampling post-operative with a core biopsy needle through the tumour.

3 | Sectioning into fresh blocks and then using a punch biopsy to sample cores of tissue from each block.

Guidelines on sampling from specific tumour types is available within the sample handling guidelines here:
https://www.genomicsengland.co.uk/information-for-gmc-staff sample-handling-guidance/

Advanced Metastatic Disease

Patients with inoperable cancer can now be included by sending biopsy samples. These patients are most likely to benefit directly from sequencing of their cancer in terms of which chemotherapy is given. If a case can be made that a particular patient would benefit from having a fast track turn around on their sample in order to decide a course of treatment then this should be put in writing to be considered for inclusion as a compassionate fast track case.

Tumour content assessment

Once frozen tissue has been sampled it is necessary to take a frozen section to enable assessment of the proportion of tumour nuclei present. Cases can be batched and assessments carried out in bulk. Samples with less than 40% tumour content cannot be sequenced at the moment.

Reports

Reports will be sent as a PDF document with three sections: actionable mutations; other mutations recognised in cancer; all other mutations. Each of the patients mutations appear as a link to further information on the relevant evidence base. It is up to regional Genetic Medicine Centres to validate the results before sharing with treating clinicians.

Example reports:
https://www.genomicsengland.co.uk/information-for-gmc-staff/cancer-programme/genome-analysis/

Importance of correct data entry

The 100,000 Genomes Project is a data driven project and correct and complete data entry is critical to enable the full benefits of the programme to be realised. The upfront data we ask for is essential diagnostic information without which interpretation of the sequence will be less reliable and details of sample processing which can affect whole genome sequencing. The project links up to existing cancer data entry within hospitals so this should not require extra manual entry but it makes it even more important that the current data registries are completed accurately and kept up to date.

Data security

All data is kept in a secure monitored environment by Genomics England. Any identifiable data such as name and date of birth is kept in a separate part of the data infrastructure and will be only accessible by the patient's direct clinical team. For research purposes the data is de-identified and collated with many other patients.

Education

Further information on all aspects of this work is available on the Genomics England website, NHS England's website and the regional GMC websites. Health Education England have a Genomics Education Programme to ensure NHS staff have the knowledge, skills and experience to ensure that the health service remains a world leader in genomic and precision medicine. More information can be found at **www.genomicseducation.hee.nhs.uk.**

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