# Supplementary Materials 1

## Additional detail of types of genomic/genetic tests with examples

Single genes from a patient’s own DNA (rather than tumour DNA) may be used in the diagnosis of disease. They are also widely used in cancer care as what have become known as ‘companion diagnostics’ (CDx). Here, the status of a particular gene in a tumour sample determines whether a patient is likely to respond to a given therapeutic. An example of a CDx used in determining treatment in metastatic colorectal cancer is Kirsten Rat Sarcoma gene (KRAS). Patients with wild-type (unmutated) KRAS are more likely to respond to Epidermal Growth Factor Receptor (EGFR) targeted therapy (for example, Cetuximab). Alternatively, single gene tumour variants may indicate better or worse prognosis and either tumour or healthy tissue samples may be used to identify patients who are likely to have adverse reactions to particular treatments.

Multiple-gene tests are frequently referred to as panels. This indicates that multiple genes are being tested simultaneously. This is particularly useful when symptoms may be caused by more than one pathogen as in gastroenteritis. Panels have also been developed for certain cancer types where multiple genes may have therapeutic or prognostic significance. For example, in non-small cell lung cancer, a panel may be used to identify actionable mutations (which can be targeted with therapeutic agents) (1). Such panels can also accelerate the referral of patients to relevant clinical trials.

Polygenic risk scores are a development of multiple-gene tests that take data from a number of molecular targets (possibly combined with demographic or clinical information) and apply an algorithm to provide a score to a patient. This score may indicate the risk of developing a particular condition or the risk of recurrence of cancer, for example Oncotype Dx produce tests which provide risk of recurrence scores in breast and prostate cancer. These algorithm-based tests have been referred to as ‘black box’ tests (2) as they provide validated clinical guidance rather than a set of results from a panel requiring separate interpretation.

Whole genome sequencing involves sequencing all genes whether or not they are involved in the production of proteins. Whole exome sequencing involves only those genes know to be involved in the production of protein so making processing and data quantities more manageable. Whole transcriptome sequencing refers to the sequencing of RNA rather than DNA. The difficulty with this broad ranging group of tests is in the volume of results obtained. Some mechanism of interpretation of the results is required in order to render them clinically useful and much of the data produced will not be of immediate relevance.

Note all four test types could act as companion diagnostics if the purpose of the test was to determine a patient’s likely response to a particular therapy.

These four test types are shown in Table 1 together with examples of genes and indications of use.

**Table 1: Examples of types of genomic/genetic tests**

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| **Test type** | **Example target/s/test. (First author, date)** | **Indication** | **Function** |
| **Single gene** | CYP2D6 (3) | Estrogen receptor positive early breast cancer | To inform the targeted use of tamoxi­fen for treatment in the adjuvant setting |
| **Multiple gene** | Epidermal growth factor receptor (EGFR)  Anaplastic lymphoma kinase (ALK)  BRAF  RET  ROS1  HER2  MET mutations (1) | Advanced Non-Small Cell Lung Cancer | To identify patients who could benefit from targeted therapies |
| **Polygenic risk score** | Oncotype Dx (4) | Estrogen receptor-positive (ER+), node-negative or micrometastatic (pN1mic) early-stage breast cancer | To inform adjuvant chemotherapy recommendations |
| **Whole genome/exome/ transcriptome** | Whole exome sequencing  (5) | Paediatric muscle diseases | Diagnosis |

## References

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