Genomics and cancer

10 top tips

This edition: August 2021
Next planned review: March 2022

Macmillan Cancer Support, registered charity in England and Wales (261017), Scotland (SC039907) and the Isle of Man (604). Also operating in Northern Ireland. MAC18860_Genomics_and_cancer_tips

1 GPs have an important role to play in supporting patients through the diagnostic and treatment processes for cancer.

2 Cancer is a disease of the genome. The past decade has seen breath-taking advances in the characterisation of mutations and better understanding in a wide range of cancers due to the next-generation sequencing technologies.

3 The genomic changes in cells are either acquired over time or hereditary (Acquired):

- Acquired mutations are the most common cause of cancer caused by "wear and tear" damage on genes over time: aging, exposure to hormones, environmental toxins, and certain viruses can cause mutations
- Germline mutations are less common genetic mutations and play a role in 5–10%. They have the following features:
  - Multiple primary tumours in the same organ or different organs
  - Younger-than-usual age at tumour diagnosis
  - Tumours occurring in the sex not usually affected (e.g., breast cancer in men)
  - Tumours associated with other genetic traits or another rare disease
  - Family history of a cancer type or cancer syndrome.

4 Germline mutations or variants form around 5–10% (1 in 10) of cancers and are due to familial cancer syndromes such as breast or ovarian cancer associated with mutations in the BRCA1 or BRCA2 genes. This is relevant for the care of the patient with cancer, and for the identification of risk in family members to enable prevention, in the form of increased monitoring, screening (e.g. mammography) or treatment (e.g. chemotherapy or prophylactic mastectomy).

5 Individuals carrying inherited gene variants are susceptible to certain types of cancer. There are many hereditary genetic variants that increase lifetime risk of cancer and a higher than usual chance of recurrence after primary cancer. For example, people who have a CDK4 mutation have a high lifetime risk of melanoma, up to 80% compared to 2.5% without the variant.

6 Different germline gene variants present different lifetime risks of developing cancer, for example BRCA1 carriers have a 60–90% risk but for BRCA2 carriers it is 45–55%. Additionally, prevalence may vary in different populations, for example BRCA prevalence in the general population is 1 in 400 but is 1 in 40 In the Jewish population.

7 Somatic mutations occur in the genome of cancer cells and can be caused by environmental factors. For example, damaging UV rays from the sun cause changes of the C base in DNA to a T, which can lead to tumour formation. These can be detected by whole genome sequencing, by comparing the sequence from the patient's blood sample and the sequence from a sample of their tumour.

8 Detection of a tumour's genetic signature with somatic testing is used to make a precise diagnosis, enabling a more accurate prognosis and better tailored treatment. Increasingly, drugs are available that are targeted to the genetic features of a cancer, requiring genetic testing of the cancer cells to determine potential response.

9 It is important for GPs to understand the concept of germline testing for hereditary predisposition to cancer and somatic testing and its role within targeted therapies by identifying a tumour's genetic signature. This is because language is important, when patients hear the term "genetics" linked to their cancer diagnosis this can generate considerable anxiety and result in inappropriate referral for testing of family members when the reference is to somatic testing.

10 Macmillan has a wealth of information which can be shared with patients to support discussions about family history and genetics. You can find this information on our **website** or through our **information booklets**.

MACMILLAN CANCER SUPPORT