

The Contemporary Contribution of genetics in the diagnosis and treatment of Cancer

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Cancer is the second leading cause of mortality and morbidity and in 2015 nearly 9 million people died from cancer (1). Although cancer encompasses more than 200 different types, they all share the common characteristic, in that cancer develops as a result of genetic mutations. These mutations may be inherited in the germline, or they may arise as a result of somatic mutations, which develop due to the interactions between the genome and the environment (2,3). It is no surprise then that in the era of molecular medicine, cancer represents the model disease, where advances in DNA technologies and the ability to analyse the whole human genome, is transforming the field of cancer diagnosis, prognosis and disease management. In particular, there are two main areas where genetics is impacting the management of cancer. The area that has been historically developed first is the use of genetics, in identifying individuals who are at a high risk of developing cancer. This has been made possible since the early 1990s when key genes such as the APC and BRCA genes were discovered. Molecular analysis which detects mutations in the genes, enables the identification of individuals who have a strong family history and carry mutations in these highly penetrant genes (2,4). Currently more than 40 familial cancer syndromes are known in which more than 100 genes are involved, fuelling the use of application of NGS panels, for performing such molecular genetic testing across many cancer types (5,6).

The second area that currently represents one of the most exponentially advancing fields in medical practice, is precision medicine and personalized treatment. The major interest in this field is to analyse tumour DNA, in order to detect mutations in driver genes which are actionable and can be inhibited, by the use of small molecule inhibitors, such as Tyrosine kinase inhibitors (7). Indeed over the past decade the Cancer Genome Atlas (TCGA) has generated a vast amount of molecular profiling data across 33 cancer types, leading to the identification of key driver genes (<https://cancergenome.nih.gov/publications>) (8).

In future it is anticipated that cancer will no longer be classified based on its primary anatomic location, such as colorectal cancer, breast cancer, lung cancer or its histological features, but rather based on its specific molecular profiles. Indeed at the Institute we established a department of Molecular Pathology since the early 1990s and have built an extensive experience in the development of molecular genetic tests related to both cancer genetics and personalized medicine. The aim of this presentation is to provide a contemporary overview of the significant contribution of genetics in the diagnosis, prognosis and management of cancer patients.

References

1. Global Burden of Disease Cancer Collaboration, Fitzmaurice C, Akinyemiju TF, et al Global, Regional, and National Cancer Incidence, Mortality, Years of Life Lost, Years Lived With Disability, and Disability-Adjusted Life-years for 32 Cancer Groups, 1990 to 2015. A Systematic Analysis for the Global Burden of Disease Study. *JAMA Oncol.* 2017; 3(4):524-548. doi:10.1001/jamaoncol.2016.5688
2. Foulkes WD. Inherited susceptibility to common cancers. *N. Engl. J Med.* 2008 Nov 13;359(20):2143-53. doi: 10.1056/NEJMra0802968.
3. Parkin, DM, Boyd, L, Walker LC. The fraction of cancer attributable to lifestyle and environmental factors in the UK in 2010. *British Journal of Cancer* (2011) 105, S77–S81; doi:10.1038

4. Pomerantz MM, Freedman ML. The genetics of cancer risk. *Cancer J.* 2011 Nov-Dec;17(6):416-22, doi: 10.1097/PPO
5. Mauer, CB, Pirzadeh-Miller, SM, Robinson LD et al. The integration of next-generation sequencing panels in the clinical cancer genetics practice: an institutional experience. *Genetics in medicine*, 2014, 16, 5, 407-12.
6. Berger, MF, Mardis, ER. The emerging clinical relevance of genomics in cancer medicine. *Nature Reviews. Clinical Oncology*, 2018, 15(6):353-365.
7. Saijo, N. Targeted therapies: Tyrosine-kinase inhibitors--new standard for NSCLC therapy. *Nat Rev Clin Oncol.* 2010 Nov;7(11):618-9. doi: 10.1038/nrclinonc
8. Bailey MH, Tokheim C, Porta-Pardo E et al, Comprehensive Characterization of Cancer Driver Genes and Mutations. *Cell.* 2018 Apr 5;173(2):371-385.e18. doi: 10.1016/j.cell