

Genetics of Cancer

Author: Keeley Sullivan

Major: Microbiology

Department of Microbiology and Molecular Genetics, Oklahoma State University, Stillwater, OK 74078, USA

Key Words:

Oncogene, Proto-oncogene, Tumor Suppressor Gene (TSG), Polymerase Chain Reactions (PCRs), electrophoresis, mass spectroscopy, and microarrays and genotyping, protein arginine methyltransferase (PRMT) 5, E2F1, lncRNA, CD8, Tumor Mutation Burden (TMB), guanine nucleotide-binding protein subunit beta-2 (GNB2).

Cancer is greatly affected by genetics in the human body in a multitude of ways. Certain mutations in genes can lead to the development and proliferation of cancerous cells. These mutations can happen randomly as errors occur in DNA as cells divide and multiply. Genetic mutations that lead to cancer may also be caused by carcinogens, or harmful environmental factors like UV radiation, cigarette smoke, or HPV. Another way genetic mutations can occur is by being passed from parent to offspring. Genetic alterations typically don't harm healthy cells on their own but accumulating them over a long period of time can make healthy cells cancerous. While there are many ways cancer can be developed; by utilizing genetic coding, testing, and treatment, scientists continue to develop more and more ways to battle cancer. In genetic testing, gene mapping, and other genetic tools, specific mutations on genes can be targeted to prevent and treat many types of cancers. In this article, we will discuss the specific genetic tools being used to recognize cancerous genetic mutations.

Introduction

A gene is a sequence of DNA arranged on specific locations on chromosomes in the nucleus of a cell. The gene is the basic unit of heredity that is passed from one generation to the next. Information contained in these genes is used to make certain proteins that lead to the expression of a physical characteristic, such as hair or eye color, or to the function of a cell. A genetic mutation occurs when your cells divide and make copies of themselves, causing changes to your DNA sequence. Cancer is a broad term used to describe several diseases that can emerge from all cell types of the human body. Genetics affect cancer in many ways including gene mutations as well as specific genes and proteins that may lead to cancer if they are not regulated. There are two types of genes that are responsible for causing cancer: tumor-suppressor genes (TSGs) and proto-oncogenes. Tumor-suppressor genes lead to cancer when they are genetically mutated because they control cell division, and a mutation can disrupt TSGs from preventing cancer cells from rapidly dividing. Proto-oncogenes are normal genes found in cells, and when mutated they become oncogenes which can then become tumor cells.

Recent Progress

The overall concept of the role that genetics have in cancer is that abnormal genes cause the multitude of diseases. To pinpoint and examine the genetic alterations

that trigger tumor formation and growth, scientists have developed increasingly powerful tools to study the human genome (Bunz). These tools include Polymerase Chain Reactions (PCRs), electrophoresis, mass spectroscopy, and microarrays and genotyping. These tools aim to map DNA base codes, isolate DNA templates, analyze oligonucleotides, and determine similarities and differences in sequences respectively. Screening and therapeutic measures based upon the cancer gene theory will undoubtedly reduce the overall burden of cancer on future generations (Bunz). Panel tests look at multiple genes, single gene tests look at a particular gene, and single mutation tests look at particular area for a gene mutation. All of these genetic tests identify mutations so that cancer can be prevented, or treatment can be set in place for that specific cancer if necessary.

In a variety of cancers, protein arginine methyltransferase (PRMT) 5 is overexpressed, and E2F1 is an important target for methylation (Barczak. et al., 2023). The repertoire of lncRNA-derived peptide antigens displayed by tumor cells was qualitatively altered by pharmacological inhibition of PRMT5 or adjusting E2F1 levels (Barczak et al., 2023). Tumor growth was significantly delayed by lncRNA-derived peptides that induced an antigen-specific CD8 T lymphocyte response (Barczak et al., 2023).

Mutations in the genome, including deletions, insertions, substitutions, and translocations, are measured by Tumor Mutation Burden (TMB) (Cui et al., 2023). In a study that mapped 994 breast cancer patients' genomes it showed that 88.74% (875) of the patients had somatic mutations. The top 10 mutated genes were as follows: TP53 (34%), PIK3CA (33%), TTN (16%), CDH1 (13%), GATA3 (12%), MUC16 (9%), MAP3K1 (8%), KMT2C (8%), MUC4 (8%) and PTEN (6%) (Cui et al., 2023). In almost all human cancers, TP53 is hypermutated, playing a central role in cancer pathogenesis (Cui et al., 2023).

A guanine nucleotide-binding protein subunit beta-2 (GNB2) in the guanine nucleotide-binding protein family encodes the GNB2 protein, which regulates the alpha subunit of G-protein and various other signal transduction pathways (Zhang et al., 2024). In a study by Kotani et al., It was discovered that the GNB2 gene can accurately assess the prognosis of liver hepatocellular carcinomas (LIHC), and rectal adenocarcinomas (READ) (Zhang et al., 2024). In the same study, tumor cells were also found to be less likely to proliferate when GNB2 was decreased (Zhang et al., 2024).

Discussion

Because there are so many genes in the human body it can be difficult to determine exactly which ones to target. However, with recent developments in genetic testing it is becoming increasingly accessible for oncologists to find and target specific genes in patients. Our knowledge of cells, the body's basic building blocks, has been improved to advances in genetics and molecular biology. Instruments such as Polymerase Chain Reactions (PCRs), electrophoresis, mass spectroscopy, microarrays and genotyping have allowed scientists a new perspective into the genetic makeup of a human body. These devices show where abnormal genes lie within the genome, which will grant the ability to target genes with precise accuracy. As shown by the study by S. Cui and associates in 2023, through gene mapping they determined that the TP53 gene is hypermutated in most human cancers. Another example is shown in the findings of Kotani and associates documented by Zhang and associates. The study found that the GNB2 gene can help estimate the prognosis of certain cancers as well as decrease proliferation when the GNB2 protein is suppressed. In the study by Barczak and associates it was discovered that hindrance of PRMT5 and

E2F1 markedly delayed tumor growth. These findings further prove that genetics play a huge role in cancer. With the continuation of break throughs in the field of molecular genetics, it is likely that cancer diagnosis and treatment will drastically change in the next coming decades.

References

- Barczak, W., Carr, S. M., Liu, G., Munro, S., Nicastri, A., Lee, L. N., Hutchings, C., Ternette, N., Klenerman, P., Kanapin, A., Samsonova, A., & La Thangue, N. B. (2023, February 25). *Long non-coding RNA-derived peptides are immunogenic and drive a potent anti-tumour response*. Nature News. Retrieved March 8, 2023, from <https://www.nature.com/articles/s41467-023-36826-0>
- Bunz, F. (2022). *Principles of Cancer Genetics. Principles of Cancer Genetics* (Third). Springer. Retrieved 2023, from <https://link.springer.com/content/pdf/10.1007/978-3-030-99387-0.pdf>.
- Cui, S., Feng, J., Tang, X., Lou, S., Guo, W., Xiao, X., Li, S., Chen, X., Huan, Y., Zhou, Y., & Xiao, L. (2023, February 20). *The prognostic value of Tumor Mutation Burden (TMB) and its relationship with immune infiltration in breast cancer patients - European Journal of Medical Research*. BioMed Central. Retrieved March 8, 2023, from <https://eurjmedres.biomedcentral.com/articles/10.1186/s40001-023-01058-x>
- Zhang, L., Sahar, A. M., Li, C., Chaudhary, A., Yousaf, I., Saeedah, M. A., Mubarak, A., Haris, M., Nawaz, M., Reem, M. A., Ramadan, F. A., Mostafa, A. A. M., Feng, W., & Hameed, Y. (2024). *A detailed multi-omics analysis of GNB2 gene in human cancers*. Scielo. Retrieved March 7, 2023, from <https://www.scielo.br/j/bjb/a/LKDj7VGwzpqYvvhvBfV9ccB/?format=pdf>