Crimson Publishers
Wings to the Research

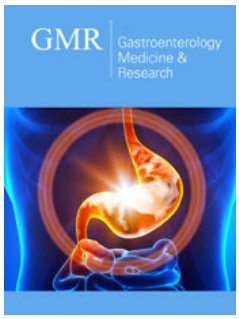
Mini Review

Cancer Genomics: Transforming Precision Diagnostics and Therapeutics

Chen Yeh*

OncoDxRx, Los Angeles, CA, USA

ISSN: 2637-7632



***Corresponding author:** Chen Yeh, OncoDxRx, LLC, 150 N Santa Anita Ave., Suite 300, Los Angeles, CA 91006, USA

Submission: October 01, 2024
Published: October 16, 2024

Volume 8 - Issue 1

How to cite this article: Chen Yeh*. Cancer Genomics: Transforming Precision Diagnostics and Therapeutics. Gastro Med Res. 8(1). GMR. 000677. 2024.
DOI: 10.31031/GMR.2024.08.000677

Introduction

Cancer is the leading cause of disease worldwide, with an estimated 19.3 million new cases and almost 10 million cancer deaths in 2020 [1]. Overall, the burden of the disease is rapidly increasing, with the global incidence projected to increase to 28.4 million cases by 2040 [1]. While there have been dramatic improvements in survival for some cancers, there has been limited progress against others. Many current therapies, such as conventional chemotherapies, broadly target all rapidly dividing cells causing unwanted side effects. New treatment approaches are needed to both improve patient survival and quality of life. Advances in technologies have led to exponential growth in the understanding of the genetic basis of cancer, opening up new avenues for treatment. This has led to the development of a new generation of targeted cancer drugs that are designed to exploit vulnerabilities in tumor cells. As these novel therapeutics specifically target cancer cells, they should theoretically cause fewer side effects than traditional chemotherapies. In recent decades, cancer medicine has evolved from the traditional" one-size-fits-all" approach – based on broad categorizations of the location of a person's cancer and its stage – into a new era of precision medicine. Genetic testing can now reveal detailed molecular information about a person's cancer – enabling doctors to match therapies that target specific alterations driving the growth and spread of their disease. In this short communication, we discuss how cancer genomics is changing how some patients are diagnosed and treated – and highlight ongoing challenges that still need to be overcome to unleash the full potential of precision medicine.

Genes and cancer

Cancer is caused by an accumulation of mutations in a person's genome that triggers a cell to start growing out of control. These gene changes can be randomly acquired during a person's lifetime as a result of natural cellular processes or from exposure to environmental factors, such as ultraviolet light or tobacco smoke. People can also inherit certain genes from a parent that can increase their risk of cancer, such as faulty versions of BRCA1 or BRCA2 that increase the chances of developing certain cancers, most notably breast and ovarian cancer [2]. A major goal in cancer genomics is to identify all the genes which, upon acquiring mutations, play a role in driving tumor growth and spread. In recent decades, the list of these cancer genes has continued to grow – thanks to vast quantities of data coming from cancer sequencing screens of many thousands of tumor samples. These include large-scale global collaborations such as the International Cancer Genome Consortium (ICGC) [3] – which was established to analyze more than 25,000 cancer genomes from 50 different tumor types – and The Cancer Genome Atlas (TCGA) that has sequenced more than 20,000 samples across 33 cancer types [4]. Building on the work from these initiatives, the ICGC/TCGA Pan-Cancer Analysis of Whole Genomes (PCAWG) was set up to identify common mutations patterns in more than 2,600 whole cancer genomes across 38 tumor types and is the largest, most comprehensive analysis of cancer genomes to date [5]. The Network of Cancer Genes (NCG), which aims to gather a comprehensive and curated collection of cancer genes from cancer sequencing screens, currently contains 3,347 genes whose modifications have known or predicted roles in driving cancer [6].

Targeting the mutation

Cancer genomics is already having an enormous impact on treatment decisions- enabling doctors to match patients with new targeted therapies that offer the possibility of better outcomes. An early example of a successful targeted drug is imatinib, which has revolutionized the treatment of Chronic Myeloid Leukemia (CML) after its approval by the US Food and Drug Administration (FDA) in 2001 [7]. It works by blocking the action of an abnormal protein made as a result of a genomic alteration in the cancer cells. Imatinib was the first example of a small molecule targeted cancer treatment to be approved for use in patients. The drug is also the second successful targeted therapy overall after trastuzumab, which targets the human Epidermal Growth Factor (EGF) receptor-2 (HER2) that is overactive in around a quarter of all breast cancers [8]. Since then, many other targeted cancer treatments have been developed. For example, gefitinib, which targets the EGF receptor (EGFR) that is faulty in some lung cancers, was approved in 2003 [9]. In 2011, vemurafenib was approved for the treatment of malignant melanomas with a specific mutation (V600E) in the B-Raf proto-oncogene (BRAF) gene [10]. Three years later, the FDA approved the first poly (ADP ribose) polymerase (PARP) inhibitor, olaparib, for the treatment of advanced ovarian cancers with inherited faults in BRCA1 or BRCA2 [11]. More recently, the first targeted treatment against the Kirsten rat sarcoma proto-oncogene (KRAS) gene was approved for treating certain lung cancer patients [12]. This was hailed as a milestone as faulty versions of this gene are the root cause of a significant proportion of cancers but for many years it was considered an "undruggable" target.

Advanced diagnostics

Molecular diagnostics is playing an instrumental role in driving the uptake of precision medicine and is increasingly used to guide therapeutic decisions in daily clinical practice. For example, genetic testing for the presence of a specific mutation in the BRAF gene in metastatic melanomas is used to identify people who may benefit from BRAF inhibitors like vemurafenib [13]. The same approach can identify patients with EGFR-positive Non-Small Cell Lung Cancer (NSCLC) who may benefit from targeted EGFR inhibitors [14]. In other cases, identifying a genetic alteration may significantly influence the choice of treatment, but this may not be for a treatment that directly targets that particular mutation. For example, identifying mutations in the KRAS gene in colorectal cancers will indicate that patients will not respond well to drugs targeting EGFR, such as cetuximab or panitumumab [15]. Certain mutations can also flag that cancer is more likely to develop resistance to treatment. For example, in Acute Myeloid Leukemia (AML), some people have mutations that increase the likelihood of their cancer becoming resistant to targeted drugs called isocitrate dehydrogenase inhibitors [16].

Liquid biopsies

Liquid biopsies can provide a rapid, simple alternative to standard tissue biopsies – providing a new tool for obtaining genetic information about a person's cancer and enabling doctors to devise precision treatment strategies [17]. A standard tissue biopsy involves a surgical procedure to remove a tumor sample for analysis. But this is an invasive procedure and can be difficult to perform, particularly if the tumor is located deep inside the body or close to vital organs. In contrast, a liquid biopsy is carried out on a sample of body fluid – most often a blood sample – to detect and analyze cancer-derived materials, such as Circulating Tumor Cells (CTCs) or circulating tumor DNA (ctDNA), which are released by a tumor as it grows [17]. As the procedure is minimally invasive and can be serially repeated, it can also enable doctors to monitor any changes to the disease in real time so that their treatment can be changed as needed. A liquid biopsy may also reveal more information about the complexity of an individual's cancer compared to a tissue biopsy. As a tumor grows, it evolves – and so most are made up of a tapestry of cancer cells with different genetic alterations. As a result, testing one tissue sample collected from a single region of a tumor is unlikely to capture every mutation that exists. However, as liquid biopsies detect materials shed from different parts of a tumor and its metastases, they may provide a more comprehensive picture of the evolving genetic landscape of the disease.

Future perspectives

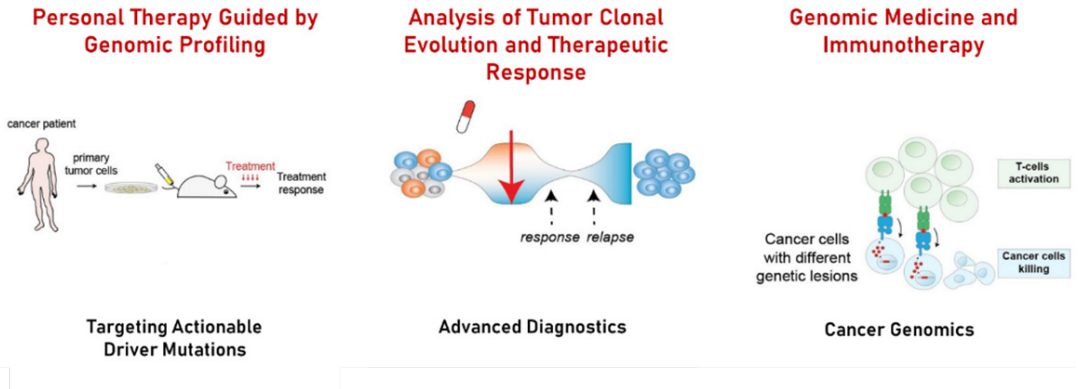


Figure 1: Overview of modern molecular genomics approaches deployed to advance precision diagnostics and therapeutics in oncology.

Precision medicine and targeted cancer therapeutics are already transforming the lives of some patients – improving their chances of survival and reducing side effects (Figure 1). But to date, the number of cancer genes still far outweighs the number of targeted treatments available – and so the vast majority of patients currently do not have "actionable" mutations in their tumors. Cancer is enormously complex and can also adapt and evolve in response to changes in its environment – including drug treatment. So, while many of the latest targeted therapies may be initially effective, a person's cancer can develop resistance and stop responding. Despite these challenges, the future of precision medicine remains bright. The number of cancer patients who could benefit from the approach will continue to expand as more genomic alterations are identified, along with agents that target them. And combining therapies that work in different ways could help prevent the disease from becoming resistant to treatment early on – improving the long-term outlook for patients.

References

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, et al. (2021) Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 71(3): 209-249.
2. BRCA gene mutations: Cancer risk and genetic testing. NIH National Cancer Institute.
3. (2010) International network of cancer genome projects. Nature 464(7291): 993-998.
4. Tomczak K, Czerwińska P, Wiznerowicz M (2015) The Cancer Genome Atlas (TCGA): An immeasurable source of knowledge. Contemp Oncol (Pozn)19(1A): A68-77.
5. (2020) Pan-cancer analysis of whole genomes. Nature 578(7793): 82-93.
6. NCG7.0 Network of Cancer Genes & Healthy Drivers.
7. Ren R (2005) Mechanisms of BCR-ABL in the pathogenesis of chronic myelogenous leukaemia. Nat Rev Cancer 5(3): 172-183.
8. Shepard HM, Jin P, Slamon DJ, Pirot Z, Maneval DC (2008) Herceptin. Handb Exp Pharmacol (181): 183-219.
9. Cohen MH, Williams GA, Sridhara R, Chen G, Pazdur R (2003) FDA drug approval summary: Gefitinib (ZD1839) (Iressa) tablets. Oncologist 8(4): 303-306.
10. Bollag G, Tsai J, Zhang J (2012) Vemurafenib: The first drug approved for BRAF-mutant cancer. Nat Rev Drug Discov 11(11): 873-886.
11. Kim G, Ison G, McKee AE, Zhang H, Tang S, et al. (2015) FDA approval summary: Olaparib monotherapy in patients with deleterious germline BRCA-mutated advanced ovarian cancer treated with three or more lines of chemotherapy. Clin Cancer Res 21(19): 4257-4261.
12. Nakajima EC, Drezner N, Li X, Mishra-Kalyani PS, Liu Y, et al. (2022) FDA approval summary: Sotorasib for KRAS G12C-mutated metastatic NSCLC. Clin Cancer Res 28(8): 1482-1486.
13. Cheng L, Lopez-Beltran A, Massari F, MacLennan GT, Montironi R (2018) Molecular testing for BRAF mutations to inform melanoma treatment decisions: A move toward precision medicine. Mod Pathol 31(1): 24-38.
14. Sheikine Y, Rangachari D, McDonald DC, Huberman MS, Folch ES, et al. (2016) EGFR testing in advanced non-small-cell lung cancer, a mini-review. Clin Lung Cancer 17(6): 483-492.
15. Wong SQ, Scott R, Fox SB (2016) KRAS mutation testing in colorectal cancer: The model for molecular pathology testing in the future. Colorectal Cancer 5(2).
16. Zhuang X, Pei HZ, Li T, Huang J, Guo Y, et al. (2022) The molecular mechanisms of resistance to IDH inhibitors in acute myeloid leukemia. Front Oncol 12: 931462.
17. Lianidou E, Pantel K (2019) Liquid biopsies. Genes Chromosomes Cancer 58(4): 219-232.