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Precision Medicine and Translational Therapeutics: A Precise Way to Deal with Cancer?

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ABSTRACT:

The review paper focuses on precision medicine and its uses in oncology. Precision medicine is the future of treatment specifically in cancer. Ongoing research and advancement will give direction to the patient-driven treatment where the symptoms are going to be managed with the designing of the medicine as per the requirement. In today's era, the demand for precision medicine is increasing in cancer, genetic disorder, and other illness. It helps in overcoming the side effects and complications associated with the treatment. In cancer, it has been noticed that conventional treatment is imposing a vast range of adverse effects. To overcome that precision medicine came into the role that is resulting in the target and personalized approach. The review is going to give insight into precision medicine and its journey. Cancer and its variable that makes it different from other illnesses, the role of precision medicine and comparison with genomics medicine, and the future of precision medicine.

Keywords: Precision medicine, genomics medicine, oncology, AI, and cancer.

1. Introduction:

Precision Cancer Medicine and Translational Therapeutics is one of the emerging research fields present. Research and innovation are going on that will bring effective cancer treatment. Cancer is one of the most deadly illness exist in human history. To date, cancer treatment is happening on a hit-and-trial method that outcomes as the complication and complexity (Adir et al., 2020). With the use of AI, the journey of precision medicine can compile a wide range of factors. To overcome the compilation and to understand the behavior of oncogenic genes, precision medicine, and translational therapeutics are serving great options. One of the factors that are traced down in the cancer is that cells develop and respond to therapies differently from one patient to the next which is creating a challenge in the treatment (Zhao et al., 2019). A gain of insight that what is the driver of tumors and abnormalities in the cell allows for tailored therapeutic strategies that are more effective with minimal side effects. With the profiling of mutation and abnormalities in the tumor, therapies are designed that is imposing minimal complications and side effects. It is done by making a permutation and combination of the contributing factor that will define the target for the tumor. With this additional molecular information taken from genomics, proteomics will help(Horak et al.,2022). Defining the response of the experimental models will lead to dramatically improved outcomes in the oncology field. Precision medicine is the tailoring of medical treatment to the individual that is holding the characteristics of the patient to which it is going to be applied. Translational therapeutics is the term present that is used to describe the pathway between the discovery of the basic disease mechanism or a novel therapeutic approach. In simple words, it is the translation of the treatment for the patient with specific diseases like cancer. One of the milestones that are achieved to date is the human genome project which is not only there to provide the essential reference map for the human genome (Ozturk et al., 2018). In addition, it gives birth to the technology and analytical tools that lead to the impact of massive quantities of genomic data. The results of the genome project are used in the advancement of DNA sequencing technology. The use and innovation that have been done over the decade led to the advancement and cost-effectiveness that contributes to the designing of the new treatment. Although, it is noticed that the innovation and development of the technologies are leading to the basic contribution to cancer genomics (Gambardella et al., 2020). The discoveries are crucial in clinical cancer research where a genetic alteration in a patient with a tumor will serve the high efficacy treatment with a high percentage of molecularly matched targets. Therefore, the fact is established that precision medicine is the new era of medicine that deliver efficacy outcomes with no or fewer complications (Schloss et al., 2020). The review article reflects on cancer and its mechanism, the role of precision medicine, and translational therapeutics followed by clinical research models that contribute to the discovery of precision medicine (Sherman et al., 2020). In the last section, the discussion is about new advancements and future research in precision medicine in cancer.

1.1 Cancer: A mutational event

Cancer refers to the event in which there is a large number of diseases present that are characterized by the uncontrolled differentiation of the cells abnormally. It holds the ability to spread to other cells and destroy normal body tissue. It often has the capability of spreading to nearby and far-located tissues (Hegde & Chen, 2020). As per the data shared World Health Organization(2022), it is one of the leading causes of death worldwide; accounting

for nearly 10 million deaths in 2020, or nearly one in six death of cancer. The most common types of cancer are breast, lung, colon, and rectum (World Health Organization, 2022). Cancer is a generic term that can be replaced with the terms like malignant tumor and neoplasm. The process that outcome in the wild stages of cancer is known as metastasis; becoming the primary cause of death from cancer. One of the basic features that are there in cancer is the clonality of tumor cells that is making the single cells initiate and proliferate in an abnormal manner (Hanahan, 2022). At the cellular cell, the development comprises the multistep process where mutation and selection of cells with the progressively increased capacity for proliferation, survival, invasion, and metastasis are there (Ferlay et al., 2021). Initial steps involved the initiation of the tumor that is resulting in the genetic alteration that makes the proliferation of the cells in an unorganized way, followed by the progression of the tumor that continues as the additional mutation is getting introduced in the cell. The descendants of cells having such sort of mutation act as the dominating ones within the tumorous cells.

1.2 Role of cell cycle and regulator proteins:

Genes that code for normal proteins with control over the critical processes of the cell cycle is proto-oncogenes (Zhang & Yu, 2019). Induction of any kind of alteration in the genes makes them an oncogene that is an abnormal protein product and exhibits the characteristics like an increase in activity that is making the promotion of tumor growth. The impact of mutation is seen in that instead of stopping in the G phase, it will take participation in the subsequent cell cycle steps. The results came in terms of uncontrolled growth (Brown et al., 2020). The active and inactivation of the states lead to cancerous growth. For example, Ras protein acts as the molecular switch that gets turned off and off depending on the form of the nucleotide that is bounding to it. In the protein, if there is any modus of mutation arises the changes in the structure will be introduced that will be impacting the activity and give rise to tumor growth because it is acting as the oncogenes (Mukhopadhyay et al., 2021). Apart from mutation, another type of alteration that happens at the genetic level is translocation where the chromosomal material gets reattached leading either to the formation of the N-terminus of one protein or the C-terminus of another protein that is going to deliver the altered regulation of expression of proteins. An example of such translocation is the Philadelphia chromosome which is comprised of the N- terminus of the Bcr and the C-terminus of Abl (Soverini et al., 2019). The development of cancer takes place in the four stages, there are multiple factors lies that is involving the size and location of the tumor. Stage 1 is cancer in a small area and will not be spreading to the lymph nodes or any other tissues. Stage 2 is cancer growing to other regions but not having the potential to spread. Stage 3 is the growth of cancer to get larger and spread to the lymph nodes. Stage 4 is about the spread of cancer to other organs and holds the capacity to introduce it to other cells as well (Frick et al., 2022). The stage is the advanced one and difficult to deal with and treat. Continuous involvement of the carers is required that will manage the advanced stages.

1.3 Risk Factors contribute to cancer and its progression:

There are two sorts of risk in certain people that is absolute risk and relative risk. Absolute risk is the event that person will develop the condition during a given period. It is one of the parameters to identify that what is the percentage of people at risk of diseases among the population (Momenimovahed & Salehiniya, 2019). The second one is the relative risk that will be taking the comparison of the risk of diseases between the two groups of people. The aim and motive that is there is the comparison of certain risk factors in the population. Following are some of the risk factor present that gives rise to the absolute and relative risk of cancer among the population and groups of people. Older age, cancer can develop at any age but when an individual grows older the chances of developing cancer get increase as the damage to cells is there. An unhealthy lifestyle will be there due to the eating of high and sugary food. The functioning of the system gets modified that is leading to physiological changes and an increased risk of many types of cancer. Exposure to chemicals and radiation, the exposure of asbestos, pesticides, insecticides, and radon will eventually be resulting in a cancerous situation. Apart from this, radiation like UV rays will increase the risk of skin cancer as it makes DNA alteration. Apart from this, geography is another factor that will be acting as the differentiator and causes variation in the prevalence of cancer. It is a multifactorial thing that comes up with the combination of genetics, diet, and environment (Wu et al., 2018). Infection, several viruses are known for causing cancer in humans. For example, The human papillomavirus is causing cervical cancer in women and anal cancer in men. Drugs and medical treatment, intake of drugs, and interventions might be the reason for the occurrence of cancer (Brown et al., 2018). For example, Diethylstilbestrol (DES) is increasing the risk of breast cancer in women who are taking the drugs. The spread of cancer is seen with the cell break from the original tumor and travels to the bloodstream via the lymphatic system that is going to form new tumors in other organs and the process is known as metastasis. For the prevention of the risk of cancer, following a healthy and active life is important.

1.4 How cancer is different from other diseases and illnesses:

One of the main differences that are there in cancer and other illness is the involvement of genes. Cancer is a genetic condition that occurs to the alteration in the genes and the way gene controls cell functioning. Genetic changes can happen because of error while a division of cells, damage due to the harmful exposure to the DNA, and inheritance from parents to a child.

Three main types of genes that tend to cause cancer are proto-oncogenes, tumor suppressor genes, and DNA repair genes(Brown et al., 2020). Changes in the genes are also known as the drivers of cancer.

Proto-oncogenes are the one that participates in the cell cycle and contributes to the normal growth and division of cells. The alteration in the gene in certain ways makes them more active than the normal state which outcomes in the formation of cancer-causing gene " oncogenes". The gene allows the cells to grow and survive which is not demanded in the faulty one. In this manner, the regulator becomes the driver of cancer.

Tumor suppressor genes that again involved in controlling and regulating cell growth. Cell encompass the mutation or levels of alteration will resulting in the division of the cells in an uncontrolled manner (Kontomanolis et al., 2020).

DNA repair genes hold the major responsibility of fixing damaged DNA. cells having a mutation in the gene tend to develop the additional mutation that will give rise to the change in the chromosomes. Such a sort of mutation is known as duplication or deletion. Altogether mutation will cause the cells to become cancerous. Molecular changes (MYC gene) are one of the significant reason lies that leads to several symptoms appearing that requires dealing with radiation and chemotherapy. Chemo drugs are going to provide in combination usually resulting the side effects like fatigue, hair loss, bleeding, infection, and gastrointestinal changes (Dhanasekaran et al., 2022). In addition, the interaction of the medication might lead to worse side effects. One example is platelet help in the clotting of blood and stops bleeding. Taking medication will lead to an impact on the count of platelet and weaken the blood platelets. The consequence is seen in unstoppable bleeding. Apart from this, the intake of vitamins will be resulting in less effectiveness of the chemotherapy. Radiation therapy is also used for the treatment of cancer but at the same time, it will lead to the destruction of the nearby cell as well. The side effect of the therapy is seen in the second or third week of treatment and goes on for several weeks (Zakiryanova et al., 2018). One of the possible later effects that are going to develop is second cancer which is a new type of cancer. To deal with the contraindication, side effects, and complication of the standard therapy; recent researches show that personalized medicine and translational therapeutics hold promising nature that is going to revolutionize the field of oncology.

2. Precision medicine:

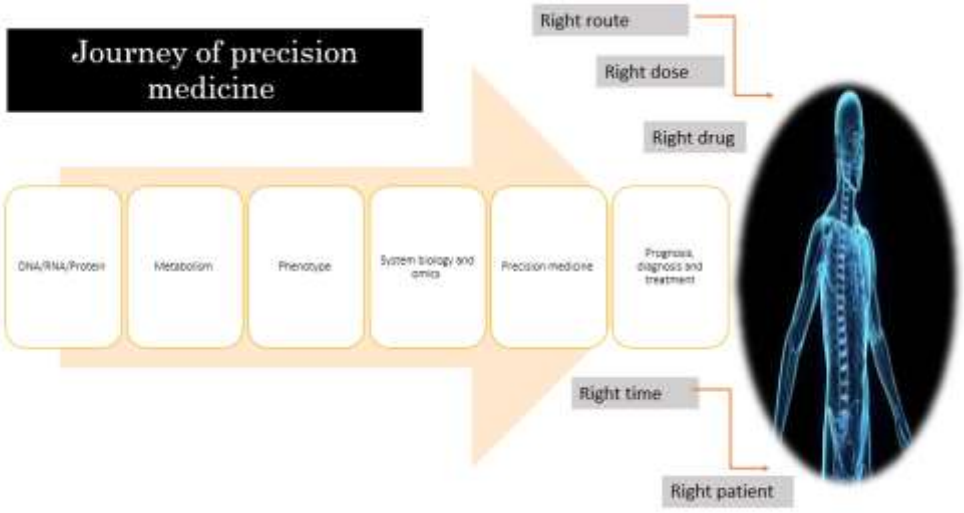

Fig. 1 Journey of precision medicine: Experiment with practices

(Source: Love-Koh et al., 2018; Mahmud et al., 2019)

The term has gained significant popularity in the past few years that is full of scientific aspects and some controversial points. The terms that are more often used to replace precision medicine are stratified medicine, targeted therapy, or deep phenotyping (Ginsburg & Phillips, 2018). Precision medicine is a medical model that aims to purpose the customization of healthcare with the medical decision, treatment, practices, and products that are going to be tailored to a sub-group of the patient. It is about the designing of the medical care that is going to optimize the efficiency of the benefits for the patient with the use of genetic and molecular profiling. There is a broad range of scientific areas coming in the discovery of precision medicine the discovery of the drug, genetics/genomics, health communication, and integration of the evidence-based approach (Bzdok et al., 2021). The approach is very different from the traditional one as it is not about the signs and symptoms. It takes the large-scale data that comprise the clinical, lifestyle, genetics, and further biomarkers. The principle of precision medicine is to tailor the treatment based on the person's genes, lifestyle, and other factors. With the sequencing of the human genome in 2001, the technology of precision medicine gets a pace that will be presenting the opportunity of making medicine that is going to deliver patient care in a customized manner. Sorafenib is the systemic therapy present for advanced-stage HCC (Llovet et al., 2018). The role of precision medicine is getting edges closer to getting approval for the diseases. The characteristic that defines precision medicine is that requires patient data. The health records and genetic codes of the patient play a vital role that will be influencing people's healthcare and giving direction to research. The movement of medicine toward the use of precision one going to serve several advantages that are in terms of the higher resolution and use of other technologies to bring more precise targets to deal with the subgroups of the diseases (Kosorok & Laber, 2019). Prominent examples that are going to deal with these are cancer and cystic fibrosis. The existence of the field is based on the sequencing-led discovery of genetics in population and low throughput approaches in genetics diagnosis in the patient. It is going to make things possible in terms of bringing the integration of two fields that is the technologies and algorithms that are providing the phenomenal discovery of genomics that is required to eliminate the error before making it applied to clinical medicines. The areas and points that require extensive work are the quality and coverage of the sequential data for clinical genetic testing (Koenig et al., 2017). The

main idea of precision medicine is to improve health outcomes by tailoring treatment to individual characteristics. It is based on evidence-based data that is making the medicine as specified as the condition. With the help of the approach, the error can be eradicated that is going to be generated with the application of a combination of drugs (Ginsburg & Phillips, 2018).

2.1 Origin of precision medicine and recent research:

The origin of precision medicine is not known as no one can precisely say that on that day a particular drug is invented as it is dependent on ongoing research. After the successful completion of the human genome project, a new field emerged as precision medicine. There is a huge number of investment is made by the national institute of health under Francis collins that will be leading to the road of new knowledge that is bringing the transformation in genetic medicine and going to take that direction too far away from mutations and chromosomal aspects. A handful of newly discovered drugs are based on the genetics of cancer cells. Examples: Herceptin, imatinib, and others (Phillips, 2020). The discovery of drugs is leading to the hope that the deadliest disease like cancer will be cured. A second thought that espouses the idea of precision medicine is that it holds the ability to gather new and evidence-based data that is concerning the treatment of diseases. The main motive lies in the identification of specific genes and biomarkers researchers will be able to design a more precise intervention (Ahmed et al., 2020). Taking the insight into the history of precision medicine NIH become the largest funder in medical research. The areas covered in the duration include the "comparative effectiveness research" and "patient-centered outcomes research". Using electronic means to address the growing demand for the collection of medical data incorporation of "big data method". It has been over 100 years since the term gene is introduced (Benjamin, 2019). It is the hereditary unit that carries out genetic information. The chemical structure is known as the genome and the human genome is made up of 3 billion bps. Genes comprise the coding (exons) and non-coding regions (introns). On average, the human gene encompasses nine exons and the longest human gene is known as titin(TTN) with 365 exons, 109224 base pairs, and encoding for 35991 amino acids. All these disclosures about the existing feature and their role will be going hands-on hand which is growing with the support of technological advancement. Integration of science, technology, and statistics will lead to the generation of an amazing field that is going to improve lives (Yu et al., 2019). With this discovery of trastuzumab happens, the first drug that is developed by the implication of the drug-diagnostic development model is taking the diagnostic assay with the gain of understanding of the pathophysiology of disease and mechanism of action of the drug. The main aim of a drug is to deliver the right drug to the right patient via the right route at right time (Yu et al., 2019). The model has proven tremendous numerous times specifically in the field of oncology and hematology. It was the first targeted cancer drug that is using the drug-diagnostic co-development model successfully.

To make the drug, the first steps have been taken 2 decades earlier with the combination of drugs and diagnostics. Just after the turn of the century, another milestone that is achieved is the approval for the small molecule tyrosine kinase inhibitor imatinib. The main action of the drug is to inhibit the BCR-ABL protein that is present in the chronic myeloid leukemia patient. The cause behind CML is the translocation of regions of the BCR and ABL gene that is resulting in the formation of a BCR-ABL fusion gene (Ahmed et al., 2019). The drug is producing great and high responses in cytogenetic and hematologic patients with CML. Back 20 years, Langreth and Waldholz came up with the idea of a" new era of personalized medicine" there is still no clear and precise definition present in the area of hematology and oncology (Jørgensen, 2019). After so many years, the National cancer institute tries to define the concept of personalized medicine:

"A form of medicine that is formed by the use of information regarding the genes, proteins, and environmental factors to incorporate the prevention, diagnosis, and treatment of the diseases. In cancer, personalized medicine takes up unique information about the person's tumor and will lead to the planning of treatment. The targeted therapies are used for the treatment of specific types of tumors. That is also called precision medicine".

From the discovery of Herceptin and imatinib; the research still going on that is reaching new edges in oncology. The discoveries are promoting outcomes in treatment that is higher in efficacy and efficiency.

2.3 Latest discovery in precision medicine (PROTAC):

- Recent advancement in precision medicine shows outstanding results that are evident with the availability of new drugs. Targeted protein degradation has emerged as a phenomenal creation in domains of chemical biology and the discovery of drugs.
- PROTAC are heterobiomolecules that is having an E3 ligase ligand fused to the POI ligand via a chemical linker (Nalawansha & Crews, 2020).
- As soon as the tertiary complex formation happens, E3 ligase induces the ubiquitination and proteasomal degradation of the targeted protein. In the last five years, understanding and insight about PROteolysis TArgeting Chimera (PROTAC) technology has expanded in terms of its unique mode of action and its advantages.
- It emerges as a novel therapeutic strategy. It holds great promising nature as the therapeutic modality that is requiring only transient interaction with any service on the target site to promote the degradation. The main action occurs via the event-driven mode of action that is going to eliminate the protein. Thus, eradicating the possible functions that are related to it (Sakamoto 2010).
- These moieties are specific, versatile, and biologically active that is leading to the induction of degradation of protein that is promoting the process of tumorigenesis and will lead to the inhibitory effects on the growth of cancer cells.
- The application of PROTACs seems to be dependent on the success of ubiquitination and degradation of protein targets by endogenous ubiquitin ligases and proteasomes within the cells. It is emerging as a novel technology as it is directly hitting the mechanism of cancer cells.

2.4 Comparative analysis of Genomics medicine and precision medicine:

The essential role that is seen in precision medicine is to make the right match of drugs for the right patients. In cancer, precision medicine is taken as a near synonym for genomics. With the increase in the practices of precision medicine, it is found that it is way far different from genomic medicine. The aim of genomic medicine is that it is used for somatic genetic alteration that is point mutation, deletion, and chromosomal abnormalities. Now, precision medicine is taking actionable and informative alterations. Genomics-based drugs are only having insight that what the mutation is there but precision medicine is much beyond that perspective. The wholesome vision is the best-targeted intervention that is serving less the complication and side effects in conditions like cancer. Understanding of microbiome is the key factor of precision medicine that is not only focused on the genomics data but take the integration of demographic and family history (Petrosino, 2018). Altogether, it is making coverage all the factor that is related to the condition. It also contributes to the refinement of the process of precision biomarker discoveries (Kolde et al., 2018). Routine patient care is one of the challenges that is seen in terms of patient care that can be overcome with the use of precision medicine. As it identifies the root cause and the mechanism of action that will lead to the eradication of the cause that is behind the condition. It will be making the efficacy and care of the patient to get increase in terms of dealing and outcomes (Peterson et al., 2019). Another difference is seen in terms of the identifiable mutation that is quite important for the success of genomics medicine. sometimes, it is acting as a misleading factor as one is unable to identify the faith of mutation in the cell that is limiting the outcomes. This sort of bias can be overcome for the sake of personalized medicine. The transformation will be occurring with the use of AI that is in terms of huge cohorts, performing routine clinical genomics, and considering the value across the population that is going to define the future possibilities.

3. Future of precision medicine: a roadmap toward practices:

With time, one thing that has changed is the need of an individual in terms of care and requirement that is making a shareholding in the process of discovery of new domains in medicine and research. The approach that is going to be used in precision medicine is about combining the knowledge of cancer and its vulnerabilities that is allowing clinical progression (Johnson et al., 2021). It requires the intake of both omics and functional approaches that is generating the option for the individual need. Precision medicine is the future of medicine that is not only making the symptoms and conditions overcome in addition allowing the high efficacy of results with limiting the number of side effects. The vast range of tools and experiments is showing how much potential it holds. The use of Artificial intelligence will be presenting so much leverage at the interface of computation and omics that help in generating insight, enables the system to learn and give reasoning, and empowers clinician decision through advanced intelligence (Denny & Collins, 2021). AI contributes to the digitalization of health-related data with the use of technologies that promises to bring the best with the rapid uptake of advancement and fueling transformation. The principle of AI is to secure data, analytics and insight, and expertise that is helping in the use of data into knowledge that is going to impact human history. Supramolecular photothermal effects will take the integration of the binary system that is leading to drug delivery and targeted therapy(Zhao et al., 2019)

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References:

Adir, O., Poley, M., Chen, G., Froim, S., Krinsky, N., Shklover, J., ... & Schroeder, A. (2020). Integrating artificial intelligence and nanotechnology for precision cancer medicine. *Advanced Materials*, *32*(13), 1901989.https://doi.org/10.1016/j.jmb.2018.06.016

Ahmed, Z., Zeeshan, S., Mendhe, D., & Dong, X. (2020). Human gene and disease associations for clinical-genomics and precision medicine research. *Clinical and Translational Medicine*, *10*(1), 297-318.https://doi.org/10.1002/ctm2.28

Ahmed, Z., Zeeshan, S., Xiong, R., & Liang, B. T. (2019). Debutant iOS app and gene-disease complexities in clinical genomics and precision medicine. *Clinical and Translational Medicine*, *8*(1), 1-11.https://doi.org/10.1186/s40169-019-0243-8

Benjamin, R. (2019). Assessing risk, automating racism. *Science*, *366*(6464), 421-422.https://doi.org/10.1126/science.aaz3873

Brown, K. F., Rumgay, H., Dunlop, C., Ryan, M., Quartly, F., Cox, A., ... & Parkin, D. M. (2018). The fraction of cancer attributable to modifiable risk factors in England, Wales, Scotland, Northern Ireland, and the United Kingdom in 2015. *British Journal of Cancer*, *118*(8), 1130-1141.https://doi.org/10.1038/s41416-018-0029-6

Brown, R. A., Richardson, K. L., Kabir, T. D., Trinder, D., Ganss, R., & Leedman, P. J. (2020). Altered iron metabolism and impact in cancer biology, metastasis, and immunology. *Frontiers in Oncology*, *10*, 476.https://doi.org/10.3389/fonc.2020.00476

Bzdok, D., Varoquaux, G., & Steyerberg, E. W. (2021). Prediction, not association, paves the road to precision medicine. *JAMA Psychiatry*, *78*(2), 127-128.https://doi.org/10.1001/jamapsychiatry.2020.2549

Denny, J. C., & Collins, F. S. (2021). Precision medicine in 2030—seven ways to transform healthcare. *Cell*, *184*(6), 1415-1419.https://doi.org/10.1016/j.cell.2021.01.015

Dhanasekaran, R., Deutzmann, A., Mahauad-Fernandez, W. D., Hansen, A. S., Gouw, A. M., & Felsher, D. W. (2022). The MYC oncogene—the grand orchestrator of cancer growth and immune evasion. *Nature Reviews Clinical Oncology*, *19*(1), 23-36.https://doi.org/10.1038/s41571-021-00549-2

Ferlay, J., Colombet, M., Soerjomataram, I., Parkin, D. M., Piñeros, M., Znaor, A., & Bray, F. (2021). Cancer statistics for the year 2020: An overview. *International Journal of Cancer*, *149*(4), 778-789.https://doi.org/10.1002/ijc.33588

Frick, J., Gebert, P., Grittner, U., Letsch, A., Schindel, D., & Schenk, L. (2022). Identifying and handling unbalanced baseline characteristics in a non-randomized, controlled, multicenter social care nurse intervention study for patients in advanced stages of cancer. *BMC Cancer*, *22*(1), 1-13.https://doi.org/10.1186/s12885-022-09646-6

Gambardella, V., Tarazona, N., Cejalvo, J. M., Lombardi, P., Huerta, M., Roselló, S., ... & Cervantes, A. (2020). Personalized medicine: recent progress in cancer therapy. *Cancers*, *12*(4), 1009.https://doi.org/10.3390/cancers12041009

Ginsburg, G. S., & Phillips, K. A. (2018). Precision medicine: from science to value. *Health Affairs*, *37*(5), 694-701.https://doi.org/10.1377/hlthaff.2017.1624

Hanahan, D. (2022). Hallmarks of cancer: new dimensions. *Cancer Discovery*, *12*(1), 31-46.https://doi.org/10.1158/2159-8290.CD-21-1059

Hegde, P. S., & Chen, D. S. (2020). Top 10 challenges in cancer immunotherapy. *Immunity*, *52*(1), 17-35.https://doi.org/10.1016/j.immuni.2019.12.011

Horak, P., Leichsenring, J., Goldschmid, H., Kreutzfeldt, S., Kazdal, D., Teleanu, V., ... & Stenzinger, A. (2022). Assigning evidence to actionability: An introduction to variant interpretation in precision cancer medicine. *Genes, Chromosomes and Cancer*, *61*(6), 303-313.https://doi.org/10.1002/adma.201901989

Johnson, K. B., Wei, W. Q., Weeraratne, D., Frisse, M. E., Misulis, K., Rhee, K., Zhao, J., & Snowdon, J. L. (2021). Precision Medicine, AI, and the Future of Personalized Health Care. *Clinical and Translational Science*, *14*(1), 86–93. https://doi.org/10.1111/cts.12884

Jørgensen J. T. (2019). Twenty Years with Personalized Medicine: Past, Present, and Future of Individualized Pharmacotherapy. *The Oncologist*, *24*(7), e432–e440. https://doi.org/10.1634/theoncologist.2019-0054

Koenig, I. R., Fuchs, O., Hansen, G., von Mutius, E., & Kopp, M. V. (2017). What is precision medicine?. *European Respiratory Journal*, *50*(4). .https://doi.org/10.1183/13993003.00391-2017

Kolde, R., Franzosa, E. A., Rahnavard, G., Hall, A. B., Vlamakis, H., Stevens, C., ... & Huttenhower, C. (2018). Host genetic variation and its microbiome interactions within the Human Microbiome Project. *Genome Medicine*, *10*(1), 1-13.https://doi.org/10.1186/s13073-018-0515-8

Kontomanolis, E. N., Koutras, A., Syllaios, A., Schizas, D., Mastoraki, A., Garmpis, N., ... & Fasoulakis, Z. (2020). Role of oncogenes and tumor-suppressor genes in carcinogenesis: a review. *Anticancer Research*, *40*(11), 6009-6015.https://doi.org/10.21873/anticanres.14622

Kosorok, M. R., & Laber, E. B. (2019). Precision medicine. *Annual Review of Statistics and its Application*, *6*, 263.https://doi.org/10.1146%2Fannurev-statistics-030718-105251

Llovet, J. M., Montal, R., Sia, D., & Finn, R. S. (2018). Molecular therapies and precision medicine for hepatocellular carcinoma. *Nature reviews Clinical Oncology*, *15*(10), 599-616.https://doi.org/10.1038/s41571-018-0073-4

Love-Koh, J., Peel, A., Rejon-Parrilla, J. C., Ennis, K., Lovett, R., Manca, A., ... & Taylor, M. (2018). The future of precision medicine: potential impacts for health technology assessment. *Pharmacoeconomics*, *36*(12), 1439-1451.https://doi.org/10.1007/s40273-018-0686-6

Mahmud, I., Kabir, M., Haque, R., & Garrett, T. J. (2019). Decoding the metabolome and lipidome of child malnutrition by mass spectrometric techniques: present status and future perspectives. *Analytical Chemistry*, *91*(23), 14784-14791.https://doi.org/10.1021/acs.analchem.9b03338

Momenimovahed, Z., & Salehiniya, H. (2019). Epidemiological characteristics of and risk factors for breast cancer in the world. *Breast Cancer: Targets and Therapy*, *11*, 151.https://doi.org/10.2147%2FBCTT.S176070

Mukhopadhyay, S., Vander Heiden, M. G., & McCormick, F. (2021). The metabolic landscape of RAS-driven cancers from biology to therapy. *Nature Cancer*, *2*(3), 271-283.https://doi.org/10.1038/s43018-021-00184-x

Nalawansha, D. A., & Crews, C. M. (2020). PROTACs: an emerging therapeutic modality in precision medicine. *Cell Chemical Biology*, *27*(8), 998-1014.https://doi.org/10.1016/j.chembiol.2020.07.020

Ozturk, K., Dow, M., Carlin, D. E., Bejar, R., & Carter, H. (2018). The emerging potential for network analysis to inform precision cancer medicine. *Journal of Molecular Biology*, *430*(18), 2875-2899.https://doi.org/10.1002/adfm.201806877

Peterson, J. F., Roden, D. M., Orlando, L. A., Ramirez, A. H., Mensah, G. A., & Williams, M. S. (2019). Building evidence and measuring clinical outcomes for genomic medicine. *The Lancet*, *394*(10198), 604-610.https://doi.org/10.1016/S0140-6736(19)31278-4

Petrosino, J. F. (2018). The microbiome in precision medicine: the way forward. *Genome medicine*, *10*(1), 1-4.https://doi.org/10.1186/s13073-018-0525-6

Phillips, C. J. (2020). Precision medicine and its imprecise history.https://hdsr.mitpress.mit.edu/pub/y7r65r4k/release/4

Sakamoto K. M. (2010). Protacs for treatment of cancer. *Pediatric Research*, *67*(5), 505–508. https://doi.org/10.1203/PDR.0b013e3181d35017

Schloss, J. A., Gibbs, R. A., Makhijani, V. B., & Marziali, A. (2020). Cultivating DNA sequencing technology after the human genome project. *Annual review of genomics and human genetics*, *21*, 117-138.https://doi.org/10.1146/annurev-genom-111919-082433

Sherman, R. M., & Salzberg, S. L. (2020). Pan-genomics in the human genome era. *Nature Reviews Genetics*, *21*(4), 243-254.https://doi.org/10.1038/s41576-020-0210-7

Soverini, S., Bassan, R., & Lion, T. (2019). Treatment and monitoring of Philadelphia chromosome-positive leukemia patients: recent advances and remaining challenges. *Journal of Hematology & Oncology*, *12*(1), 1-14.https://doi.org/10.1186/s13045-019-0729-2

World Health Organization.(2022). Cancer. https://www.who.int/health-topics/cancer#tab=tab_1

Wu, S., Zhu, W., Thompson, P., & Hannun, Y. A. (2018). Evaluating intrinsic and non-intrinsic cancer risk factors. *Nature Communications*, *9*(1), 1-12.https://doi.org/10.1038/s41467-018-05467-z

Yu, Y., Wang, Y., Xia, Z., Zhang, X., Jin, K., Yang, J., ... & Shi, L. (2019). PreMedKB: an integrated precision medicine knowledgebase for interpreting relationships between diseases, genes, variants and drugs. *Nucleic Acids Research*, *47*(D1), D1090-D1101.https://doi.org/10.1093/nar/gky1042

Zakiryanova, G. K., Wheeler, S., & Shurin, M. R. (2018). Oncogenes in immune cells as potential therapeutic targets. *ImmunoTargets and therapy*, *7*, 21.https://doi.org/10.2147%2FITT.S150586

Zhang, L., & Yu, D. (2019). Exosomes in cancer development, metastasis, and immunity. *Biochimica et Biophysica Acta (BBA)-Reviews on Cancer*, *1871*(2), 455-468.https://doi.org/10.1016/j.bbcan.2019.04.004

Zhao, L., Liu, Y., Chang, R., Xing, R., & Yan, X. (2019). Supramolecular photothermal nanomaterials as an emerging paradigm toward precision cancer therapy. *Advanced Functional Materials*, *29*(4), 1806877.https://doi.org/10.1002/gcc.22987