Cancer Precision: An Overview

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ABSTRACT

Cancer precision, universally talked as personalized healthcare is the methodology to health care on the specific individual basis. The leading benefit of cancer precision can be reflected as the more specific and target therapy. Whenever there is a mention of cancer precision it narrates with reviewing the initiation, advancement and genetics/heredities of an individual’s cancer in order to design a therapy which is chiefly related to the evidences. In other words, it can be compared to as simple as blood group matching, for blood transfusion the matched blood group is used and in the same way the therapy is matched to patient’s individual condition rather cancer subtype. The review article deals with different aspects and approaches of cancer precision treatments along with a brief explanation regarding study driver mutations and role of genomics and how a few personalized medications applications of the precision treatment based on individual gene difference.

Keywords: Cancer precision, Personalized healthcare, Driver mutations, Personalized medication

INTRODUCTION

Cancer precision commonly addressed as tailored healthcare is the approach to health care on the individual basis. And when mentioned as cancer precision it relates with studying the induction, progression and genetics of individual’s cancer in order to design therapy related to the evidences. It is as simple as blood group matching, for blood transfusion the matched blood group is used and in the same way the therapy is matched to patient’s individual condition rather cancer subtype. The main advantage of cancer precision can be considered as the more specific and target therapy. The precision medicine uses multiple type of data to classify patients into the precise groups and use the treatments approaches that they will benefit from [1]. And the process for complying starts with the genome sequencing of the tumour and finding out about the driver and the passenger mutations [2]. Once we have this we can use many strategies for precision medicine like finding out the potent target for drug, by designing a genomic therapies, by evaluating the response of the individual patients and finding out the responsive factors [3,4]. Breast cancer served as the basis of the precision medicine in context to hormone replacement [5]. It is very promising technique although it also faces the challenge of effective integration of genomic technology into clinical oncology [6], but new study platforms are being designed to make things clear and easy for the more effective designing [7].

Study of driver mutations and role of genomics

Cancer is a result of accumulation of mutations and other heritable changes in susceptible cells [8]. Driver mutations are those that confer a selective growth advantage to the cell while passenger mutations are those which do not alter the net replication rate of the cell but occurred in a cell that coincidentally or subsequently acquired a driver mutation.

So every cell that has driver mutation, passenger mutation will be there. As these passenger mutations have got nothing to with the net replication rate of the cell, they don’t play any role in the tumor growth rate [9]. Driver mutations play a vital role in tumorigenesis, these mutations can be targeted in order to increase the increase the sensitivity of the cells or the inactivation of these can also help and while we argue on the origin of the cancer, these driver mutations play a vital role for the treatment so these molecular basis can be used to classify and characterize the cancer [10].

In order to use these driver mutations as target for the treatment purpose, we use tumor profiling to identify them [11]. Apart from acting as a guide for the precision medicine these driver mutations show us the mutational patterns helping us to detect the known and novel DNA damage as well as repair process [12]. Analysing these mutations is not very difficult as we have computational tools that can predict these driver genes on the basis of population scale genomic data [13].

In the process of transformation the evolution and natural selection of clones take place which is called natural clonal evolution and the factors responsible for it are linked to the instability driven by or initiated by the driver mutations and it is also possible to have treatment on the basis of these evolutions and they can also be precision therapies by evaluating certain responses [14]. Mutation in IDH1 gene is found to be driver gene mutation in most of low grade gliomas and it has been used as target for treatment as well as diagnostic assay [15]. For non-small cell lung
cancer, inhibitors for tyrosine kinase targeting one of the most common driver mutation which epidermal growth factor mutation have been developed [16,17].

Obtaining the gene expression profiles by screening the large population of tumor samples can help a lot in stratifying to classify and design the therapy by inducing the genes into various models and understand the progression of that particular subtype and exploit the vulnerable checkpoints to design the targeted therapy. Omics data gives the specified information about the patients which in certain cases are very unique to the individual [18]. With the help of this information many opportunities can be created by linking the genome transition and interaction of the biological systems and cycles with the drug or the designed therapy which can provide us the complete picture rather than just the pieces of puzzle. And with the complete catalogue of mutation in sight we can find out the exact target.

**Personalized medication application based in individual gene difference**

Trastuzumab medication and HER2+ breast cancer treatment

Trastuzumab is a very well-known popular medicine for certain breast cancers. Trastuzumab, to be exact is a monoclonal antibody which is specifically designed to target Human Epidermal Growth Factor Receptor-2 (HER-2) receptor. This drug is implied in the treatment only if the patient displays an over expression of HER2/neu receptor. Essentially, certain tissue typing test are carried along initially, in order to screen the patients before confirming them the above stated medication. These tissue tests Include Immunohistochemistry (IHC) and Fluorescence *In Situ* Hybridization (FISH). With the help of these tests, Her2+ patients are identified and thus are placed on trastuzumab drug therapy [19,20].

Melanoma and individual gene differentiation

High-throughput sequencing technologies have been of great efficacy in detecting genetic alterations marking their presence in melanoma genesis. BRAF mutations in melanoma are related with younger patient age and with its prime location on trunk and lower extremities. However, BRAF mutations were found to be poor projecting markers in patients identified at stage III or IV. Researchers have also shown shoddiest prognosis for NRAS-mutant tumors at stage III or IV.

Similarly, the presence of KIT aberrations was shown to be associated with reduced overall existence in a large study of Asian patients. Congruently, another study initiates KIT-mutant stage IV melanomas to have an inferior prognosis than comparable KIT wild-type tumors. All this observation concludes that melanoma is very much susceptible to genetic differentiation.

Therefore, before placing the patients on a treatment, individual gene differenting tests are carried on them to identify the possible mutation and over-expression. For example, Trametinib is a MEK inhibitor (FDA approved in May 2013). It is indicated for unresectable or metastatic melanoma with BRAF V600E or V600K mutations, which is confirmed by the THxID BRAF mutation test [21].

Colon cancer gene differentiation

A rising amount of drugs are now obtainable for the treatment of colon cancer, and a genetic examination can be implied to appraise which drugs may be the preeminent or poorest candidates. For example, about 40% of patients with metastatic colon cancer are questionable to respond to cetuximab and panitumumab as their tumors have a mutated form of the KRAS gene. Recent practice strategies commend that only patient with the normal (wild-type) form of the KRAS gene must be treated with these drugs in combination with chemotherapy [22].

Cytochrome P450 enzymes, drug toxicity and individual gene differenting

Rendering to numerous researcher’s observations, around 5.3% of all infirmary admissions are linked with Adverse Drug Reactions (ADRs). Several ADRs are the outcome of differentiations in genes that encrypt for drug-metabolizing enzymes. One of the chief examples are cytochrome P450. These variations lead drugs to be metabolized either at a higher or a lower rate than normal. Consequently, some patients have problems disabling a drug and removing it from their bodies, which results into “overdose toxicity,” whereas others remove the drug too quickly beforehand the medication had a fortuitous to work. If these genetic differences are not carefully identified while treating, the results of the therapy may range from unpleasant to lethal. In order to avoid such consequences, certain tests that can perceive variations in CYP450 genes are carried along [23,24].

For example, warfarin treatment used to prevent blood clots is intricate by genetic dissimilarities in a drug-metabolizing enzyme (CYP2C9) and an enzyme that triggers vitamin K (VKORC1). Appropriate dose is characteristically accustomed for the individual patient by multiple sequences of trial-and-error, throughout which the patient is susceptible to risk of unwarranted hemorrhage or additional blood clots. The Food and Drug Administration (FDA) now acclaims genotyping for all patients prior to warfarin management, which permits for more exact dosing. Though the datasets are still being calculated, there is a clear evidence that this helps patients avoid serious and possibly fatal adverse effects [25].

**Approaches towards cancer precision**

Use of molecular diagnostics on the basis of predictive biomarkers is in clinical practice for personalized oncotherapy or in other words for cancer precision and these markers serve as a link to the target [26]. Finding out the novel biomarkers from different sources can also play as a strong base for the new diagnostic molecules as well as the precision design, biomarkers were isolated from the serological biopsy samples for the gastric cancer and these can be used to find out the individual’s risk of developing GC, this somehow is the other side of precision medicine which can be termed as precision prevention [27]. Some targeted therapies can also be personalized as precision medicine on the basis of the same expression level of mutation. As the mutation in the enhancers, promoters and insulators can be the hallmark of the level and the further phenotype [28]. High EREG-expression is taken as a biomarker of the cells, in order to be targeted by 9E5-conjugated PCNP [29] and this strategy can be personalised in the near future according to the mutation, type of mutation and level of mutation rather hierarchy of mutation.

Also the use of gene profile rather expression profiles has been used for the optimization of the chemotherapy for breast cancer using different sets of regimens to observe the improvement in the response by personalised cancer therapy [30]. ER is the major driver in ER+ breast cancer, that is why it is targeted for many types of therapies [31]. It has seen reported that thromboxane A2 pathway is essential for cancer progression and anchorage independent growth and invasion capabilities in breast cancer and switching off the biosynthesis of this thromboxane A2 subsequently turns off other molecules responsible for the cancer progression [32].

Comparison of genome profile of the normal cell and cancer cell takes us directly to the target, likewise the expression of Neural Cell Adhesion Molecule (NCAM) on tumor epithelial cells is a biomarker as the expression is not observed in the normal cells. NCAM targeted polymer drug
Conjugate serves the target molecule for the one characterized by its expression as well as the tumor cells that have the higher expression of this molecule [33]. Patient-Derived Xenografts (PDX) is a crucial platform to elucidate the new treatments as well as the biomarkers and with help of PDX on the basis of heterogeneity, the drug response pattern can be understood in presence of other interfering factors [34].

TGAs and AGCR have been able to classify the gastric cancer of the basis of molecular platforms; they have also been able to develop PDX models which in turn help to understand the histology as well and the genetic features of the patient [35]. mRNA by regulating various pathways play a significant role in the tumor development and progression. mRNA replacement therapy is one more strategy which can be used after having the genomic data of the tumor but it faces a challenge of having a successful delivery system. But with the development of nonvaccine this approach can be used [36,37].

Also by inducing the forced expression of some microRNA cancer cells can be targeted, in gastric cancer by inducing the expression of miR-491-5p it was possible to inhibit proliferation, colony formation and induce apoptosis in gastric cancer cells. miR-491-5p was able to act anti-oncogene by targeting Wnt3a/β-catenin signalling pathway [38]. One more interesting approach toward cancer precision medicine is use of combination of imaging with the theranostic nanoparticles, it was observed that miRNA/F-PNDs can be a potential theranostic platform for synchronous tumor imaging and miRNA-based modulation therapy against cancer [39].

CONCLUSION

Considering the aspects and prospects of precision medicine and treatment, it can be said that cancer treatments in near future will be significantly benefitted by the same. Moreover, personalized medicinal approach towards cancer treatment based on the gene difference might open up a completely new field of research and treatments. Although there are certain constraints and obstacles in the current phase for cancer precision, the vision of effective integration of precision treatment along with the personalized medication and genomic technology gets prominent with every novel step in the field of research. Form the most common cancer to the rarest of them, precision treatment and medication advancement would be extremely beneficial towards the patients with lowered rates of adverse effects and less contraindications. Although, the cancer precision treatments have a long way to go, it can be said that a constructive, precision method can be related as a very progressive and beneficial stepforward in highly improved diagnosis and patient treatments.

REFERENCES

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