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Editorial

Journey through Memory Lane and Trends in Neoantigens for Cancer Immunotherapy

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Cancer is a source of worry in some countries of the world, despite its having a global distribution in occurrence. The human immune system is critical in helping against infections and associated diseases of which includes cancer. Cancer shows more pronounced pathogenesis or progress of effects of the disease when the immune system which does surveillance of the body components cannot recognize these abnormal cells (cancer cells), or the body sees these abnormal cells as "self" and fails to attack them, or when the surveillance of the immune system has been degraded in strength such as by mutations occurring in the tumour cells that creates mutated antigens.

Creating added problems to the body's immune system during immune response is the release of metabolites into the body by tumour cells during angiogenesis and metastasis [1], as these released metabolites often block the functioning and performance of the immune system surveillance and responses. This selectively suppresses the immune system [2] and is most pronounced around tumour tissue(s) micro-environment. This explains the failure or non-optimal effectiveness of immunotherapeutic approach in some cancer patients.

Cancer neoantigens (Tumor specific antigens TSAs) are cancer specific abnormal proteins generated as direct outcome of non-synchronous somatic mutations on the surface of individual cancer cells.-They can activate the body's immune system to prepare the Tumor associated antigens (TAAs) based vaccines. Tumor associated antigens (TAAs) and cancer germline antigens (CGAs) are usually expressed on tumour cell surface - on healthy or immune tissues at low levels. The third type of tumour antigens is called tumor specific antigens (TSAs)-neoantigens. Tumour neoantigens have stepped into the options of tumour immunotherapeutic techniques. These neoantigens include antigens produced by mutant proteins that are abundantly expressed only ion tumour cells have strong immunogenicity and tumour heterogeneity [2].

There are several types of cancer treatment for patients depending on the type of cancer and how advanced it is (National Cancer Institute NCI, United States, 2022a). Single type treatment (immunotherapy) or in most cases the use of combination therapy are chosen to treat each patients. Typical types of treatment include chemotherapy, radiation, surgery, hormone therapy, hyperthermia (by using heat on the body to help kill particularly pre-cancers), immunotherapy (that prods the immune system to attack cancer cells and its shed toxic metabolites, photodynamic therapy (using light activated drugs), stem cell transplant to restore damaged baseline body stem cells ferried into blood system) and surgery [3]. Screening tests help select treatment plan and course for the patient.

Use of combined therapy for cancer was first introduced in the mid 1960s with a team Emil Frei., *et al*. playing a pivot role by applying combinatorial therapy with success in cases of acute leukemia based cancer in children [4]. Combination or combinatorial therapy gives room to create different avenues to combat the deranged cells and often help kill more cancer cells compared to single treatment option

plan. Basically, this technique probes into creating anti-cancer generated activities on different pathways in the body to create a strong anti-cancer flux in the body and more options are coming up for synergized clinical use to administer combinatorial treatment options. Coupled to it is the enlarged pool of options upon which systemic tests can be carried out against different types of cancer cells, and stages of cancer (pre-cancerous and cancerous stages) to determine most effective combinatorial options to treat cancer. New neoantigens are being discovered and this is supporting combinatorial approach to cancer treatment.

The molecular tools of genomics-including high throughput omics, metagenomics, proteomics, and microfluidics among others have been useful in the discovery of new targets for clinical oncology therapeutics applications against cancer, flowing from design pipelines to detect new molecules, and translation onto bedside for clinical tests for effectiveness, immunogenicities, pharmacokinetics of such molecular designs, and adverse reactions to ascertain if they truly qualify to enter pool combinatorial therapy. Frontier molecular tools of gene and protein/amino acid sequencing technology, industrial biotechnology, bioinformatics and its wonder algorithms, metabolomics have helped prop-up discoveries of new neoantigens and avenues for use as targets to develop cancer immunotherapy for those eliciting high levels of immunogenicity during bedside clinical tests to evaluate such neoantigen based cancer therapeutic vaccines development.

The entry justification of neoantigens for cancer therapy, some patients who do not respond to checkpoint inhibitors administered alone, they can now be tailored towards personalized vaccines treatment [5-7]. In addition, neoantigens have been found to induce immune responses with high specificity to cancer cells because of their underlying mutations, whilst exerting minimal toxicity to non-cancerous cells [8].

Neoantigens can be classified into two categories which are, Shared neoantigens (mutated cancerous cell antigens that are common across different cancer patients and not present in normal genome of the body, for which those with high immunogenicity can be screened for selection to be used to develop cancer vaccines for patients with the same mutated gene [9] and Personalized neoantigens (mutated antigens that are unique to particular neoantigens and completely different across different patients and are screened to be selected for use in personalized vaccine therapy) [6,8].

Attributes of different types, quantities of neoantigens in different individuals of same type of tumour caused by specificity of mutations to create heterogeneity has an inclination for use of selected neoantigens in each of these patients for personalized therapeutic clinical health management.

Historically, in the early twentieth century, many findings revealed that the immune system can recognize and eliminate tumor cells, but the type of non-self molecules that can offer this patterned immune challenge against tumor cells was not definitive at this period, until the first of such non-self bio-molecules was found to be recognized by T-cells in 1998 [7,10-12]. This is reminiscent to a struck antigenic mutant bio-molecular mine for immunotherapy.

The mutant gene has to be at a level that is quantitatively enough, and must be specific in characterization as part of requirements to be featured as a neoantigen. Invariably, De Plaen., *et al*. [13] played a critical role in discovery of this neoantigen.

Conceptually, two typical clever insights and observations in neoantigen based immunotherapy that is cascading and propelling cancer immunotherapy have been that: neoantigens molecules in the blood or other body tissues (such as blood leucocyte antigen neoantigens) are not affected by thymus selection or central tolerance while the accompanying T-cells exhibit high avidity [14]. Secondly is the discovery that tumour cells metabolically generate mutant proteins such as neoantigens that have been found to be recognized by the immune system as antigenic molecules which elicit typical mainstream immune characteristic of prodding both cellular and humoral arms of the body's immunity, particularly downstream.

But how are tumour neoantigens generated? They can mainly be in form of tumour specific antigens (TSA), generated by non-synchronous mutations in tumour cells, can be produced by viral infection and can develop alternative splicing and gene rearrangements [2].

Challenges in neoantigens for immunotherapy includes determination of the precise nature of inoculation, method of identification and detection of neoantigens, sequencing to identify mutant antigens and abnormal proteins, prediction of promising mutants, maximizing use of mass spectrometry-based immunoproteomics, proteogenomics, *in-vivo* and *in-vitro* immunological analysis to cross-check and validate neoantigens, adequate levels of immunogenicity and development and selection of suitable carriers to be used to convey neoantigen based treatment to reach target sites in the body (typical delivering carriers are liposome nanocarriers. Typically developed means of identification of neoantigens include: detecting neoantigens from biopsies obtained from tumor and normal cells [1,15].

Techniques are been developed to tackle challenges, such as use of DNA to deliver multiple neopeptide epitopes incorporating cytokines as adjuvant, which hindered tumor growth [14].

As an emerging clinical tool against cancer in translational features, neoantigens in cancer biology and clinical applications include roles found for neoantigen molecules in developing new predictive biomarkers (tumour markers) and synergistic combinatorial therapy [8], with some levels of successes [2].

Typical approaches to creating tumour immunotherapy against diverse types of cancer include tumour vaccines (there are now neoantigen peptides candidates on clinical trials), immune enhancement therapy, immune checkpoint blockade therapy, and adoptive cell therapy (ACT) in which T-cells are given to a patient to counter a disease [3].

Typical approved immune checkpoint blockers targeting PD-1/PD-Ligand (L)1 signaling pathway now exist for clinical oncology treatment of cancer approved in the United States. The success of immune checkpoint blockade targeting CTLA-4, PD-1 and PDL1 has sparked a breakthrough in cancer therapy through technique of tumor immunotherapy [1,2,8].

Several tumour neoantigen based vaccines are on different stages of clinical trials for various solid tumours [2], products mostly from these Europe, North America, Asia and Australia major axes of tumour immunotherapy research.

What are the clinical manifestations that indicate positive effects of combinatorial neoantigen based therapy? (1) Increased strength of killing effect on tumour. (2) Increased durability of anti-tumor experience. (3) Improved state of health and quality of life of patient. (4) Reduced burden of cancer on patients in area of morbidity. (5) Reduced chances of eventual mortality of patient.

How is individualized neoantigen therapy used? (1) It can be used alone. (2) It can be used in combinatorial treatment with other therapies.

Invariably, cancer immunotherapy, alongside metabolomics, microfluidics, bioinformatics wonder algorithms, synthetic biology based protein and gene bioengineering have become hotspots in scientific research, and the emergence of more scientific bioinformatics driven, wet lab driven and clinical data driven data, are assisting to develop new neoantigens for diverse types of cancer immunotherapeutic approaches. Synthetic biology tools will help shape future trends, developing and improving efficacy of new neoantigens for cancer immunotherapy. This will likely include biosynthetically neoantigenic peptide molecules with improved functionalities for priming and strengthening the immune system to improve killing qualities against cancerous cells. In this editorial, I took journey through: introduction to cancer, cancer neoantigens and types of cancer treatment, justification of neoantigens for cancer therapy, historical features, conceptual features, challenges, translational features, and a round-off of this editorial report.

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Bibliography

1. Ozurumba-Dwight LN., *et al*. "Neoantigens based molecules as clinical tools for cancer immunotherapy: conception and translational attributes". *Journal of Medical and Dental Science* 9.2 (2022): 46-50.
2. Zhang ZM., *et al*. "Neoantigens: A breakthrough in Tumour immunotherapy". *Frontiers in Immunology* (2021).
3. Pucci C., *et al*. "Innovative approaches for cancer treatment: current perspectives and new challenges". *Ecancer Medical Science* 13 (2019): 961.
4. Frei E., *et al*. "The effectiveness of combinations of anti-leukemic agents in inducing and maintaining remission in children with acute leukemia". *Clinical Trial Multi-analyte Blood Test* 25.5 (1965): 642-656.
5. Ott PA., *et al*. "A Phase 1b trial of personalized neoantigen therapy plus anti-PD-1 in patients with advanced melanoma, non-small cell lung cancer, or bladder cancer". *Cell* 183 (2020): 347-362.
6. Fang Y., *et al*. "A Pan-cancer clinical study of personalized neoantigen vaccine monotherapy in treating patients with various types of advanced solid tumours". *Clinical Cancer Research* 26 (2020): 4511-4520.
7. Ozurumba LN., *et al*. "Artemisia annua (Qing Hao): Solved and Adaptively Met the Drug Resistance Challenge by Plasmodium Malaria Parasite. It's other Chemotherapeutic attempt against Cancer; and Overall Implications on Public Health". *Greener Journal of Biomedical and Health Sciences* 2.1 (2016): 001-011.
8. Fang X., *et al*. "Neoantigens and their potential applications in tumour immunotherapy". *Oncology Letters* (2022).
9. Zhao W., *et al*. "Shared neoantigens: ideal targets for off-the-shelf cancer immunotherapy". *Pharmacogenomics* 21 (2020): 637-645.
10. Oiseth S and Aziz M. "Cancer immunotherapy: a brief history, possibilities and challenges ahead". *Journal of Cancer Metastasis and Treatment* (2017).
11. Abbas AK., *et al*. "Properties and Overview of Immune Responses". In: Cellular and Molecular Immunology, 9th edition. Amsterdam: Elsevier (2017): 1-11.
12. Brodin P and Davis MM. "Human immune system variation". *Nature Reviews Immunology* 17 (2017): 21-29.
13. De Plaen E., *et al*. "Immunogenic (tum) variants of mouse tumour P815 cloning of the gene of tum-antigen P91A and identification of the tum- mutation". *Proceedings of the National Academy of Sciences* 87.7 (1988): 2274-2278.
14. Jiang T., *et al*. "Tumour neoantigens from basic research to clinical applications". *Journal of Hematology and Oncology* 12.1 (2019): 93.
15. Stephens AJ., *et al*. "Beyond Just Peptide Antigens: The Complex World of Peptide-Based Cancer Vaccines". *Frontiers in Immunology* 12 (2021): 696791.

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