The OMICAS, Can-IT: Onco-Molecular Immunotherapeutic Constellation Analytics Spectrum in Cancer Immunotherapy.

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According to the International Agency for Research on Cancer (IARC), the number of cancer patients rose to 17.0 million and there are 9.5 million deaths due to cancer worldwide. The immune system is a complex network of defense mechanisms against foreign bodies and also terminally differentiated cancer cells. The immune system can distinguish foreign bodies and cancer cells from healthy cells except in the tumor microenvironment (TME). Cancer-Immunotherapy (Can-IT) is a biologics-based therapy for the treatment of diseases by modulating the immune system. Can-IT is an excellent synergistic approach along with chemotherapy either with/without radiation. Failure in patient response to Can-IT has been a challenging medical task to date. Although different research groups have evaluated various reasons for the failure of Can-IT, we believe that more accuracy can be achieved by using a multi-omics approach for a deeper investigation and analysis. Thus, we propose an Immunomics-based approach that considers multi-omics for the evaluation of patient's immune system in the context of Can-IT.

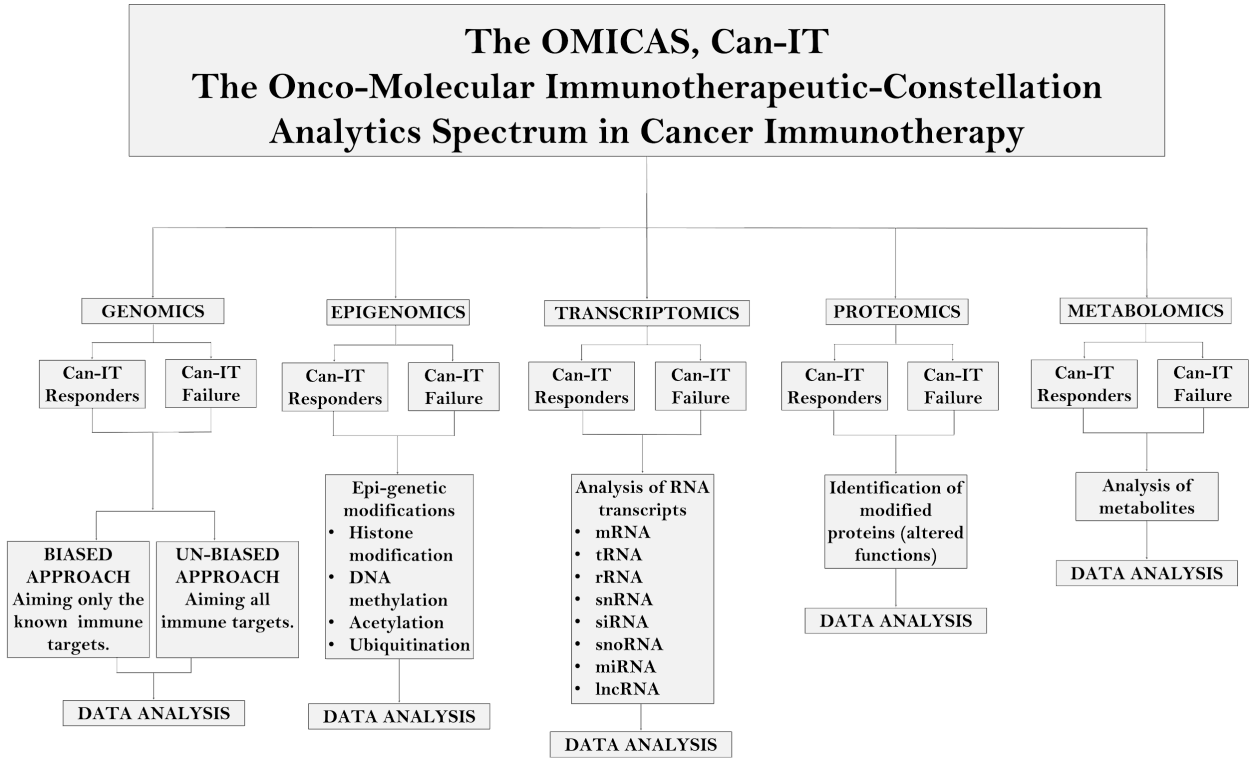

Figure 1. Flowchart of the proposed multiomics (Genomics, Epigenomics, Transcriptomics, Proteomics and Metabolomics) initiative of Can-IT.

The human immune system is a network of biological processes that can identify and destroy foreign bodies and cancerous cells. Cancer Immunotherapy (Can-IT) uses the patient's immune system to fight cancer. Checkpoint inhibitors, Chimeric antigen receptors T-cell therapy (CAR T-cell therapy), Cancer vaccines, Monoclonal antibodies, and Oncolytic virus are different types of Can-ITs (1). Some specific types of immune cells are utilized to boost the patient's immune cells that have the potential to fight the cancer cells and it is observed that only 15-20% of the cancer patients respond to the treatment (2). Though the efficacy of the immunotherapy is found to be better, only a few sets of patients were found responding to the treatment (3,4). For example, in CAR T-cell therapy, the potential T-cells are cultured *in vitro* and are intravenously transferred into the patient. But this seems to not work for some of the cancer patients. The failure of Can-IT might have several reasons and it is necessary to evaluate this issue using a multiomics approach. The multiomics-based approach gives rise to a huge amount of data that opens doors to many research aspects of cancer biology and the immune system that provides a higher level of understanding with deeper insights into the problem. A multiomics-based approach involves Genomics, Epigenomics, Transcriptomics, Proteomics and Metabolomics. Each level of the multiomics generates data that are needed to be evaluated and involves a broad view of each aspect.

To understand the modifications and changes that occur in the tumor microenvironment it is also necessary to analyze the immune cells and their interactions with healthy cells as a control experiment. This part of the investigation involves both biased and unbiased approaches at each stage of the multiomics (Figure 1). The biased approach is to aim at the known immune targets while the unbiased approach is to aim at all the immune targets. Genomics is to investigate the failure of Can-IT at the genomic level and epigenomics involves epigenetic modifications like DNA methylation, acetylation, ubiquitination, and histone modifications. Transcriptomics, proteomics, and metabolomics are the broad view of the analysis of RNA transcripts, the target of the possible neoantigens, and their modified proteins that are leading to altered functions in the patient's body and the metabolites respectively. The data obtained helps us not only to analyze the mutations that help the cancer cells escape the immune system but also the mutations that lead to altered functions of the mutant proteins.

Currently, we are in the process of collecting and analyzing patient samples for the multiomics study proposed above. Among the samples collected, we have been categorizing them based on gender, age, type of cancer, etc. The data obtained from the *in vitro* and *in vivo* studies will be published in the future issues of TCABSE-J.

References

1. https://www.cancer.org/treatment/treatments-and-side-effects/treatment-types/immunotherapy/what-is-immunotherapy.html.
2. https://www.cancer.org/research/cancer-facts-statistics/global.html
3. Manpreet Sambi, Leila Bagheri, Myron R. Szewczuk, "Current Challenges in Cancer Immunotherapy: Multimodal Approaches to Improve Efficacy and Patient Response Rates", Journal of Oncology, vol. 2019, Article ID 4508794, 12 pages, 2019. https://doi.org/10.1155/2019/4508794
4. Drew Pardoll, Cancer and the Immune System: Basic Concepts and Targets for Intervention, Seminars in Oncology, Volume 42, Issue 4, 2015, (523-538), ISSN 0093-7754,https://doi.org/10.1053/j.seminoncol.2015.05.003.(https://www.sciencedirect.com/science/article/pii/S0093775415001013).

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