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Editorial

Harnessing the Power of the Immune System: Future of Immunotherapy in Gastrointestinal Cancers

Rajesh Gacche*

Department of Biotechnology, Savitribai Phule Pune University, Pune, MS, India

***Corresponding Author:** Rajesh Gacche, Department of Biotechnology, Tumour Biology Laboratory, Savitribai Phule Pune University, Pune, MS, India.

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Engineering immune system: New vision for gastrointestinal cancers

Gastrointestinal (GI) cancers, including colorectal, gastric, and hepatocellular carcinomas, are a significant global health burden along with progressive financial toxicity. In the current state-of-the, certain types of GI tract and digestive system cancers, such as pancreatic and liver cancers have demonstrated more aggressive phenotype and poor prognosis. The aggressive nature of these cancers is one of the limiting factors in achieving successful treatment outcomes and improved prognosis. Another important factor which limits the conventional therapy is the evolving drug resistance [1]. Nevertheless, the current therapeutic regime for GI tract and digestive system cancers is associated with significant side effects, such as nausea, vomiting, diarrhoea, fatigue, weight loss, hair loss, and immune system suppression. These side effects adversely affect the patient's quality of life and may require supportive care. Of note, the other risk factors such as smoking, excessive alcohol consumption, obesity, poor diet, chronic inflammation, certain infections (e.g. *Helicobacter pylori*), and genetic predisposition contribute towards disease progression and complicate the treatment [2].

Traditional treatment approaches like surgery, chemotherapy, and radiation therapy, have improved outcomes and disease prognosis of few patients; however, the prognosis for majority of patients remains suboptimal especially the metastatic cancer patients. The immune system is a complex network and repertoire of cells, organs, and molecules that work in coordinated fashion to defend against harmful pathogens and abnormal cells, including cancer. Cancer cells can evade immune surveillance through various mechanisms, enabling them to proliferate and spread. Immunotherapy aims to restore and enhance the immune system's ability to recognize and eliminate cancer cells, offering a novel therapeutic strategy for GI cancers. In recent years, immunotherapy has emerged as a ground-breaking and game changing approach in the mainstream of cancer treatment. The pioneering research of James Allison, and Tasuku Honjo who awarded Nobel prize in 2018 have unravelled the molecular mechanisms which blocks the key proteins and activate the immune system against cancer cells. Especially unravelling the role of PD-1 (programmed cell death protein-1), PD-L1 (PD-1 ligand), and CTLA-4 (cytotoxic T-lymphocyte-associated protein 4) in creating immunosuppressive niche [Altmann, 2018] inspired the scientific community to target these proteins and develop immune check point inhibitors [3]. The independent work of these two Nobel Laureates has created a foundation for entirely new therapeutic paradigm to fight against cancer and many other human ailments. In the present state-of-the-art, besides surgery, chemotherapy, and radiation, cancer immunotherapy is represented as a new pillar and game-changer in cancer therapy. By leveraging the body's immune system to recognize and eliminate cancer cells, immunotherapy has revolutionized the management of various malignancies and other human ailments.

Intervention of immune checkpoint inhibitors

One of the most promising approach of immunotherapy in GI cancers is the use of checkpoint inhibitors. Checkpoint proteins are the molecules involved in regulating the immune cells that regulate immune responses, keep check and arrest excessive activation or autoimmune reactions. Cancer cells explore and perhaps exploit these checkpoints, such as programmed cell death protein 1 (PD-1) and cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4), to evade immune destruction. Checkpoint inhibitors block the interactions between these checkpoints and their ligands, unlocking the immune system to target and destroy cancer cells [4].

Improved prognosis in colorectal cancer (CRC)

Checkpoint inhibitors have shown remarkable success in treating a subset of patients with advanced CRC. Pembrolizumab and nivolumab, PD-1 inhibitors, have demonstrated efficacy in patients with mismatch repair deficiency or high microsatellite instability, which are associated with a greater immune response. These patients often experience durable responses and improved survival rates, leading to the approval of checkpoint inhibitors as a standard therapy for this subgroup [5]. Besides the promising potential of immune check point inhibitors, there are some concerns over the global efficacy of check point inhibitors, for example, immunologically "cold" tumours of CRC, only a limited number of patients are currently getting benefits from check point inhibitors owing to individual differences and low response rates [6]. The future research should focus more on such issues for increasing the therapeutic index of check point inhibitors.

Gastric cancer: Progressive complexities leading to difficulties in treatment

Treatment options for gastric cancer depend on the stage of the disease and can include surgery, chemotherapy, radiation therapy, targeted therapies, and immunotherapy. However, the effectiveness of these treatments varies based on the stage, location, and characteristics of the tumor. Some gastric cancers may be resistant to available treatments, limiting treatment options and leading to poorer outcomes. Gastric cancer treatments, particularly chemotherapy, can cause significant side effects. These side effects may include nausea, vomiting, hair loss, fatigue, decreased appetite, and compromised immune function. Additionally, patients with advanced disease may have reduced tolerance to treatments due to overall poor health and nutritional status [7]. Besides aforesaid problems, Gastric cancer tends to recur or metastasize even after successful initial treatment. The cancer cells may spread to distant organs, making it challenging to achieve long-term remission or cure. Ongoing monitoring and surveillance are necessary to detect recurrence or metastasis early and provide appropriate treatment [8]. Gastric cancer has traditionally been challenging to treat, with limited options for advanced-stage disease. Immunotherapy has shown promise in this setting, particularly in patients with programmed death-ligand 1 (PD-L1) overexpression. The addition of checkpoint inhibitors, such as pembrolizumab and nivolumab, to standard chemotherapy regimens has demonstrated improved overall survival and progression-free survival rates, providing new hope for patients with advanced gastric cancer [9,10].

Hepatocellular carcinoma (HCC): "An ounce of prevention is worth a pound of cure"

This proverb clearly emphasizes the importance of prevention and early detection. Hepatocellular Carcinoma is closely associated with risk factors such as chronic liver diseases, including hepatitis B or C infections, excessive alcohol consumption, obesity, and exposure to certain toxins. Taking preventive measures and managing these risk factors can significantly reduce the chances of developing HCC. HCC is the most common primary liver cancer, and its treatment options have been limited [11]. Immunotherapy has emerged as a transformative approach for HCC, particularly in patients who have progressed on sorafenib, the standard first-line therapy. Immune checkpoint inhibitors, such as nivolumab and pembrolizumab, have shown efficacy in advanced HCC, leading to improved overall survival and offering a new treatment avenue for patients with limited options [12]. In summary, while checkpoint inhibitors have shown promising results in gastrointestinal cancers, not all patients respond to monotherapy. Combination approaches, such as combining checkpoint inhibitors with other immunotherapeutic agents, targeted therapies, or chemotherapy, are being explored to enhance treatment efficacy. Additionally, efforts are underway to identify predictive biomarkers that can help identify the most likely benefits of immunotherapy. Undoubtedly, immunotherapy has revolutionized the treatment landscape for gastrointestinal cancers, offering new hope for patients with

limited therapeutic options. The use of checkpoint inhibitors has shown remarkable efficacy in subsets of patients with colorectal, gastric, and hepatocellular carcinomas, leading to improved survival rates and durable responses. Ongoing research, including the exploration of combination therapies and the identification of predictive biomarkers, holds promise for further advancements in this field. Immunotherapy represents a paradigm shift in cancer treatment, harnessing the power of the immune system to combat gastrointestinal cancers and potentially transform patient care in the future, however the emerging drug resistance, side effects and its benefits to fewer number of cancer patients, warrants further research in the mainstream of GI cancer treatment.

Bibliography

1. Huang WJ., *et al*. "Multidrug Resistance of Gastric Cancer: The Mechanisms and Chinese Medicine Reversal Agents". *Cancer Management and Research* 2.12 (2020): 12385-12394.
2. Huang J., *et al*. "Updated epidemiology of gastrointestinal cancers in East Asia". *Nature Reviews Gastroenterology and Hepatology* 20.5 (2023): 271-287.
3. Basudan AM. "The Role of Immune Checkpoint Inhibitors in Cancer Therapy?" *Clinics and Practice* 13 (2023): 22-40.
4. Petricevic B., *et al*. "Neoadjuvant immunotherapy in gastrointestinal cancers - The new standard of care?" *Seminars in Cancer Biology* 86.2 (2022): 834-850.
5. Al Zein M., *et al*. "Immunotherapy and immunoevasion of colorectal cancer". *Drug Discovery Today* 14 (2023): 103669.
6. Liu JL., *et al*. "Cold" colorectal cancer faces a bottleneck in immunotherapy". *World Journal of Gastrointestinal Oncology* 15.2 (2023): 240-250.
7. Alsina M., *et al*. "Current developments in gastric cancer: from molecular profiling to treatment strategy". *Nature Reviews Gastroenterology and Hepatology* 20.3 (2023): 155-170.
8. Jiang H., *et al*. "Revealing the transcriptional heterogeneity of organ-specific metastasis in human gastric cancer using single-cell RNA Sequencing". *Clinical and Translational Medicine* 12.2 (2022): e730.
9. Xu X., *et al*. "Immunology and immunotherapy in gastric cancer". *Clinical and Experimental Medicine* (2023).
10. Narita Y and Muro K. "Updated Immunotherapy for Gastric Cancer". *Journal of Clinical Medicine* 12.7 (2023): 2636.
11. Ganesan P and Kulik LM. "Hepatocellular Carcinoma: New Developments". *Clinics in Liver Disease* 27.1 (2023): 85-102.
12. Sangro B., *et al*. "Advances in immunotherapy for hepatocellular carcinoma". *Nature Reviews Gastroenterology and Hepatology* 18.8 (2021): 525-543.

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