The Future Perspective of Combination of Artificial Intelligence, Oncolytic

Virotherapy, and Immunotherapy against Gastric Cancer

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4 Piruz Shadbash*1,2

- 5 1. Basic and Molecular Epidemiology of Gastrointestinal Disorders Research Center, Research Institute for
- 6 Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran
- 7 2. Department of Microbiology and Microbial Biotechnology, Faculty of Life Sciences and Biotechnology,
- 8 Shahid Beheshti University, Tehran, Iran.

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*Corresponding author: Piruz Shadbash

- 11 E-mail: shadbashpiruz@gmail.com
- 12 Tel. (+98) 9366522792

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- 15 Dear Editor,
- Gastric cancer (GC) is one of the leading causes of cancer deaths worldwide, especially in East
- 17 Asia. Despite recent advances in diagnosis and therapy, the prognosis for advanced GC is poor due
- 18 to late diagnosis, tumor heterogeneity, and immune evasion mechanisms. Therefore, there is an
- 19 urgent need for innovative and synergistic approaches to improve treatment outcomes. The
- 20 integration of artificial intelligence (AI), oncolytic virotherapy (OV), and immunotherapy has
- 21 transformative potential in this context.
- 22 Artificial intelligence has revolutionized cancer care through its ability to process large-scale
- datasets and identify patterns beyond human ability. AI algorithms have shown significant
- 24 performance in detecting early-stage GC from endoscopic and histopathological images with high
- accuracy, which helps in timely diagnosis and risk stratification (1). Additionally, machine learning
- 26 models are being increasingly used to forecast patient response to immunotherapies and to optimize
- 27 therapy planning (2).
- 28 Oncolytic viruses selectively replicate in tumor cells, causing direct oncolysis and increasing anti-
- 29 tumor immune responses. In GC models, engineered viruses like adenovirus, reovirus, and herpes
- 30 simplex virus have demonstrated promising preclinical efficacy (3). OV-induced immunogenic cell
- death can convert "cold" tumors into "hot" tumors, thereby enhancing the responsiveness to
- immune checkpoint inhibitors (ICIs) (4).

- Immunotherapy, especially ICIs targeting PD-1/PD-L1 and CTLA-4, has demonstrated modest
- success in GC, with only a subset of patients responding favorably. Combining OV with ICIs has
- 35 emerged as a rational approach to overcome resistance and increase efficacy. Clinical trials
- investigating this synergy are currently underway and may redefine treatment paradigms (5).
- 37 The integration of AI can further strengthen this combination. AI-based analysis of tumor genomics
- and immune landscapes can guide the selection of optimal oncolytic vectors and immunotherapy
- 39 regimens. Predictive modeling may also detect biomarkers for response, enabling real-time
- 40 adaptation of treatment (6).
- In conclusion, the convergence of AI, oncolytic virotherapy, and immunotherapy provides a
- 42 multifaceted and personalized strategy against gastric cancer. Collaborative translational research
- and clinical validation are crucial to harness the full potential of this triad. We support accelerating
- 44 interdisciplinary efforts and the establishing of AI-based clinical trials to pave the way for precision
- 45 oncology in GC.
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