Correction to: Next-generation immunotherapy for pancreatic ductal adenocarcinoma: navigating pathways of immune resistance

Thatcher Heumann¹ · Nilofer Azad¹

Published online: 19 October 2021

© Springer Science+Business Media, LLC, part of Springer Nature 2021

Correction to: Cancer and Metastasis Reviews
<https://doi.org/10.1007/s10555-021-09981-3>

The original published version of this article contained a mistake in the figure captions. The figure captions captured the title of the figures, but the figure descriptions were not included. Below are the correct figure captions:

Fig. 1 Adaptive Immune Response in Cancer. Immunotherapy relies on the ability of host immune cells to recognize cancer as cells that need to be eliminated. For this to happen, a tumor cell needs to alert surveilling antigen presenting cells (APCs), such as dendritic cells (DC), that they are abnormal by expressing antigens on their cell surface. When APCs recognize this abnormal signal, they take up the antigen, traffic to lymph nodes to mature and, in turn, activate cytotoxic and helper T cells with T cell receptors (TCR) specific to that tumor antigen. Once these T cells are activated, they should further differentiate, expand, and migrate to the tumor bed and kill that tumor cell. Adapted from “Antigen Presentation in Cancer”, by BioRender.com (2021). Retrieved from <https://app.biorender.com/biorender-templates>.

Fig. 2 Mechanisms of Immune Resistance in Pancreatic Cancer. Pancreatic cancer (PDAC) has several protections against the generation and execution of an anti-tumor host immune response. A) PDAC’s low antigen burden, sequestration of MHC/HLA-I molecules, and local tolerogenic TME signaling all contribute to poor immune surveillance and stunt normal dendritic cell maturation. Without

normal antigen processing and presentation, anti-tumor effectors are not activated. B) If activation and clonal expansion of effector T cells still does not occur, trafficking to the tumor bed is complicated by disrupted chemokine gradients, abnormal vasculature, and the desmoplastic tumor stroma that acts as both a physical & chemical barrier to entry. C) Anti-tumor immune cells that are able to penetrate the TME are quickly exhausted by local metabolic conditions combined with immunosuppressive molecular crosstalk (e.g. upregulated interleukin 1 beta [IL-1b], transforming growth factor beta [TGFb], interleukin 10 [IL-10], and beta-catenin [b-catenin]) between tumor and tumor-coopted immune cell populations (cancer-associated fibroblasts [CAF]; tumor associated macrophages [TAM]; tumor associated neutrophils [TAN]; tolerogenic dendritic cells [DC]; myeloid derived suppressor cells [MDSC]; type II T helper cells [Th2]; T regulatory cells [Treg]; B regulatory cells [Breg]). Adapted from “Challenges for CAR T-Cell Immunotherapy in Solid Tumors” and “Tumor Extracellular Matrix Reduces Therapeutic Efficiency in Solid Tumors”, by BioRender.com (2021). Retrieved from <https://app.biorender.com/biorender-templates>.

Fig. 3 A Framework for Successful IO-based Treatment in PDAC. To block immune escape, next generation IO-based approaches for PDAC must be built on targeting immune priming/activation pathways simultaneously with modulating local TME immunosuppression and blocking immune checkpoints blockade for effective sustained anti-tumor immune trafficking and sustained cytotoxic response. This will require several IO and targeted agents on top of conventional therapies. Standard chemotherapy with combinatorial cocktail of an anti-tumor vaccine, co-stimulatory agent (aCD40), TME crosstalk modulator (CXC4Ri or TGFb trap), and ICB (aPD-1) is one such potential combination. Key (selected terms): [cDC] conventional dendritic cell; [CSF-1Ri] colony-stimulating factor-1 receptor inhibitor; [CTL] cytotoxic T lymphocyte; [CTLA-4] cytotoxic T lymphocyte antigen 4; [DDRi] DNA damage repair

The original article can be found online at <https://doi.org/10.1007/s10555-021-09981-3>.

✉ Nilofer Azad
Nazad2@jhmi.edu

¹ Department of Medical Oncology, Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University School of Medicine, Baltimore, MD, USA

inhibitor; [DNMTi] DNA methyltransferase inhibitor; [FAKi] focal adhesion kinase inhibitor; [FLT3L] Fms-related receptor tyrosine kinase 3; [HDACi] histone deacetylase inhibitor; [Hyal] hyaluroninases; [LAG3] lymphocyte activating 3; [M1] tumor associated macrophage, type I phenotype; [mAbs] monoclonal antibodies; [N1] Neutrophil, type 1 phenotype; [NK] – natural killer; [NK1] natural killer cell, type 1 phenotype; [PARPi] Poly (ADP-ribose) polymerase inhibitor; [PD-L1]– programmed death-ligand 1; [RT] radiation

therapy; [TGFb] transforming growth factor beta; [Th1] T helper cell, type 1 phenotype; [VEGFi] Vascular endothelial growth factor inhibitor. Created with BioRender.com.

The original article has been corrected.

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.