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Editorial
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Drug-Induced Neoantigens: A New Horizon in Cancer Immunotherapy?

Franzese O[1], Aquino A[1], Fuggetta MP[2], Roselli M[3], Bonmassar E[1,2], De Vecchis L[3] and Torino F[3]*

[1]Department of Systems Medicine, School of Medicine, University of Rome Tor Vergata, Rome, Italy

[2]Institute of Translational Pharmacology, National Council of Research, Rome, Italy

[3]Department of Systems Medicine, Medical Oncology, University of Rome Tor Vergata, Rome, Italy

Editorial

Tumor immunology has been neglected for many years. With the recent appearance on the scene of Immune Checkpoint Inhibitors (ICpI, 1) tumor immunology gained a lead role in cancer therapy. In general, classical cytotoxic chemotherapy and targeted therapy has been, at least in part, disappointing due to the almost inevitable onset of resistance in the majority of solid malignancies mostly as a result of mutations affecting target susceptibility to the drug [2]. However, also resistance against ICpI-based immunotherapy in cancer cells of different histological types was soon evident in the clinics, and this is due predominantly to the emergence of scarcely immunogenic neoplastic cell clones [3].

More than 40 years ago, we were the first to demonstrate that in vivo treatment with an antitumor compound of triazene family induces the appearance of strong transplantation antigens in murine leukemia cells [4]. Since then, this phenomenon that we called "chemical xenogenization" and more recently "Drug-induced Xenogenization" (DIX, reviewed in 5) was found to be generated by somatic mutations [6, 7] capable of inducing the synthesis of abnormal proteins. The intracellular processing of these proteins leads to the appearance of non-self peptides that are presented to T cells in the context of MHC [7].

Up-to now, ICpI, that are able to amplify exceedingly T-cell immune reactivity of the host, rely on tumor-associated antigens naturally present in cancer cells, especially in case of cells endowed with high mutation load [8]. We propose now to consider the possibility of a pharmacological control of mutation load. Up-to-date DIX has been found to be generated preferentially by triazenes (e.g. temozolomide). Therefore, in the near future a new tactic seems to appear on the skyline of cancer immunotherapy. This consists in the adoption of triazene derivatives or other compounds endowed with potent DIX activity for a successful cancer treatment based on ICpI and Drug-Induced Neoantigens.

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Correspondence:
Enzo Bonmassar, Department of Systems Medicine, National Council of Research, Rome, Italy, E-mail: bonmasse@yahoo.com

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