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REVIEW

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Non-invasive biomarkers for monitoring the immunotherapeutic response to cancer

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Abstract

Immunotherapy is an efficient way to cure cancer by modulating the patient's immune response. However, the immunotherapy response is heterogeneous and varies between individual patients and cancer subtypes, reinforcing the need for early benefit predictors. Evaluating the infiltration of immune cells in the tumor and changes in cell-intrinsic tumor characteristics provide potential response markers to treatment. However, this approach requires invasive sampling and may not be suitable for real-time monitoring of treatment response. The recent emergence of quantitative imaging biomarkers provides promising opportunities. In vivo imaging technologies that interrogate T cell responses, metabolic activities, and immune microenvironment could offer a powerful tool to monitor the cancer response to immunotherapy**.** Advances in imaging techniques to identify tumors' immunological characteristics can help stratify patients who are more likely to respond to immunotherapy. This review discusses the metabolic events that occur during T cell activation and differentiation, anti-cancer immunotherapy-induced T cell responses, focusing on non-invasive imaging techniques to monitor T cell metabolism in the search for novel biomarkers of response to cancer immunotherapy.

Keywords: Cancer metabolism, Immunotherapy, T cells, Tumor microenvironment, Imaging biomarkers

Introduction

Cancer immunotherapy has emerged as a treatment method for various cancers by targeting the mechanisms that govern the interplay between tumor microenvironment and immune cells. The general premise of immunotherapy for cancer is to stimulate, enhance, or improve the antitumor immune response of the host. Despite the advances in immunotherapy, only some patients showed a significant clinical benefit while the majority of patients depicted substantial side effects. Therefore, the immunotherapies must be targeted to the patients who are likely to benefit, suggesting an urgent need to identify biomarkers that can direct patient selection and help determine the response to treatment at an early stage. Non-invasive molecular imaging has become an essential diagnostic modality in cancer management. Because of molecular imaging's potential to test biological processes with high precision in vivo non-invasively at the whole-body level, it is of great importance to improve these technologies to direct treatment under many oncological conditions. Several immunotherapeutic techniques are employed in cancer therapy, including modulation of T cell activity through adoptive cell transfer (ACT), monoclonal antibodies (mAbs), checkpoint inhibitors, and cancer vaccines [1–3]. The common denominator for successfully implemented immunotherapies in the clinic is their ability to stimulate or increase cytotoxic T cells' infiltration into the tumor. Thus, in vivo imaging technologies that target T cell responses in patients are powerful tools for further development of immunotherapy. The following sections provide an overview of T cells' metabolism and

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