Editorial

Advances, Limitations and Future Challenges in the Management of Immunotherapy for Hematological Diseases and Solid Tumors

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Our immune system is able to attack cancer cells by recognizing cellular mistakes and destroying them. To date, we still do not have sufficient knowledge on how well the immune system can fight degenerate cells that are developing. The idea of utilizing the patients' own immune system to fight tumors has led to the remarkable progress in the field of cancer therapy in the last decade [1]. However, errors during the cell division process and multiple genetic mutations promoting oncogeneses allow the damaged cells to escape the immune system, which usually patrols and eliminates such cellular mistakes before they become uncontrollable. This Special Issue reviews diverse immunotherapeutic strategies, approved treatments and possible methods to predict therapeutic response. The experts in the field do not only summarize the recent breakthroughs and successful evidence in many types of cancers, but also the failures and the unexpected limitations in clinical practice. The contents should help us better understand the mechanisms of different immunotherapies and intend to discuss the challenges and opportunities in improving current strategies.

Capietto and colleagues have focused on the mutated peptide ("neoantigens") induced by oncogenic events and presented on the histocompatibility complex (MHC) molecules to evoke potent anti-tumor immune responses [2]. The tumor-specific neoantigens can be generated from different sources: single-nucleotide variations or small insertions/deletion, gene fusions, alternative splicing variants and post-translational modifications. Since such cancer-specific neoantigens are known to induce potent immune response, numerous efforts to modulate the neoantigen expression, and different approaches to enhance the anti-tumor-specific T cell response are made [3,4]. Capietto and colleagues describe in their review the recent updates on the identification of neoantigens and prediction methods for therapeutic responses, as well as studies showing promising results for the DNA/RNA aberrations as novel sources of neoantigens [2]. One of the mentioned challenges was, for example, the identification and modulation of neoantigens arisen from non-coding DNA regions, e.g., long and short non-coding RNA transcripts (lncRNA) or pseudogenes. LncRNA influence the processes of regulation of transcription, splicing and translation, and pseudogenes can regain the lost protein-coding function in tumor cells. Moreover, the T-cell response varies with the type of neoantigens or targeting approaches, and may not be sufficient enough to fight the tumor cells effectively. The improvement of antigen quality and overcoming some manufacturing challenges requires more studies in this field.

From a therapeutic perspective, certain dysregulated kinase signaling cascades found in tumors, which could mediate different immune responses by targeting, are discussed by Kim and colleagues [5]. Among others, the Rho-kinase (ROCK) pathway is known to promote tumor cell progression, migration, metastasis, and extracellular matrix remodeling. ROCK is a serine/threonine kinase [6] and has two isoforms, ROCK1 and ROCK2, which are differentially expressed in specific tissues [7]. In tumors, an increasingly stronger expression of Rho-K with tumor progression has been observed [5]. There are already two

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