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Editorial

Getting visible with exciting IO tech!

For any new journal, starting is the most challenging part. With help from the Editorial Board members we have managed to receive a collection of manuscripts on technological developments of which some have already been accepted. ESMO IOTECH's first issue is now out and will be available in print and online [1] at ESMO 2019 in Barcelona. As IOTECH is an open access journal, all manuscripts can be read on line as soon as they are accepted.

In this second issue of IOTECH, Drs Bentzen and Reker Hadrup explain how the diversity of the T-cell repertoire that our bodies possesses, can manage to recognize and deal with the billions of antigens, coming mostly from pathogens, that we encounter during life [2]. The hallmark for this is, that a single T cell receptor displayed by the T cell is not unique for a single MHC-peptide complex, but cross-reacts with many antigens, estimated to be around a million. However, this degeneracy of TCR specificity poses a number of important challenges to the now rapidly emerging field of adoptive cell therapy using TCR gene modified T cells, of which safety is the most important one. How should we predict whether and to what extend a tumor-specific TCR could lead to toxicity as a result of off-target recognition? Currently, new assays are in development that aim to give a risk prediction for any cross-reactivity. These are based on unraveling points of interaction between the TCR and peptide/MHC complexes and predict with how many peptides the TCR could interact. Especially for the so-called affinity optimized TCRs, cross-reactivity is a main concern and knowledge about potential cross-reactivity will be crucial to rationally design optimal receptors for gene modification of T cells for adoptive transfer with the highest efficacy.

Imagine a surgeon spraying a nanoparticle fibrin gel on the surgical wound just after having removed the tumor in order to stimulate local immune cells to destroy some micrometastases or single cancer cells left at the tumor side. Chen, Ci and Gu recently developed such a technology using a spray of nanoparticles filled with an anti-CD47 monoclonal antibody [3]. Tumor cells abuse expression of CD47, a molecule normally present on erythrocytes, which helps them hide from innate immune cells such as monocytes/macrophages expression the ligand SIRP-α that otherwise would eliminate these cells. CD47, also called “don't eat me” signal can be blocked by amongst others anti-CD47 antibodies. Recently, a study was published showing clear anti-tumor efficacy of anti-CD47 antibodies as systemic treatment for cancer patients, illustrating the potential importance of blocking this new checkpoint. Here, the sprayed nanoparticles not only form a fibrin layer that promotes would healing, they also deliver anti-CD47 following degradation of the nanoparticles to the fresh surgical wound, thus stimulating locally present immune cells to engulf and destroy the persistent tumor cells, and at the same time elicit an anti-tumor adaptive immune response.

Why do some patients develop immune related toxicities on treatment with immune checkpoint blockade while others do not? This question has become increasingly important now so many patients are being treated with these new drugs. It has been known for a long time that germline host genetic factors play a role in the development of autoimmune diseases. Chat, Ferguson and Kirchhoff asked the question, whether development of immune related adverse events during treatment with anti-CTLA-4, anti-PD-(L)1 or their combination, resembling autoimmune diseases, could also be influenced by the presence of host genetic factors [4]. They argue for performing genome wide association studies (GWAS) to search for single nucleotide polymorphisms that are highly correlated with high grade IO toxicities, which when confirmed could serve as biomarkers for toxicity and ideally could be utilized to counsel patients before initiating an IO treatment.

In my opinion, these three papers are great examples of how the IO field is evolving. They discuss innovative and important new developments in the IO space, and fit perfectly within the focus of IOTECH. I challenge you to provide us with manuscripts on either original new results or write a review or perspective on a novel development that is “hot” in the IO field.

I hope you enjoy reading this issue as much as I did.

References

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[4] Chat Vylyny, Ferguson Robert, Kirchhoff Tomas. Germline genetic host factors as predictive biomarkers in immuno-oncology. Immuno-Oncol Technol 2019. Pii: S2590-0188(19)30018-8.

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