Cancer Immunology

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Immune modulation in cancer: implications for novel cancer therapies

Exploiting the immune system for cancer has become a paradigm-shifting therapeutic arsenal in oncology. Thus, cancer immunotherapy is increasingly considered to be one of the most important advances in the field of medicine following outstanding clinical successes with adoptive T cell therapies or blockade of immune checkpoints (Nobel Price in Medicine, 2018). Yet, therapeutic benefits are currently limited to a minority of treated patients and many patients are either refractory ab initio or develop resistance to such therapies, through yet poorly understood mechanisms. Our research group is a translational science laboratory in cancer immunology and immunotherapy. We are applying basic science research in immunocompetent murine tumor models and primary human tumor specimens and translating our discoveries and knowledge directly into early clinical testing (clinical trial unit including a phase I unit).

The understanding of cellular and molecular mechanisms of primary and acquired resistance to checkpoint blockade therapy allows for designing novel combination immunotherapy approaches to overcome these resistance mechanisms. In the last years, our research has been dedicated to mechanistically understand the immunomodulating capabilities of novel anti-cancer therapies in order to pave the way for rationally designed treatment algorithms. We have recently provided insights into the therapeutic activity of immune-modifying chemotherapy that can elicit strong anti-tumor immunity in patients and mouse models. In addition, we showed that resistance to immunotherapy can be successfully overcome by synergistic combinations of immunotherapeutic agents and approaches specifically targeting immune-suppressive pathways. Figure 1 provides an overview with references. A major barrier for effective cancer immunotherapy is intra-tumoral immune cell exhaustion. A comprehensive understanding of molecular initiators and promoters of T cell exhaustion is key to develop more effective strategies to restore antitumor immunity. Our group is interested in dissecting mechanisms underpinning T and NK cell exhaustion in human cancer patients; accordingly, recent work elucidated the diversity and functional impact of inhibitory T cell receptors expressed in cancer patients. To develop strategies to overcome tumor-induced T cell dysfunction, immunotherapeutic agents endowed with specific immune-activating capacities have been evaluated to induce a functional T cell recovery, thereby enhancing the effector functions in tumor-infiltrating immune cells. Figure 2 provides an overview with references.

We are currently working on implementing emerging technologies for multidimensional characterisation of the tumor microenvironment. E.g. CODEX is a novel multiplex imaging platform, which is capable of providing information on expression of up to 50 markers from a single tissue slide coupled with spatial coordinates of the cells (Figure 3). It is an excellent tool to study immune cells in their in situ environment. In addition, CyTOF (mass cytometry) is a multi parameter tool allowing for detailed quantification to study the cell subsets in suspension. Therefore, combining CyTOF with CODEX allows for through immune and tumour cell characterisation, also in the samples where material for analysis is limited.

Selected Publications


