ImmunoTools *special* Award 2018

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Unraveling a novel combination strategy of CD70 immunotherapy and chemotherapy for non-small cell lung cancer

Non-small cell lung cancer (NSCLC) represents an estimated 85% of all lung cancers, accounting for approximately 1.3 million deaths per year worldwide. NSCLC remains the leading cause of cancer mortality worldwide with a 5-year overall survival rate of only 15% for all stages, according to the World Health Organization. The first-line treatment of advanced NSCLC in the majority of patients still consists of conventional chemotherapy to achieve tumor response or stable disease.

However, survival outcomes for the majority of NSCLC patients still remain very poor. In the last decade, several important therapeutic advances took place in the treatment of NSCLC. Among these advances are the identification of specific genetic alterations (mutations, re-arrangements) and the development of small molecular tyrosine kinase inhibitors (TKIs) targeting these alterations, with promising response rates up to 70% and improvement of both median progression-free survival and quality of life for metastatic NSCLC patient. Although these personalized treatment options show successful results in the clinic, targeted therapies are limited to only a minority of NSCLC patients harboring targetable driver alterations, pointing out the need for new therapeutic strategies for the majority of NSCLC.

Immunotherapy, which is now considered a pillar of cancer treatment alongside surgery, chemotherapy and radiation, is another promising treatment strategy for NSCLC patients. Especially the emergence of immune checkpoint inhibitors represents a landmark of success in a broad range of tumor types with a great number of ongoing clinical trials and recent FDA and EMA approvals to treat different tumor types, including NSCLC. Unfortunately, despite these novel effective therapeutic strategies, objective responses in monotherapy still remain below 25%. In addition, the high degree of non-responders as well as patients who initially respond, but later on acquire resistance, represent a significant challenge in the field of cancer therapy.

Thus going beyond monotherapy to combination therapies is a worthwhile strategy to circumvent this challenge.

In this regard, CD70, recently recognized as immune checkpoint, has emerged as a promising novel target to be blocked in various hematological and solid malignancies. In contrast to the restricted expression of CD70 in normal lymphoid tissue and the absence of CD70 in other normal (healthy) tissue, constitutive overexpression has been described in multiple hematological and solid tumor types. Its overexpression on tumor cells is associated with immune suppression in the tumor microenvironment. We have previously demonstrated constitutive CD70 overexpression on tumor cells in a subset of primary non-small cell lung cancer (NSCLC) biopsies. More importantly, preliminary findings from our group demonstrated the ability of cisplatin to induce CD70 overexpression on NSCLC cells, which broadens the therapeutic window of anti-CD70 immunotherapy.

On the other hand, certain chemotherapeutic agents can elicit immunostimulatory changes in the tumor microenvironment by triggering immunogenic cell death and enabling tumor-specific cytotoxic T cell responses. Until now, only a few cancer drugs have been reported to trigger ICD. In this regard, the immunogenic features of chemotherapeutic agents that are clinically relevant in NSCLC remain to be unraveled. Thus, strategically combining such a chemotherapeutic agent with anti-CD70 immunotherapy has the potential to achieve enhanced anti-tumor effects.

Therefore, the use of ImmunoTools antibodies will provide us important insights into the immune activating effects of our combination strategy by assessing the important hallmarks of immunogenic cell death, expression of immune checkpoints, immune cell phenotype and cytokine production.

ImmunoTools *special* AWARD for **Tal Flieswasser**

includes 24 reagents

FITC - conjugated anti-human CD3

PE - conjugated anti-human CD4; CD8; CD14, CD80, Annexin V

APC - Annexin V

recombinant human cytokines: rh GM-CSF, rh IL-1beta, rh IL-2, rh IL-4, rh IL-12

human ELISA-set (for one 96 plate): human IFN-gamma, human IL-10, human TNF-a