PROGRAM

IUCT-O AMPHITHEATRE, TOULOUSE

SESSION 1
ADAPTATIVE IMMUNITY AND CLINICAL APPLICATIONS

WORKSHOP OPENING 9:00 - 9:15

KEYNOTE 1 : PR. PEDRO ROMERO 9:15 - 10:05

University of Lausanne and Novigenix, CH
Harnessing metabolic modulation to promote T cell memory formation for cancer immunotherapy

CELIA RAMADE (CRCT) 10:05 - 10:25

The presence of CD8 T-cell responses to neoantigens predict responsiveness to PD-(L)1 axis blockade in non-small cell lung cancer

GUILHÈN PRUNIER (INFINITY) 10:25 - 10:45

Co-stimulatory Receptors in Action: Shaping CD8+ T Cell Immunological Synapse for Target Cell Elimination

COFFE BREAK AND POSTER SESSION 10:45 - 11:15

PR. LOÏC YSEBAERT 11:15 - 12:00

Cancer Research Center of Toulouse, Institut Universitaire de Cancer Toulouse-Oncopole, FR
Novel immunotherapies of B-cell lymphomas

INDUSTRIAL'S FLASH TALK : PROMEGA, OLINK, INVIVOGEN 12:00 - 12:15

LUNCH BREAK 12:15 - 13:45

SESSION 2
INNOVATIVE IMMUNOTHERAPIES AND MICROENVIRONMENT

KEYNOTE 2 : DR. CAPUCINE GRANDJEAN 13:45 - 14:30

Pasteur Institute, FR
Real time immersion into the mode of action of anti-tumor immunotherapies in different anatomical sites : Same therapy different outcomes

LEA RIMAILHO (CRCT) 14:30 - 14:50

Study of CD39 as new therapeutic target in non-Hodgkin's lymphoma

TANIA MARGARIDO-PEREIRA (CRCT) 14:50 - 15:10

Anti-TNF to improve the efficacy of immunotherapy targeting PD-1 and CTLA-4 in advanced melanoma

COFFE BREAK AND POSTER SESSION 15:15 - 15:45

KEYNOTE 3 : DR. ALEXANDRE BOISSONNAS 15:45 - 16:30

Center of Immunology and Microbial Infections, FR
Regulatory T cells recovery after chemotherapy shape the myeloid-landscape in lung tumors

THEOTIME LAVERGNE (INFINTY) 16:30 - 16:50

Stability of tumor-infiltrating regulatory T cells in mice

BINETA RIGAUD (CRCT) 16:50 - 17:10

NK cells with adhesion defects and reduced cytotoxicity functions are associated with a poor prognosis in Multiple Myeloma

CLOSING AND AWARDS CEREMONY 17:15 - 17:30

ONCO IMMUNOLOGY

17.10.2024

1RST EDITION WORKSHOP

https://oncoimmunoworkshop.sciencesconf.org

ABSTRACT

HARNESSING METABOLIC MODULATION TO PROMOTE T CELL MEMORY FORMATION FOR CANCER IMMUNOTHERAPY

PR. PEDRO ROMERO

University of Lausanne and Novigenix SA, Epalinges, Switzerland

Adaptive immunity mediated by antigen-specific T cells is critical to protection from microbial pathogens and tumors. Tumor antigen specific CD8 T cells can control tumors but are often rendered functionally inactive in the tumor microenvironment by a multitude of suppressive factors. A prominent mechanism of blunting anti-tumor CD8 T cell activity is differentiation into exhausted T cells by chronic antigen-mediated stimulation. Exhausted CD8 T cells in the tumor microenvironment are heterogenous and two major subsets have been distinghished. Progenitor exhausted T cells (Tpex) and terminally exhausted T cells (Tex). The former share functional properties of memory T cells and the size of the Tpex subset correlates with good prognosis and sensitivity to immune checkpoint blockade therapy. Both conventional memory T cells (Tm) and Tpex share metabolic pathways including a reliance on oxidative phosphorylation (Oxphos) and fatty acid oxidation (FAO). In contrast, Tex cells exhibit features of metabolic impairment including reduced glycolyis and mitochondrial dysfunction. Mounting evidence supports a central role of memory T cells in sustaining anti-tumor immunity and in endowing adoptively transferred T cells with potent anti-tumor activity and clinical response. We and others have uncovered numerous points of metabolic modulation of activated T cells steering their differentiation towards memory type T cells. In this talk, I discuss the role of inhibitors of mTORC, mitochondrial pyruvate carrier and isocitrate dehydrogense 2 in tilting differentiation of recently activated T cells toward memory type T cells. Inclusion of such inhibitors for a limited period of time during the ex vivo expansion of T-cells for adoptive transfer therapy enhances their ability to control tumors in in vivo experimental models. These observations have important implications in both understanding the immune metabolic pathways underlying T cell differentiation and designing optimized culture protocols for the generation of potent T cell products for therapy of cancer.

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ABSTRACT

REGULATORY T CELLS RECOVERY AFTER CHEMOTHERAPY SHAPE THE MYELOID-LANDSCAPE IN LUNG TUMORS

DR. ALEXANDRE BOISSONNAS

Center of Immunology and Microbial Infections, Paris, France

Regulatory T cells (Tregs) and tumor-associated macrophages (TAMs) are major immune components of the tumor microenvironment promoting tumor progression and limiting the efficacy of chemotherapy. While Tregs are well known for their immune suppressive activity toward the adaptive immune system, their action toward the mononuclear phagocytes compartment is ill-defined. We observed that following chemotherapy in NSCLC and mouse lung tumor, that Tregs shape an anti-inflammatory myeloid-landscape by rapidly dampening the recruitment of TNFα-producing inflammatory-monocytes and increasing TGFβ expression upon differentiation into TAMs. Chemo-immunotherapy using anti-TNFR2, to preferentially target tumor-infiltrating Treg, altered their dynamic of interactions with tumor-monocytes and TAMs, limited their anti-inflammatory action and improved survival in mouse models. Chemo-immunotherapy targeting the Tregs and TAMs-mediated synergic immunosuppressive recovery has a strong therapeutic potential as an alternative or along immune-checkpoint blockade.

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ABSTRACT

REAL TIME IMMERSION INTO THE MODE OF ACTION OF ANTI-TUMOR IMMUNOTHERAPIES IN DIFFERENT ANATOMICAL SITES : SAME THERAPY DIFFERENT OUTCOMES

DR. CAPUCINE GRANDJEAN

Pasteur Institute

Paris, France

INSTITUT PASTEUR

The use of monoclonal antibodies (Ab) to eliminate malignant cells can be an effective strategy to treat patients with cancer. Rituximab, an anti-CD20Ab, was the first therapeutic Ab to be used in the clinic and has significantly improved the outcome of patients with B cell malignancies or autoimmune disorders. It acts by depleting normal and malignant B cells through several possible mode of action (MOA) extensively explored in vitro: Anti-CD20Ab trigger Ab-dependent cellular cytotoxicity (ADC) by natural killer (NK) cells, bind the complement cascade (CDC) or induce Ab-dependent phagocytosis (ADP) by macrophages. In vivo, target cells can invade multiple sites [eg. blood, bone marrow (BM), lymph nodes (LN)] and thus different MOA may occur depending on the effector composition of the anatomical site. There is a general assumption that anti-CD20mAb anti-tumor activity largely relies on FcR-dependent MOA further supported by patients' data, associating polymorphisms in Fc receptors with improved therapeutic response. Despite NK cells being often considered as the central players, depletion of macrophages/monocytes in mouse models has highlighted them as essential for mediating Ab therapeutic activity. Nevertheless, despite two decades of clinical use, linking the respective contribution of these MOA in different tumor sites, to the therapeutic response of anti-CD20Ab, remains a central question to optimize Ab use in the clinic.

Through 2 photon real time in vivo imaging, we investigate anti-CD20Ab in three common sites of B cell malignancies by using fluorescent mouse-models and lymphoma cells expressing a dual FRET-based reporter of apoptosis and phagocytosis. We visualized target B cells travelling through the liver sinusoids and being depleted efficiently by Kupffer cells within minutes. By contrast, tumor cells in the BM or LN appeared largely sessile highlighting the importance of evaluating local MOAs. Like in the liver, we find ADP by macrophages to be the dominant MOA but with a reduced efficacy: B cell tumor elimination in the BM was partial with ADP being no longer active after one hour. Moreover, macrophages were present at low density in tumor-rich regions and could only reach out for neighboring tumors further impeding anti-CD20Ab activity. More suprisingly, depletion in LNs seems to be spatially regulated raising important questions for the clinic as LNs are one of the primary site of lymphomagenesis. Here, we pinpoint both temporal and spatial constraints limiting ADP, raising important questions for treatment optimization. A fine understanding of MOA at different tumor sites is key for the rational design of next-generation therapies.

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