LEVELS OF SOLUBLE CD73 IN MELANOMA PATIENTS.

S. Morello1, C. Sorrentino1, 2, M.Capone3, G. Madonna3, D.Mallardo3, A. Grimaldi3, A. Pinto1, P. Ascierto3.

University of Salerno, Dept Pharmacy

Melanoma is one of the most aggressive types of cancer, that is difficult to manage clinically. A major feature of melanoma cells is their ability to escape immune surveillance. The first successful attempt to abolish immune-suppression in melanoma treatment has been achieved with the use of the FDA-approved monoclonal antibody (mAb) ipilimumab. Ipilimumab binds to the cytotoxic T lymphocyte antigen-4 (CTLA-4), which is expressed on activated CD4+ T cells and CD8+ T cells. Later on other immune checkpoint molecules have been discovered, such as antibodies against programmed cell death-1 (PD-1 - Nivolumab, Pembrolizumab and Atezolizumab), programmed cell death ligand 1 (PD-L1, ligand for PD1). Notably, the therapeutic outcomes in melanoma patients is improved by combining multiple immune checkpoints inhibitors. Hence, in the last few years many efforts have been made aiming to investigate novel therapeutic strategies to inhibit cancer-induced immune-suppression.

Adenosine is an ATP-derived molecule generated at the extracellular level by the ecto-nucleotidase CD73, expressed on the surface of both lymphoid and myeloid cells, and tumor cells. Adenosine accumulates within the tumor microenvironment and it critically impairs the anti-tumor immune response mainly via A2A adenosine receptor subtype. Numerous pre-clinical studies have shown that blockade of CD73 can significantly limit tumor growth and metastasis. In a syngeneic mouse model of melanoma we have demonstrated that inhibition of CD73 significantly reduced tumor growth by improving the T CD8+cells -mediated response. We determined the levels of soluble CD73 in serum samples from healthy and melanoma patients donors, by measuring the activity of soluble CD73. The specificity of CD73 activity in serum samples was tested in presence of the pharmacological CD73 inhibitor, APCP, or the anti-CD73 antibody. The activity of soluble CD73 increased in melanoma patients compared with healthy donors. The activity of the soluble CD73 was measured also in patients treated with the anti-PD1 monoclonal antibody. Altogether, the results suggest that CD73 may represent a potential therapeutic target for melanoma patients.