

Fondazione Ricerca Molinette



SEMINARI DI MEDICINA SPERIMENTALE

MAGGIO

Mercoledì 27 Maggio 2015, **ore 14:00**

Palazzina "R. Ceppellini", Aula di Genetica Medica (II piano),
Via Santena, 19.

Michail V. SITKOVSKY (Director, New England Inflammation and Tissue Protection Institute, Northeastern University and Dana Farber Cancer Institute, Harvard Institutes of Medicine, BOSTON, MA)

"Combination of anti-A2A-adenosinergic systemic oxygenation and the blocker of A2A adenosine receptor with immunotherapies (and chemotherapy?) of cancer".

(ospite: F. Malavasi)

Informazioni possono essere ottenute da: marzia.rocchia@unito.it

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Summary

The tissue hypoxia-driven accumulation of extracellular adenosine and the A2A adenosine receptor-mediated immunosuppression (Ohta & Sitkovsky, *Nature*, 2001) continue inhibiting anti-tumor T cells, even after the combinatorial blockade or depletion of all known immunological negative regulators of anti-tumor immunity.

In contrast, the inhibitors of the pathophysiological, “hypoxia-A2-adenosinergic” signaling in tumor microenvironment are effective in i) weakening - at least in part - of all other so far tested immunosuppressive mechanisms, and in ii) reprogramming the intratumoral proteome and purine metabolome away from being immunosuppressive and tumor-protecting and toward immunopermissive and tumor-death facilitating (Hatfield et al, *J. Mol. Med.* 2014; *Science Translational Medicine*, 2015).

It is proposed to re-purpose the supplemental oxygenation and the synthetic A2A adenosine receptor blockers and test them in combination with current immunotherapies of cancer. Exclusion criteria for these generally safe treatments will be also discussed.