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Combination therapy against NGcGM3 ganglioside and EGFR: A new approach for lung cancer treatment

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NGcGM3 ganglioside is tumor specific antigen from different cancers and it has been associated with bad prognosis. The epidermal growth factor receptor (EGFR) is an aggressive prognostic indicator in some tumors. Center of Molecular Immunology (CIM), Havana, Cuba has developed vaccines and monoclonal antibodies against these targets. Also, any evidences revealed a functional relationship between EGFR and NGcGM3 at the tumor cell membrane, suggesting a rational for exploring the therapeutic combinations of immunotherapies targeting them. However, limited evidence has been generated. We explored whether the survival and anti-metastatic effect of passive anti-EGFR therapy (7A7 mAb; iv) would be modulated by the co-administration of NeuGcGM3/VSSP vaccine (sc), in two murine spontaneous lung metastasis models: Lewis lung carcinoma (3LL-D122) and mammary adenocarcinoma (4T1, orthotopic). Target combination therapy increased survival in two lung metastasis models, in comparison with monotherapy groups (n=10 in each group). Moreover, depletion of NK1.1+, CD4+ and CD8+ cells *in vivo* completely abrogated the increment in survival of the combination treatment group. Concomitantly, reduction of NGcGM3 ganglioside, Urokinase Plasminogen Activator Receptor (uPAR) and $\alpha 5\beta 1$ integrin expression is leading the inhibition of pro-tumoral signaling by the activation of EGFR, FAK and Src molecules in this group. Combination treatment induces a stronger inhibition of the signaling cascades related to EGFR and NGcGM3 ganglioside at the tumor cell membrane. In summary, these two lung metastasis models are a good murine setting to validate the potential combination of NGcGM3 vaccines and anti-EGFR treatments and suggest the opportunity for cancer patients who overexpressed these two molecules.

Biography

Adriana Carr has completed her PhD from Havana University School of Medicine and Post-doctoral studies from Center of Molecular Immunology. She is the Director of Biomarker Group and Head of Combination Therapy Project based in Immunotherapy at the Center of Molecular Immunology in Havana, Cuba, an institution related with the develop of new drugs (vaccine and antibodies) for cancer therapy. She was invited to John Wayne Cancer Institute and also worked with Buenos Aires University in cancer immunotherapy. She has published more than 34 papers in reputed journals.

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