ONCOLille Seminars

L'INSTITUT DE CANCÉROLOGIE DE LILLE

On Thursday 6th of April. 2023 at ***11 am***

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ONCOThai

Impact of Nasopharyngeal Carcinoma Tumor Exosomes on Human Dendritic Cell Maturation: A Phenotypic, Functional and Pathophysiological study

Nasopharyngeal carcinoma (NPC) is an upper aerodigestive tract tumor associated with Epstein-Barr virus (EBV) infection. NPC is characterized by an immunosuppressive microenvironment that promotes tumor immune escape. Two major actors with immunosuppressive properties have been described, regulatory T cells (Treg) and NPC tumor exosomes (NPCExo). Recently, our team has shown that NPCExo promote the suppressive function of Treg as well as their recruitment via the chemokine CCL20. In this context, the objective of this work was to evaluate the ability of NPCExo to induce the emergence of tolerogenic dendritic cells (tDC), which are known to promote tumor development by inhibiting the T cell response.

The results obtained show that NPCExo promote the generation of tolerogenic mature regulatory DCs (mregDC). Indeed, DCs generated in the presence of NPCExo (NPCExoDC) have a defect in LT activation in co-culture compared to mature DCs (mDC). This defect is not related to a change in the phenotype of these cells since it is comparable to that of mDC. On the other hand, during their development we notice changes in their cytokine production. During the differentiation phase, NPCExoDC show an important activity of the IDO enzyme and a secretion of the immunosuppressive cytokine IL-10. Then, during the maturation phase, these NPCExoDC produce very little of the proinflammatory cytokines IL-6 and IL-12 in connection with a significant production of IL-4 regulating the production of IL-12. Interestingly, we observed a decrease in oxidative metabolism compared to mDCs which may be related to a decrease in effector capacity. In parallel, we studied the effect of exosomes from NPC patients (NPCpatientSEV) and we also observed the emergence of mature DCs with a defect in pro-inflammatory cytokine production and LT activation.

Then, in order to study the migration capacities of DCs generated with NPCExo, we studied their potential attraction by known chemokines such as CCL19 or CCL20 as well as for NPCExo. Our results show that mregDCs are attracted to NPCExo to a greater extent than to the chemokine CCL19. On the other hand, the attraction by NPCExo does not seem to be dependent on CCL20 as it was the case for the attraction of Treg previously demonstrated in the laboratory.

Finally, to identify exosomal players responsible for DC functional modifications, we studied the role of galectin-9 (Gal-9). Gal-9 does not alter the phenotype and cytokine secretion of DCs compared to mDCs but appears to activate LTs less efficiently in co-culture compared to mDC-induced LT activation. Finally, interestingly, the addition of a Gal-9 blocking antibody, 1g3 (patented by our laboratory) seems to restore the activating capacities of DC on LT, confirming the role of this molecule.

All our results open interesting avenues not only in the understanding of the pathophysiology of NPC but also new therapeutic perspectives via targeting tumor exosomes.

See you all in **Axel Khan Conference Room - ONCOLille**

If you can't make it, we will also stream through Zoom:
https://univ-lille-fr.zoom.us/j/94766125424
Passcode: OLille!
Meeting ID: 94766125424

Chann Lagadec
For the ONCOLille Animation Committee