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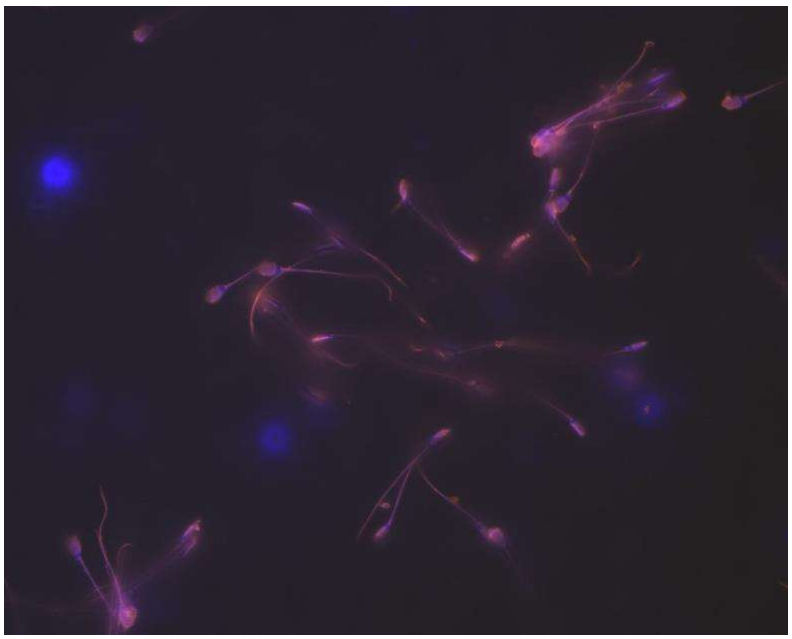
One Health

L'Animal et l'Homme, une même santé



32. Tgfβ-Tgfβ receptor signaling is essential for lung interstitial macrophage differentiation and identity

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In the lung, interstitial macrophages (IM) spontaneously produce the immunosuppressive cytokine interleukin (IL)-10, thereby maintaining lung homeostasis and preventing the development of allergic inflammation to aeroallergens. Recently, we discovered two distinct IM subsets and found that MafB was an important transcription factor that restricted local monocyte proliferation and mediated IM differentiation and identity of both subsets. While macrophage colony-stimulating factor (M-CSF) acts as a local signal contributing to this process, it remains to be determined whether additional factors from the lung microenvironment are imprinting the identity of IM. We performed single cell RNA-sequencing of whole lung cells in steady-state and performed NicheNet analysis, allowing us to identify the *Tgfb-Tgfbr* axis as a promising ligand-receptor interaction mediating IM identity. Both IM subsets expressed high protein levels of Tgfβ-RII, and BMDM stimulation with Tgfβ triggered expression of IM-associated genes. Then, we generated myeloid-restricted *Tgfbr2*-deficient mice (i.e., *LysM^{Cre}Tgfbr2$^{fl/fl}$* mice) and found that numbers of IM were lower in *LysM^{Cre}Tgfbr2$^{fl/fl}$* mice as compared to littermate controls. Of note, IM differentiation from monocytes seemed to be impaired and blocked in a monocyte-to-IM transition state in those mice. We also found that MafB directly or indirectly regulated IM-specific Tgfβ receptor expression in myeloid-restricted Mafb-deficient mice. This work adds to our understanding of IM biology by showing how the lung-specific microenvironment shapes IM identity, thus providing foundations for future IM-targeted therapeutic interventions in the context of lung chronic inflammatory disorder.

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33. Confirmed hypoglycin A toxicosis in two gnus

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In spring 2021, two gnus (*Connochaetes taurinus taurinus)* exposed to *Acer pseudoplatanus* seedlings in their zoo enclosure were found in decubitus with signs of depression and tremors. Blood samples collected from these animals at that time were tested positive for hypoglycin A (HGA) and its toxic metabolite methylenecyclopropylacetyl-carnitine (MCPA-carn). These observations highlight (i) exposition to HGA, (ii) HGA absorption and, (iii) HGA metabolization into its active metabolite. In addition, biochemical findings (*i.e.*, increased muscle enzyme activity in blood) indicated an ongoing rhabdomyolysis process. Hypoglycin A metabolization into MCPA-CoA is known to induce a severe alteration in lipid metabolism resulting in an energy deficit in type I muscle fibers. To confirm *A. pseudoplatanus* poisoning in the diseased gnus, free carnitine and twenty-one acylcarnitines (C2, C3, C3DC, C4, C5, C5-OH, C5DC, C6, C8, C8:1, C10, C10:1, C10:2, C12, C12:1, C14, C14:1, C16, C16:1, C18 and C18:1 -carnitine) were quantified in serum and compared to non-exposed gnus as controls. In the diseased gnus, HGA appears to have similar consequences on fatty acid catabolism than the one described in equids with a severe modification of the acylcarnitines profile. This study confirms HGA poisoning in Bovidae associated with exposure to *A. pseudoplatanus* and so, discloses a potential risk of toxicity for domestic ruminants and a potential risk for food safety.