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Proinflammatory role of myeloid derived suppressor cells (MDSCs) in a glucose-6-phosphate isomerase (GPI)-induced T-cell and B-cell independent rheumatoid arthritis (RA) model and tracking of granulocytic-MDSCs (G-MDSCs) *in vivo* using Positron Emission Tomography/Magnet Resonance Imaging (PET/MRI)

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Monocytic MDSCs (M-MDSC) and G-MDSCs are immature myeloid cells (CD11b+ Gr1+) and important regulators of basic immune responses. To date the role of MDSCs during RA is quite unknown; hence the aim of this study was to analyze the occurrence and homing of MDSCs during the effector phase in the GPI-serum RA mouse model. Further, we aimed to track 64Cu-PTSM or 64Cu-1A8 labeled G-MDSC after I.V. injection in RA mice by PET/MRI *in vivo*. BALB/c mice were injected with GPI-Ab to induce RA. We isolated cells from lavage of RA and healthy ankles at days 1, 3 and 6 and performed FACS analysis to identify G-MDSCs (Ly6G+) and M-MDSCs (Ly6C+). Ly6G antibody (Ab) or isotype Ab were used to deplete G-MDSCs. We labeled G-MDSCs intracellular with 64Cu-PTSM or Ly6G-Ab (1A8) 64Cu-1A8. Labeled cells were I.V. injected in RA mice on day 6 and tracked their homing patterns by PET/MRI. On day 1 less than 10%, day 3 up to 55% and day 6 up to 70% of infiltrating CD11b+ cells were identified as G-MDSCs. Contrary the expression of M-MDSCs in arthritic ankle lavage was not affected. G-MDSC depletion with Ly6G Ab on day 6 after RA induction reduced the number of GMDSC to less than 10%. *In vivo* 64Cu-PTSM-G-MDSCs from RA ankles homed to arthritic ankles 1 hour post injection (5.5±0.6 % ID/cc) and 3.9±0.5% ID/cc after 24 hours. In contrast 64Cu 1A8-G-MDSCs showed enhanced homing into GPI-arthritic ankles (1 hour: 7.2%±3.0% ID/cc; 24 hours: 7.7±2.6% ID/cc) compared to 64Cu-PTSM-G-MDSCs. Thus, our data indicate that most of the infiltrating cells in inflamed ankles are G-MDSCs and depletion of Ly6G+ cells lead to a massive decrease of G-MDSCs and arthritic joint inflammation, indicating a new therapeutic approach. 64Cu-1A8G cell labeling showed promising results for tracking G-MDSCs *in vivo*.

Kynurenine reduces memory CD4 T-cell survival early in HIV-1 infection

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Immunology and metabolism have always been considered as distinct disciplines. However, recent advances in the understanding of immune functions under HIV-1 infection associate these branches with intricate networks. Today, we show that inflammation and kynurenines whose plasma levels are higher in HIV-1-infected subjects when compared to those of uninfected controls reduced the ability of memory CD4 T-cells to respond properly to IL-2. We found that *in vitro* treatment of memory CD4 T-cells with kynurenine results in oxygen reactive species (ROS) production that was responsible for inhibiting the phosphorylation of STAT5 factor following IL-2 stimulation. Interestingly, we found that memory CD4 T-cells from HIV-1-infected subjects, even those with less than 3 months of presumed infection, displayed reduced ability to protect themselves against Fas-mediated apoptosis in the presence of IL-2 help. The effect of kynurenines and subsequent oxidative stress was abrogated when HIV-1-infected subjects were treated with combined antiretroviral therapy (cART) early during the time course of their infection. Collectively, these data highlight the key role of inflammation and perturbed metabolism during HIV-1 infection, particularly in the survival of memory cells and the nature of HIV-1 reservoir.