

**O1192 HIV-transmission from infected CD4+ T lymphocytes to microglia and astrocytes**

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**Background:** During chronic HIV infection, 20-50% of the patients exhibit neurologic disorders known as HIV-associated neurocognitive disorders (HAND). Entrance of HIV into the Central Nervous System (CNS) occurs soon after HIV systemic infection, and is mainly mediated via infected CD4+ T-lymphocytes and monocytes from the blood stream. In the CNS compartment, first cells to be infected are perivascular macrophages and microglia that together with astrocytes act as HIV reservoirs and may disseminate HIV to neighboring cells.

Our research goal was to better understand the effectiveness of HIV transmission from infected CD4+ T-lymphocytes (TCD4) to microglia and astrocytes. With this aim, we studied trans-infection of microglia and astrocytes using a well characterized HIV-2 strain, HIV-2<sub>ROD</sub>.

**Materials/methods:** Donor (TCD4) and target cells (microglia and astrocytes) were maintained in three distinct conditions: (i) co-culture during seven days; (ii) separated 15h after infection, and (iii) separated 42h after infection. The infected lymphocytes were co-cultured in mixed culture (cell-cell contact) and transwell co-cultures, as described (Furihata et al. J.Virol, 2015). Virus production was monitored by reverse transcriptase (RT) activity in culture supernatants, using an immunoenzymatic assay (Cavidy).

**Results:** Our most relevant results demonstrated that in all conditions viral replication in microglia and astrocyte is similar to that observed in TCD4. We also verified that, in the three conditions, HIV-2<sub>ROD</sub> replicates more efficiently in mixed cell cultures than in transwell co-cultures. It was also interesting to note that viral replication in astrocytes directly infected was less efficient than in those resulting from (ii) and (iii) conditions. To note that RT activity detection after 15h and 42h donor-target cells contact showed to be similar.

**Conclusions:** Although microglia displays low levels of CD4 expression and astrocytes are CD4-negative, both cells showed to be infected *in vitro*. We hypothesize that the infection of microglia, and mainly astrocytes, is mostly driven by extracellular membrane vesicles (EMVs), which are known to contain genetic material, as well as cellular and viral proteins, including microRNAs, and to disseminate inflammation.

