Interactions between antiretroviral drugs and human Arginase 1.

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The neuro-pathogenetics mechanism(s) underlying HIV-associated neurocognitive disorders are mostly unknown. HIV-infected macrophages and microglial cells play a crucial role, and the metabolic fate of L-Arginine may be highly revelant for microlgia activation. In this context Arginase(ARG), which uses L-Arginine as substrate, can be on the same time target and source of oxiditive stress and inflammation. In this research project, we investigated whether different classes of antiretroviral drugs (i.e. non nucleosidic/nucleotidic retro-transcriptase inhibitors (NNRTI), protease inhibitor (PI) and Integrase Strand Transfer Inhibitor (INSTIs)) inteact with ARG activity. We used a valitated cell model, namely the human microglia cell line (CHME-5), as well as computational chemistry approach. The purified human ARG in a cell-free in vitro system was also used. Overall evidence shows that Dolutegravir, Raltegravir, Elvitegravir and Nevirapine significantly inibit ARG activity (Lisi et al 2017), whereas Darunavir, Atazanavir and Efavirenz consistently inibit ARG activity in intact CHME-5 (Lisi et al 2016), but show no significant affects on purified human ARG (unpublished data).

Lisi L, J Neurochem 2016

Lisi L, J Neurochem 2017