The U24 protein of HHV-6A induces the expression of Alzheimer's disease risk factors of microglial cells

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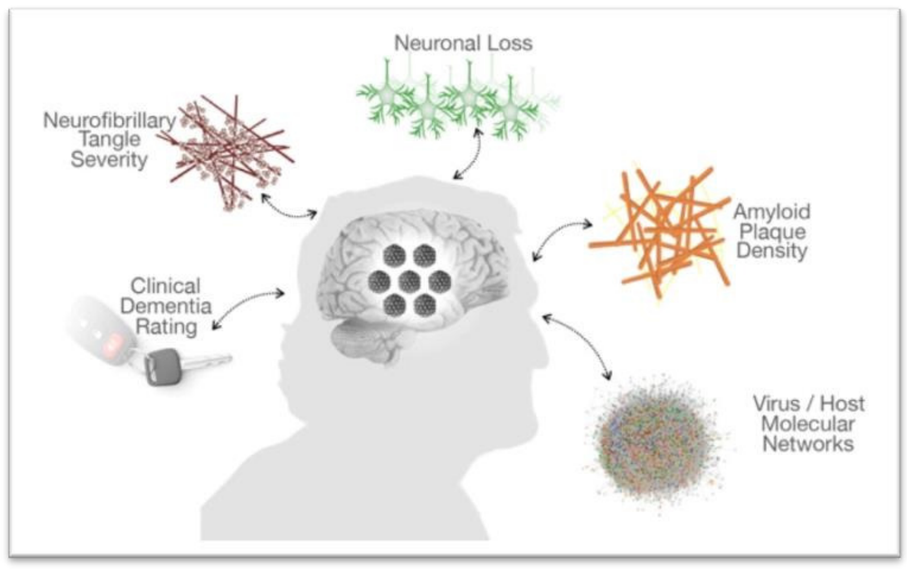
Backgroud

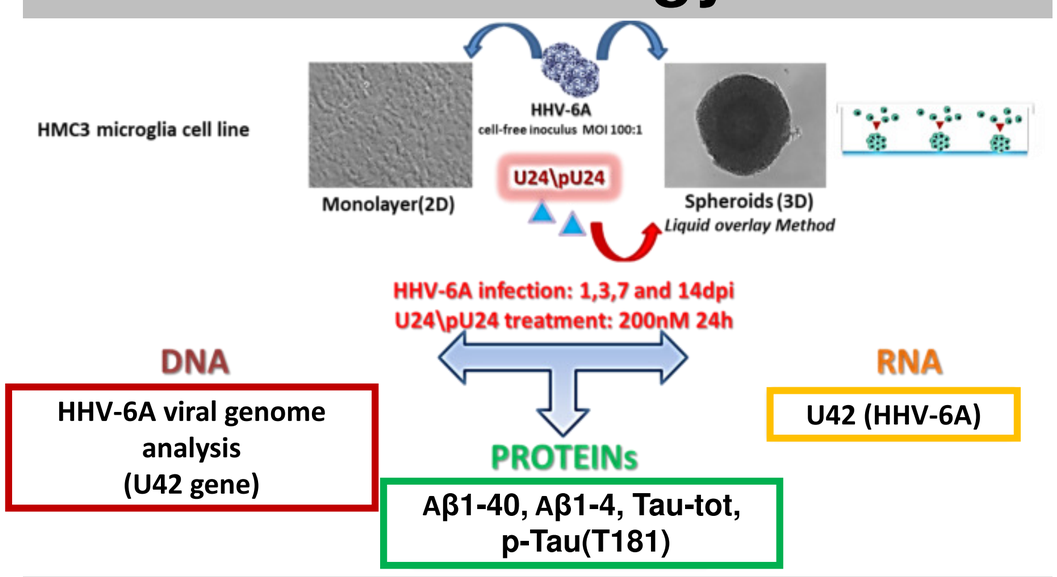
In Alzheimer's Disease (AD) brains, pathological characteristics are observed: extracellular insoluble senile plaques formed by amyloid-β (Aβ) peptide, apoE[1] and intraneuronal neurofibrillary tangles (NFT) formed by tau protein[2]. Recent findings suggest a possible implication of HHV-6A in AD[3,4], and we showed the ability of HHV-6A infection to induce the expression of apoE[5] and to be involved in Aβ expression by microglial cells and cell activation[6]. Several evidences reported that a particular HHV-6A protein, U24, appears to be involved in the neurodegenerative processes[7] due to its high homology with MBP protein. Furthermore, U24 is able to induce tau hyperphosphorylation and Aβ expression through the activation of Fyn-kinase, a kinase involved in tau phosphorylation and Aβ induction[8], suggesting its role also in AD pathogenesis.



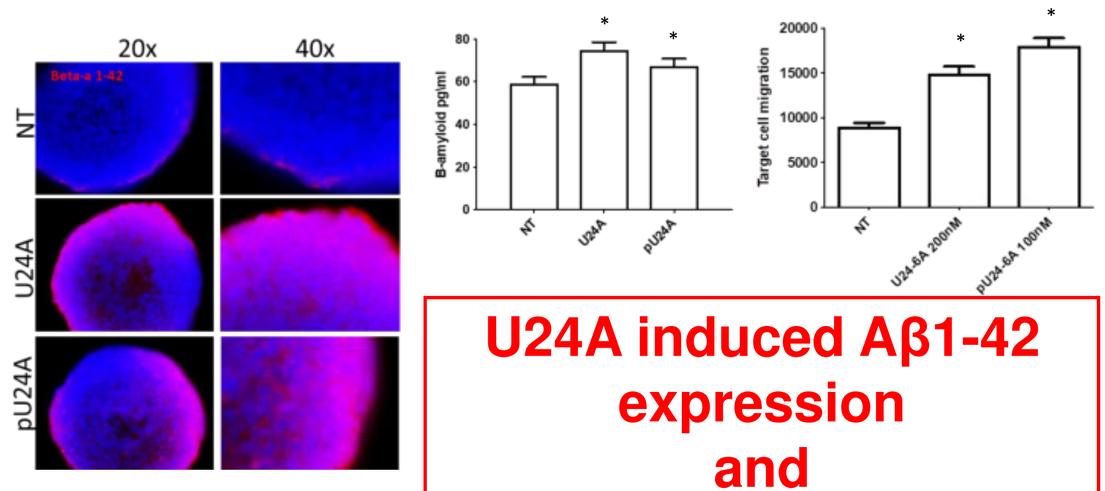
Aim

We evaluated the effect of HHV-6A infection, and particularly of U24 HHV-6A protein, on microglial cells expression of the common risk factor for AD development, Aβ and tau., and its involvement in Fyn-kinase activation and microglia migration.

Technology

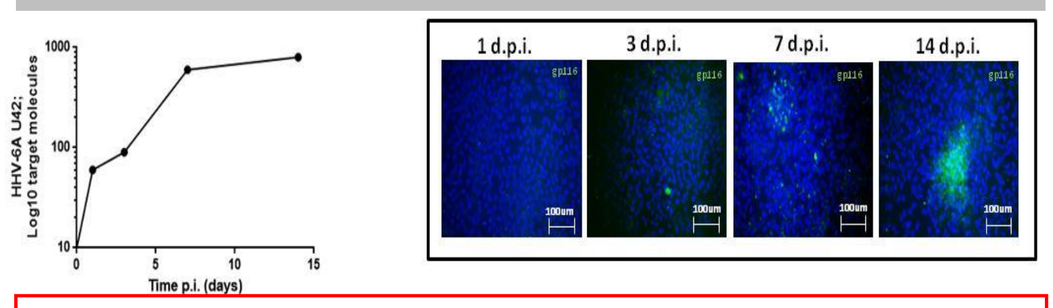


U24 effect on microglia



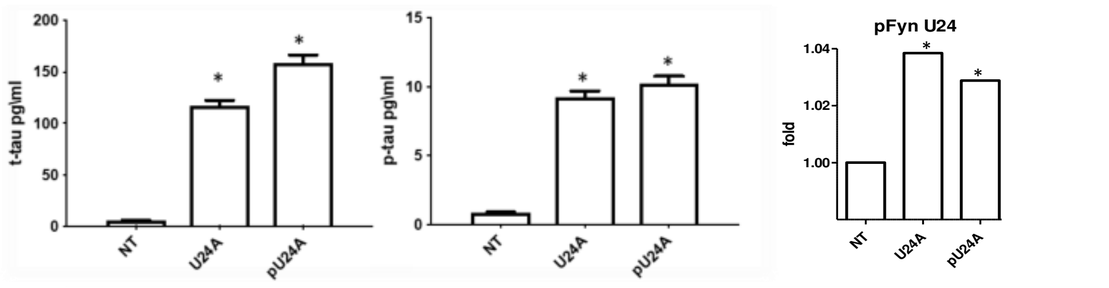
U24A induced Aβ1-42 expression and microglial cell migration

Microglial cell HHV-6A infection



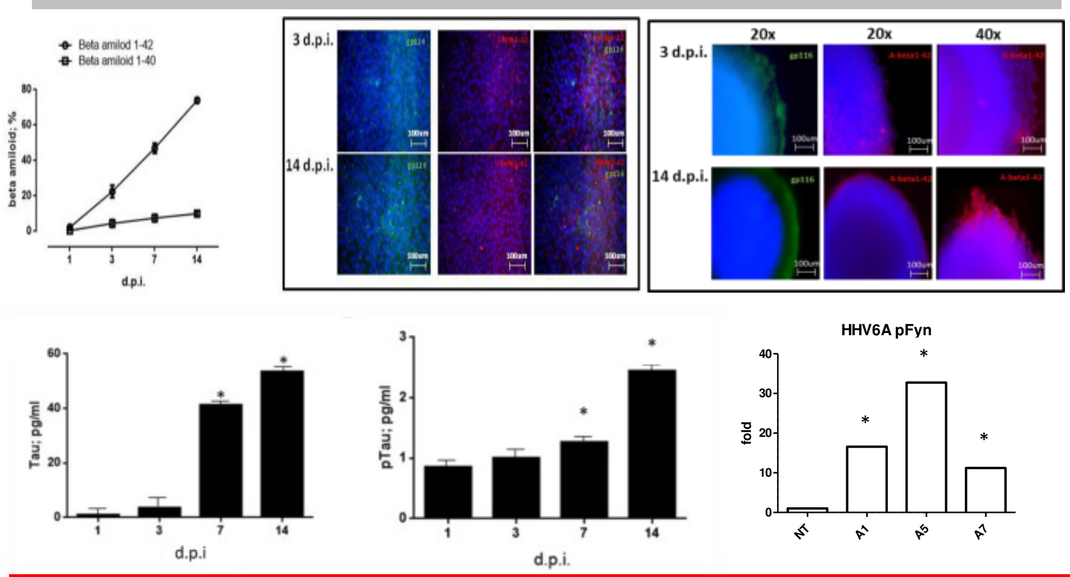
Microglial cells are permissive to HHV-6A infection

U24 effect on Tau\pTau and Fyn-K



U24 induced Fyn kinase activation and Tau\pTau expression

HHV-6A effect on Aβ, Tau\pTau and Fyn-k



Aβ1-42, Tau\pTau and pFyn-k increase during HHV-6A infection

Conclusions

Microglial cells are permissive to HHV-6A infection, that induces the expression of the common risk factor for AD development: apoE, Aβ and tau[7], together with the stimulation of microglia activation and migration. Interesting, we can observe the same induction treating microglial cell with the only HHV-6A U24 protein, with the involvement of Fyn-kinase.

References

1.Eimer WA et al. Neuron. 2018; 2.Kumar A et al. Pharmacol Rep. 2015; 3.Lazar AN et al. Acta Neuropathol. 2013; 4.Readhead B et al. Neuron. 2018; 5.Rizzo R, et al. J Alzheimers Dis. 2019; 6. Bortolotti et al. Alzheimers Res Ther. 2019; 7.Sang Y. Et al., Biochemistry 2014; 8. Larson M et al. J Neurosci, 2012