MODULATION OF MICROGLIA-ASTROCYTES INTERACTION THROUGH LXR ACTIVATION

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In neurodegenerative brain pathologies, such as Alzheimer's and Parkinson's disease, microglia are frequently activated by a local and chronic inflammation. Pro-inflammatory compounds secreted by activated microglia are responsible for astrocyte activation. These astrocytes also produce pro-inflammatory molecules leading to an inflammatory vicious circle in the brain. This toxic environment produced by both cell types seems to be one of the causes of neuronal death in patient's brain. Liver X receptor (LXR) is a ligand-activated nuclear receptor playing a role in the cholesterol homeostasis control but also regulating inflammatory responses in many cell types.

Is the LXR activation able to modulate the dialogue taking place between microglia and astrocyte during inflammation? Can LXR modulate the activation state of these two cell types in order to break this inflammatory vicious circle?

To study these cellular interactions, astrocytes and microglia co-cultures were performed. These cells were activated by pro-inflammatory molecules and LXR agonist. The pro-inflammatory gene/protein expression profile of these cells was analysed by Real-Time PCR and ELISA assay, respectively.

Our results show that activated LXR reduces microglia activation, but has no direct effect on astrocyte activation. In co-culture experiments, preliminary observations show that LXR-treated microglia is able to down-regulate astrocytic activation. Activated LXR appears to be indirectly able to modulate the phenotype of astrocyte through its action on microglia.

This work emphasizes the role of activated LXR in the cellular communication between microglia and astrocytes. Thus, LXR activation could reduce brain inflammation and consequently protect from neuronal death.