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A new CB_2R transgenic mouse model for the study of inflammation

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Introduction: Because of limited availability of research tools, cannabinoid CB_2 receptors (CB_2R) have so far been difficult to study. To solve this problem, we generated a new transgenic mouse model, which expresses the reporter gene (Green Fluorescent Protein, GFP) under the control of the endogenous mouse *Cb2* promoter. CB_2R are expressed abundantly in cells of the immune system, including immunocompetent cells of the CNS, such as microglia. Thus, in the present study we analyzed the expression of CB_2R in two models of inflammation, one affecting the CNS (Alzheimer's disease) and the second related with liver fibrosis pathology.

Method:
CB_2R mouse model: generated by inserting an EGFP reporter gene preceded by an IRES sequence in the 3' UTR of the *Cb2* mouse gene. This approach results in the expression of the reporter gene under the control of the endogenous mouse *Cb2* promoter in a bicistronic mRNA with the CB_2 protein.
CB_2R mouse model characterization in inflammation:
Alzheimer's disease: CB_2-GFP transgenic mice were crossed with 5xFAD mice. Immunohistochemical stainings were performed against EGFP in order to describe CB_2R expression in the β-amyloid (Aβ) pathology. In addition, primary cultures of microglial cells were treated with Aβ to study changes in EGFP-expression.
Bile duct ligation: Adult CB_2-GFP transgenic mice underwent bile duct ligation and sham-operated animals were used as controls. Organ histology and immunohistochemical staining were performed to assess the expression of inflammatory and fibrotic markers in the livers from CB_2GFP mice.

Results:
Alzheimer's disease: EGFP flourescence was increased in *in vitro* microglial cells treated with Aβ. EGFP was detected in microglial cells associated to neuritic plaques under chronic neuroinflammation conditions. No EGFP was evident in brain regions lacking Aβ plaques.
Liver fibrosis: Bile-duct ligation caused profound hepatic changes as showed by increases in serum AST, ALT, and total and direct bilirrubin levels. EGFP expression was induced in endothelial cells and inflammatory cells in damaged livers.

Conclusion: This new CB_2R mouse model allows for a better understanding of the expression and role of CB_2R in different models of inflammation, offering a powerful tool for the development of new therapeutic drugs.

References:

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