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Title: Age and time-dependent expression of CD74 after kainic acid-induced status epilepticus

Abstract:

In order to identify time dependent physiological changes underlying epileptogenesis, we have previously investigated time-course of hippocampal gene expression profiles of postnatal day (P)15 and P30 rats after kainic acid-induced status epilepticus (KA-SE) using high-density oligonucleotide arrays and qRT-PCR. We selected for differentially regulated genes (P30/P15) by capitalizing on age-dependent physiological responses to KA. It was observed that KA-SE causes hippocampal neurodegeneration and development of a chronic epileptic state in mature rats (P30), while KA causes neither cell death nor chronic spontaneous seizures in younger animals prior to P21.

Furthermore, through ontological databases, genes associated with the mitogen activated protein kinase (MAPK) pathways and inflammation related genes were among the most significantly regulated after KA-SE and gene expressions were more robust and sustained in P30 compared to P15. Specifically, one gene that belonged to both MAPK and inflammation pathway and that displayed a striking gene expression profile was CD74, a transmembrane receptor for macrophage migration inhibitory factor (MIF), a pro-inflammatory cytokine. In particular, CD74 upregulation exhibited an exponentially increasing trend near 240h only in P30 animals. Furthermore, microarray data from human hippocampal tissue from patients with mesial temporal lobe epilepsy (MTLE) also confirm an upregulation of CD74 compared to control.

In the present study, we performed immunohistochemistry to verify our microarray data and to localize CD74 expression in rat brains (P15 and P30) and in surgically resected cortices from patients with intractable epilepsy.