CP-07

The mechanisms of EGFR in the regulating intrinsic growth activity of central neurons

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The objections of this study was to understand the relationship between EGFR and axon regeneration and to investigate the mechanisms of how EGFR regulating the neuronal intrinsic regenerative ability. Central expressions of EGFR, total mTOR, p-mTORSer2448, total Akt and p-AktSer473 were evaluated in rats of different developmental stage using Western blot analysis and Real-time PCR. Neuron cells were cultured with different EGFR expression levels. Rapamycin was used as an inhibitor of mTOR. Axon protein Tau, neuron proteins β-tubulin and neurofilament were assessed to evaluate the extent of the axon regeneration. Expressions of EGFR, total mTOR, p-mTOR^{Ser2448}, total Akt and p-Akt^{Ser473} were detected using Western blot analysis in cultured neuron. The expressions of EGFR and mTOR dropped off with the aging of the rats. No significant differences were found in the expressions of total Akt levels between each group of rats. p-Akt^{Ser473} and p-mTOR^{Ser2448} were highly expressed in fetal and newborn rats but decreased obviously in adult rats. Tau, β-tubulin and neurofilament were up-regulated when EGFR was overexpressed and down-regulated after EGFR was blocked. The phosphorylation of mTOR and Akt were apparently elevated when EGFR was overexpressed and decreased when EGFR was blocked. The upregulation effects of the mTOR by EGFR were blocked by rapamycin. So, EGFR has the potential to regulate the neuronal intrinsic regeneration, mTOR and PI3K/Akt pathway activation may have an important role in it.

CP-08

Genetic Dissection of Glutathione S-transferase Omega-1: Identification of Novel Downstream Targets and Alzheimer Disease Pathways

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Previous studies demonstrate that *Gsto1* plays a protective role against oxidative stress and may also influence the progression of AD. Gene expression profiling of BXD family was combined with linkage analysis to characterize mechanisms controlling *Gsto1* expression and to identify network members that may contribute to AD risk or progression. Higher expression of *Gsto1* was associated ($P < 0.01$) with inheritance of the B6 allele in hippocampus, cortex, striatum, and cerebellum. Allele-specific assays verify that the expression of *Gsto1* is controlled by a *cis*-acting QTL. We leveraged endogenous variation in *Gsto1* expression to identify 1. a coexpression network, 2. downstream molecular targets, and 3. downstream phenotypes. We identified 140 transcripts that are highly correlated with *Gsto1* expression variation. Some of these have previously been implicated in AD including *Acat1*, *Chmp2b*, *Dlst*, *Optn*, and *Sod2*. We also identified *Pa2g4* as a downstream target of *Gsto1* by a combination of linkage and partial correlation analyses. To evaluate relations between *Gsto1* and candidate downstream network members we transfected astrocytes with *Gsto1* siRNA and were able to confirm a significant influence on the expression of *Pa2g4*. Both this genetic approach and the validated downstream targets provide new insight into the biological role of *Gsto1* and modifers of the risk and progression of AD.