P1-c05 Astroglial cell assemblies

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Over the past years, many studies have focused only on neurons, and astrocytes are considered to be non-excitable passive cells. Recent studies have revealed that they are active participants that may exert significant control over a huge CNS network. However, many studies have focused on properties of individual astrocytes, and little is known about their collective behavior. What are their properties as communication elements in a neuro-glial network? We therefore performed immunohistochemistry and revealed that their physical locations are arranged at almost regular intervals of 20–30 μm. Furthermore, we observed spontaneous activities of hippocampal astrocytes for as long as 1hr using Ca^{2+} imaging techniques. The cross-correlogram between all pairs of approximately 200 astrocytes showed that astrocytes in closer vicinity tended to exhibit more correlated activities. These properties are clearly different from neurons, and our findings will lead to better understanding of neuro-glial network function.

P1-c06 ZNRF1 regulates glutamine synthetase protein expression in Schwann cells via a ubiquitin-proteasome pathway

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Ubiquitin-proteasome system has been implicated in a variety of neuronal functions. We have previously identified a novel E3 ubiquitin ligase, zinc finger/Ring finger 1 (ZNRF1), which is up-regulated in Schwann cells of degenerating peripheral nerves. Here we have identified glutamine synthetase (GS) as a protein targeted by the ZNRF1-dependent proteasomal degradation mechanism. In neuro2a cells, forced expression of ZNRF1 reduced the GS protein level in a dose-dependent manner, and this effect was blocked by a proteasome inhibitor. In a mouse sciatic nerve transection model, injury induced ZNRF1 expression in a segment distal to the injury site resulted in the decreased expression of GS protein, while its mRNA remains the same. These findings suggest that, unlike most other proteins characterizing Schwann cell phenotypes, GS expression is regulated post-translationally by ZNRF1 E3 ligase-dependent ubiquitin-proteasome degradation mechanism.
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P1-c09 Extracellular S100B increases the amplitude of kainate-induced gamma oscillation *in vivo*

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S100B is predominantly synthesized by astrocytes and secreted to the extracellular space. The secreted S100B exerts various effects on neurons, astrocytes and microglia depending on the concentration. We have shown that the amplitude of kainate-induced gamma oscillation in CA1 str. radiatum is significantly smaller in S100B knockout mice (Sakatani et al., 2007). To assess the contribution of extracellular S100B to the gamma oscillation, we combined local field potential recording and local infusion of dimeric S100B at CA1 str. radiatum in S100B KO mice. Local infusion of low concentration (100 nM) S100B did not have a significant effect on kainite-induced gamma oscillation. At a high concentration (10 μM) of S100B, local infusion of S100B resulted in an increase of the gamma oscillation. In a separate set of experiments, anti-S100B antibody was locally applied in wild-type mice, resulting in a decrease of the gamma oscillation amplitude. Our results suggest that extracellular S100B increases the amplitude of kainate-induced gamma oscillation.

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P1-c10 Activity-dependent glial coverage in the rat nucleus of tractus solitarius during postnatal development

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Glial cells contribute to maturation of synapses in developing nervous system. We have previously reported that, in the rat caudal nucleus of tractus solitaries (cNTS) during postnatal development, the decrease of axosomatic synapse number in small cell soma appears to depend on increase of glial coverage by astrocytic processes. However, the factors influencing the increase of glial coverage in cNTS remain unknown. In the present study, to elucidate whether the neural activity facilitate glial coverage of small cell soma in cNTS, the effects of activity blockade in vivo were examined. Deprivation of activity with intraperitoneal injection of MK801, NMDA receptor antagonist, at P5-P8 caused less matured glial coverage in small cell somata at P10 and P21. These results suggest that glial differentiation around soma requires neural activities. Activity-dependent pathway involving astrocytes might play a role in decrease of axosomatic synapse number in small cell during developing cNTS.

P1-c11 The sensitivity of differentiated astrocytes to hydrogen sulfide is diminished in the reactive astrocytes

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Hydrogen sulfide (H_2S), which enhances the induction of hippocampal long-term potentiation and induces calcium waves in astrocytes, has been proposed to be a synaptic modulator in the brain. Here we show that differentiated astrocytes acquire sensitivity to H_2S that is diminished by their transformation into reactive astrocytes. Although NaHS, a donor of H_2S, did not increase the intracellular concentration of Ca^{2+} in progenitors, exposure to leukemia inhibitory factor, which induces differentiation into glial fibrillary acidic protein-positive astrocytes, increased the sensitivity to NaHS. In contrast, epidermal growth factor (EGF), transforming growth factor α, dibutyryl cyclic AMP and interleukin-1β induced the conversion to reactive astrocytes with diminished sensitivity to NaHS. This effect of EGF was inhibited by cycloheximide, indicating that de novo protein synthesis was required for the suppression of NaHS sensitivity.

P1-c13 mRNA expression profile of claudin subtypes in mouse blood–brain barrier

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Tight junctions (TJs) are an important component of the blood–brain barrier (BBB). To understand the contribution of each claudin subtype to TJ formation, we have measured the mRNA expression levels of claudin-1 to -23 in highly purified mouse brain capillary endothelial cells (BCECs). Mouse BCECs were isolated with anti-PECAM-1 antibody by magnetic cell sorting. Expression of Tie-2, Mdr1a and GLUT1 mRNAs was concentrated in the isolated fraction. Among claudin subtypes, claudin-5 was most highly expressed, at a level which was at least 593-fold greater than that of claudin-1, -3 or -12. Expression of mRNAs of claudin-8, -10, -15, -17, -19, -20, -22 or -23 was also concentrated in the isolated fraction, suggesting these subtypes are expressed in mouse BCECs. The levels of claudin-10 and -22 mRNAs were comparable with that of occludin mRNA. These results indicate that claudin-5 is the most abundant claudin subtype in mouse BCECs, and are consistent with the idea that claudin-10 and -22 are involved in TJ formation at the BBB in cooperation with claudin-5.