F109

Abnormal Phototransduction Cascade during Diabetes in the Rat Retina

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The phototransduction of vertevrate photoreceptor cells is a well studied G protein-mediated signaling pathway. Transducin (GT) and Rhodopsin kinase (RK), G protein-coupled proteins, are assumed to regulate light sensitivity in the retina as interact with Rhodopsin (Rho). We obtained preliminary data by northern blotting that the expressions of GT and RK are changed abnormally in the retina at early stage 6 weeks in streptozotocin (STZ)-induced diabetic rat. The alternated change and interaction might be induced abnormal photosenstivity and visual dysfunction in the retina during diabetes. For investigation more definitely about the role of photoreceptor proteinsin diabetic retina, we carried out western blotting, immunohistochemistry and immunoprecipitation using GT, RK and Rho antibodies in the retina 6 weeks after induction compared with control. Recently, signalling of photoreceptor proteins, GT, RK in retinais studing to associate with oscillatory potential, oxidative stress, vascular change as well as phototransduction, and so their changes may also induce neuronal dysfunction in diabetic rat retina. As a result, we confirmed that the photoreceptor proteins changed abnormally in the diabetic retina and interacted alternately. These could aid with understanding the complicate pathology in the retina during diabetes.

F110

A Novel Regulatory Role for Liver X Receptors in Adipogenesis

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Liver X receptors (LXRs) are nuclear hormone receptors that regulate cholesterol and fatty acid metabolism in liver and macrophages. Although adipose tissue is a major lipid metabolism organ, it is not known whether LXR activation regulates adipocyte differentiation. Here we show that LXR activation stimulated adipocyte differentiation, as determined by lipid droplet accumulation and adipogenic marker gene expression in the preadipocyte cell lines 3T3-F442A and 3T3-L1, and in primary human preadipocytes. Acute LXR activation in fully differentiated adipocytes primarily induced expression of the lipogenic genes LXR, ADD1/SREBP1c and FAS and the adipogenic genes PPARand aP2. Administration of the LXR agonist T0901317 to mice enhanced expression of most types of adipogenic genes in white adipose tissue. In addition, suppression of endogenous LXR expression by specific siRNA abolished adipogenesis. Taken together, these results suggest that LXR activation induces lipogenic gene expression in fat and liver, and identifies a novel function for LXRs in adipogenesis.

F111

Twist2, a Member of bHLH Proteins, Inhibits Transcriptional Activity of ADD1/SREBP1c through Physical Interaction

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ADD1/SREBP1c is a key transcription factor for fatty acid metabolism and insulin dependent gene expression. Although it has been extensively studied for the transcriptional and post-translational regulation of ADD1/SREBP1c, functional modulation of ADD1/SREBP1c through interacting proteins has been not well understood. To identify and characterize cellular protein(s) that physically associates with ADD1/SREBP1c, we adopted yeast two-hybrid system with adipocyte cDNA library, using the N-terminal domain of ADD1/SREBP1c as a bait. Twist2 (also known as Dermo-1), a basic helix-loop-helix (bHLH) protein, has been isolated as an ADD1/SREBP1c interacting protein. Overexpression of Twist2 potentially repressed the transcriptional activity of ADD1/SREBP1c, which was mediated by reducing the DNA binding ability of ADD1/SREBP1c to its target sequences with Twist2. Furthermore, inhibition of HDAC activity with HDAC inhibitors relieved Twist2-dependent transcriptional suppression of ADD1/SREBP1c, implying that Twist2 would also modulate the transcriptional activity of ADD1/SREBP1c with HDAC. Taken together, our data suggest that physical interaction between Twist2 and ADD1/SREBP1c would attenuate the transcriptional activation by ADD1/SREBP1c through suppressing DNA binding ability of ADD1/SREBP1c and chromatin modification with HDAC.

F112

The Modulatory Role of Nitric Oxide Increased by Ketogenic Diet in the Regulation of c-fos and Proenkephalin Gene Expressions Induced by Kainic Acid

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For a long time nitric oxide (NO) has been proposed to play role in regulation of seizure. However, the precise role of NO in the convulsive phenomina is controversial till now. Here, wehave found that ketogenic diet (KD) for 4 weeks increases the endogenous NO generation in the hippocampus.In the present study, we have demonstrated that NO increased by KD exerts an anti-convulsant effect on KA-induced seizure using NO synthase (NOS) inhibitors, L-NAME or 7-NI. NO plays an important role in inhibiting KA-induced proenkephalin (PENK) mRNA expression, and its inhibitory action maybe mediated through reducing proto-oncoprotein levels, such as c-fos. Using northern blot analysis, in situ hybridization, and western blot analysis, we found that pretreatment of KD leads to marked reduction of the KA-mediated c-fos protein expression in the hippocampus. And also found that KD strongly inhibits the KA-mediated increment of PENK mRNA levels in the dentate gyrus. Therefore, these findings indicate that the antiepileptic effects of KD is may be mediated by the inhibition of KA-induced increases of c-fos and PENK by the effect of NO, which is increased by KD, in the hippocampus.