**Fig. S1** High glucose induces reactive oxygen species (ROS) in cultured neurons. Neonatal hippocampal neurons were cultured with normal glucose (25 mmol/L) or high glucose (50 mmol/L) for 24 h. The high glucose significantly enhances ROS production as assessed by a ROS assay kit (Beyotime, Nantong, China).

**Fig. S2** Absence of CpG islands in the p2x4r gene promoter. The promoter sequence of p2x4r gene is 2000 bp before the transcriptional start site (TSS) in the NCBI Genbank database. There are no CpG islands in the p2x4r gene promoter according to online prediction by Methprimer software.