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# Chromatin structure and expression of the AMPA receptor subunit GluR2 in human glioma cells and the role of REST

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The AMPA receptors are postsynaptic ion channels that open following stimulation with glutamate. The regulatory region of the gene encoding the GluR2 subtype of AMPA receptors contains a binding site for the transcriptional repressor REST. The cell-type specific microenvironment, in particular the cell type-specific structure of the chromatin, is crucial for the ability of REST to control target gene transcription. Using antibodies directed against methylated lysine residues 4 or 9 (H3K4 or H3K9) of histone H3, we show that the GluR2 gene has an open chromatin configuration in human U87MG glioma cells, with nucleosomes carrying di-and trimethylated H3K4. In contrast, the GluR2 gene is embedded into a repressed chromatin environment in non-neuronal hepatoma cells and keratinocytes. Chromatin immunoprecipitation experiments revealed binding of REST and histone deacetylase-1 to the GluR2 gene under physiological conditions. While overexpression of REST reduced GluR2 mRNA levels, expression of a mutant of REST that contained a transcriptional activation domain enhanced GluR2 gene transcription in U87MG glioma cells. Treatment of the cells with the histone deacetylase inhibitor trichostatin A (TSA) induced an upregulation of GluR2 expression, indicating that the transcription of the GluR2 gene is dependent of the balance between histone acetylation and deactylation. Transcription of the GluR2 gene was also inducible by TSA following inhibition of Sp1 target gene transcription, indicating that the inhibition of Sp1 is not required for the upregulation of GluR2 expression following histone deacetylase inhibition.