



Protein Disulfide Isomerase A3 Modulates PKC ζ and Cdk5 Gene Expression in Primary Cortical Neuron Cultures

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PDIA3 silencing alters PKC ζ and Cdk5 gene expression, suggesting a previously unexplored link between PDIA3 and PKC ζ /Cdk5-associated signaling pathways in Alzheimer's disease.

INTRODUCTION

Protein Disulfide Isomerase A3 (PDIA3), a chaperone protein located in the endoplasmic reticulum (ER), has been demonstrated to promote axonal regeneration and inhibit amyloid beta (A β) aggregation, one of the main pathologies of Alzheimer's Disease (Gezen-Ak et al., 2017). In cortical neurons, silencing the PDIA3 gene results in increased amyloid production (Gezen-Ak et al., 2017). PKC ζ and Cdk5 are proteins involved in intracellular signal transduction, synaptic activity, and neuronal development, and have also been associated with Alzheimer's disease pathology (Lucke-Wold et al., 2014; Liu et al., 2015). However, their relationship with PDIA3 is not fully understood. The purpose of this study was to investigate how PKC ζ and Cdk5 gene expression is affected when the PDIA3 gene is silenced.

METHODS

siRNA treatment was used to silence the PDIA3 gene in primary rat cortical neuron cultures. At 24 and 48 hours after the siRNA treatment, total RNA was isolated. Quantitative real-time PCR (qRT-PCR) was used to measure the expression levels of the PKC ζ and Cdk5 genes after cDNA synthesis. The statistically analyze was carried out with one-way ANOVA using GraphPad Prism 8.

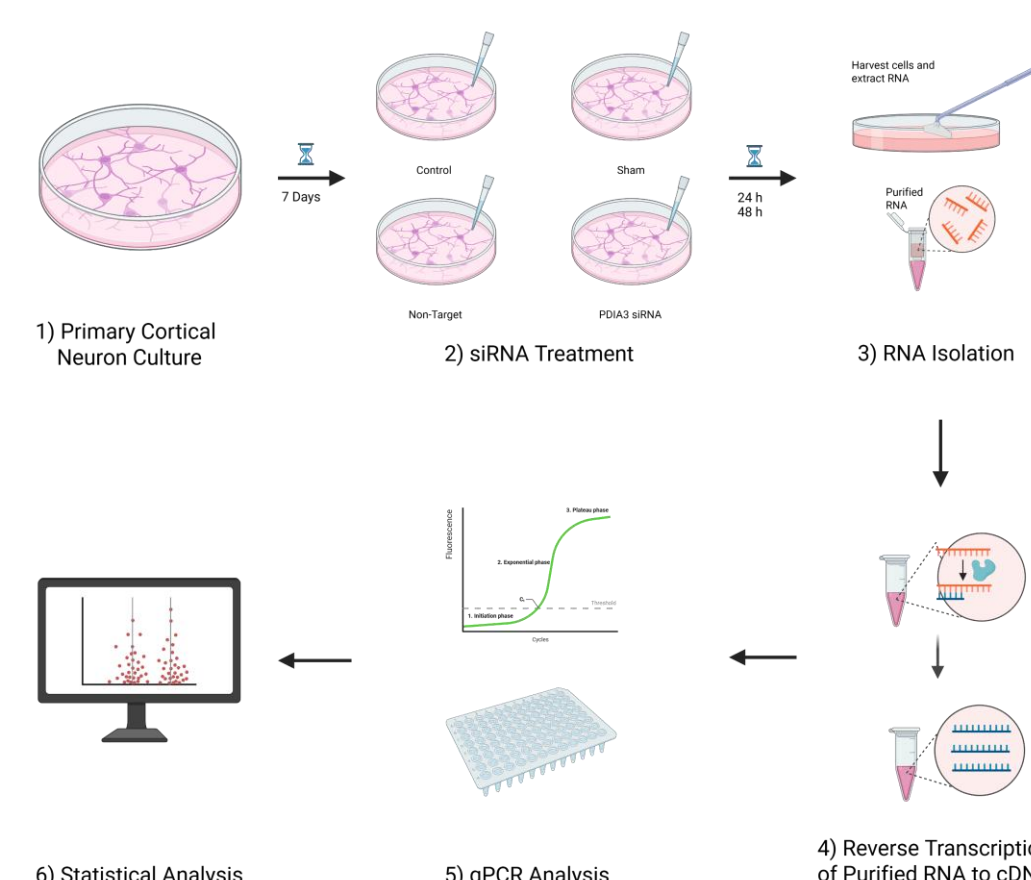


Figure 1: Workflow Diagram: The process of analyzing gene expression changes following siRNA-mediated gene silencing in cultured cells

RESULTS

PKC ζ gene expression was significantly higher in the PDIA3 siRNA group than in the non-target group at 24 hours after PDIA3 siRNA treatment ($p < 0.01$). Comparing the PDIA3 siRNA group to the control and non-target groups, Cdk5 gene expression was also significantly higher ($p < 0.001$). At 48 hours, PKC ζ gene expression was significantly lower in the PDIA3 siRNA group than in the non-target group ($p < 0.05$), although Cdk5 gene expression levels did not differ significantly across the groups.

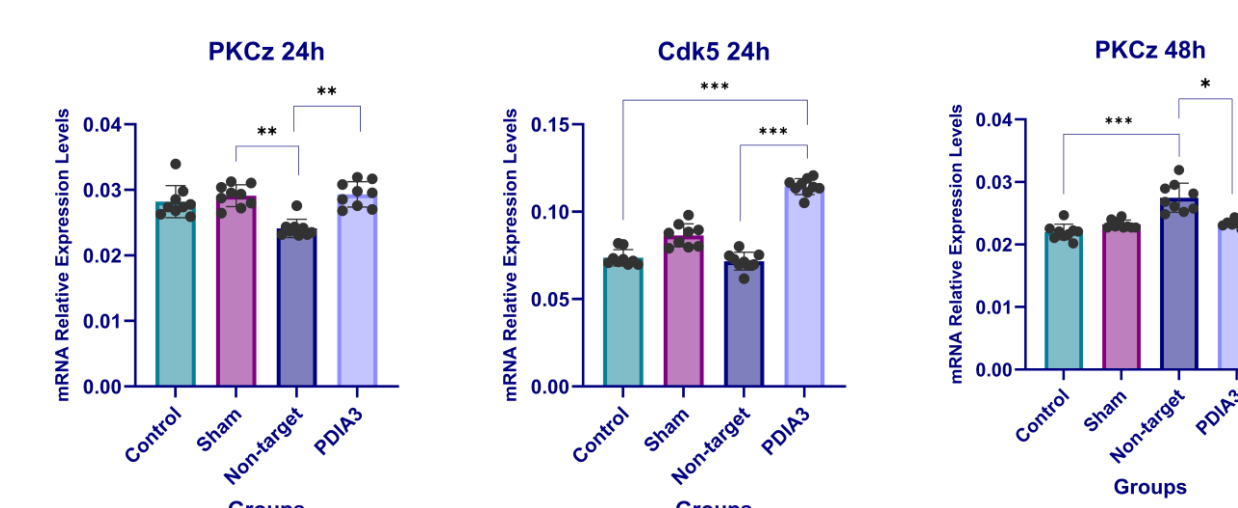


Figure 2: mRNA expression levels of Cdk5 and PKC ζ genes at 24h and 48h of primary cortical neurons with PDIA3 siRNA treatment

CONCLUSIONS

Our results indicate that silencing the PDIA3 gene, which is suggested to play a role in preventing A β aggregation in Alzheimer's disease, may affect the expression levels of the PKC ζ and Cdk5 genes. This study contributes to a better understanding of the potential role of PDIA3 in the pathology of Alzheimer's Disease. The study is supported by TUBITAK (Project No: 216S586).

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