Effect of siRNA-induced silencing of cellular prion protein on tyrosine hydroxylase expression in the substantia nigra of a rat model of Parkinson’s disease

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ABSTRACT. The most significant pathological feature of Parkinson’s disease (PD) is the progressive degeneration of dopaminergic (DA) neurons in the substantia nigra. Currently, available treatments for PD cannot prevent the loss of DA neurons. Tyrosine hydroxylase (TH) expressed in substantia nigra neurons catalyzes the conversion of tyrosine to L-3,4-dihydroxyphenylalanine (L-DOPA), which is the rate-limiting step of DA biosynthesis. Major reasons for PD occurrence include decreased TH activity in the substantia nigra and secondary DA suppression. Decreased TH activity and the resulting suppression
of DA synthesis (or neurotransmission) in the substantia nigra are key factors underlying the development of PD. Cellular prion protein (PRP) is a membrane glycoprotein expressed in the central nervous system. Although the sequence of PRP is highly conserved, its physiological function is unclear. The purpose of this study was to investigate the effect of PRP-targeted small interfering RNA (siRNA) on TH expression in a rat model of PD. Thirty male Wistar rats were injected with 6-hydroxydopamine (6-OHDA) to generate a model of PD. The rats then received injections of PRP-siRNA or nonsense siRNA in the lateral ventricles. Substantia nigra samples were collected for quantification of PRP and TH expression using real-time polymerase chain reaction and western blotting. PRP-siRNA decreased PRP expression in the substantia nigra. TH expression was decreased in PD model rats but was increased after PRP silencing. We conclude that PRP-siRNA may increase TH expression in vivo and may therefore exert protective effects on neurons in a model of PD.

**Key words:** Parkinson’s disease; Substantia nigra; Tyrosine hydroxylase; Cellular prion protein; Small interfering RNA