The tyrosine kinase inhibitor imatinib mesylate delays prion neuroinvasion by inhibiting prion propagation in the periphery.

Abstract:

Prion diseases are fatal neurodegenerative disorders with no effective therapy. A hallmark of prion disease is the conversion of the normal cellular form of prion protein PrP(C) into a disease-associated isoform PrP(Sc). The authors recently have shown that a tyrosine kinase inhibitor, imatinib mesylate, induces clearance of PrP(Sc) via specific inhibition of c-Abl in prion-infected cell culture models. In this study, the authors assessed the in vivo effects of imatinib mesylate on prion disease using a scrapie-infected mouse model and further investigated prion infectivity of the drug-treated scrapie-infected neuroblastoma (ScN2a) cells. The authors found that imatinib mesylate abolished prion infectivity to almost undetectable level in ScN2a cells and the level of PrP(Sc) was significantly decreased by the drug in scrapie-infected mouse spleens as well as in ScN2a cells. Moreover, the drug treatment at an early phase of peripheral scrapie infection delayed the appearance of PrP(Sc) in the central nervous system (CNS) and onset of clinical disease in mice. However, neither intraperitoneal nor intracerebroventricular delivery of the drug exerted any PrP(Sc) clearance effect in the CNS.