Prion diseases are fatal neurodegenerative infectious disorders for which no therapeutic or prophylactic regimens exist. Understanding the molecular process of conformational conversion of the cellular prion protein (PrP(c)) into its pathological isoform (PrP(Sc)) will be necessary to devise effective antiprion strategies. In recent years, new findings in the cell biology of PrP(c), in the molecular pathogenesis of PrP(Sc), and in the cellular quality control mechanisms involved in these scenarios have accumulated. A function of the prion protein in signalling, the possible impact of the proteasome, and aggresomes as intracellular waste deposits have been described. Here, important pathogenetic similarities with the more frequent neurodegenerative disorders are evident. The need for therapeutic, postexposure, and prophylactic possibilities was drastically illustrated by the emergence of variant Creutzfeldt-Jakob disease (vCJD), a new human prion disease caused by bovine spongiform encephalopathy (BSE) derived prions. Although prion infectivity in humans is usually restricted to the central nervous system, in vCJD patients prions are present in the lympho-reticular system, posing a theoretical risk of accidental human-to-human transmission. A variety of chemical antiprion substances have been reported in in vitro and cell culture based assays or in animal studies. Occasionally, they have also made their way into the first human trials. In addition, various promising
interference strategies have been devised in transgenic models, although they are usually hard to transfer into nontransgenic in vivo situations. New findings in the fields of peripheral prion pathogenesis and immune system involvement fuelled the search for antiprion strategies formerly considered to be entirely impossible. This opened the door towards classical immunological interference techniques. Remarkably, passive and even active vaccination approaches now seem to be realistic goals.