Conformational conversion of the recombinant hamster prion protein $SHaPrP^{90–232}$ studied by Fourier transform infrared spectroscopy and dynamic light scattering

Fabian Sokolowski[1], Ralf Masuch[2], Andreas Modler[3], Michael Baier[1], Klaus Gast[3], and Dieter Naumann[1]

[1]Robert-Koch-Institut, Nordufer 20, D-13353 Berlin, Germany. E-mail: NaumannD@rki.de
[2]Forschungszentrum Karlsruhe, Hermann-von-Helmholtz-Platz 1, D-76344 Eggenstein-Leopoldshafen, Germany. Current address: micro-biolytics GmbH, Georges-Köhler-Allee 102, D-79110 Freiburg, Germany.
[3]Max-Delbrück-Centrum für Molekulare Medizin (MDC), Robert-Rössle-Str. 10, D-13125 Berlin, Germany. E-mail: gast@mdc-berlin.de

The prion protein (PrP) is thought to be responsible for causing transmissible spongiform encephalopathies (TSE), which are neurodegenerative disorders such as BSE in cattle, scrapie in sheep and Creutzfeldt-Jakob disease in humans. The essential step in the transmission and manifestation of these prion diseases seems to be the misfolding of benign cellular PrP (PrP^{c}) to pathogenic PrP (PrP^{Sc}). Whereas PrP^{c} has a mainly α-helical structure, PrP^{Sc} seems to be predominantly folded in β-sheets. PrP^{Sc} has the strong tendency to accumulate in neural tissue and to aggregate into insoluble amyloid fibrils.

To study the folding properties of PrP in vitro we expressed a his-tagged fragment of recombinant Syrian hamster PrP^{c} (amino acids 90–232) in *Escherichia coli* as inclusion bodies. The protein was solubilized in guanidinium hydrochloride (GdnHCl), purified on nickel agarose, and oxidized. After further purification by HPLC it was examined by Fourier Transform Infrared (FT-IR) spectroscopy and dynamic light scattering (DLS) as a function of denaturant (GdnHCl) concentration, ionic strength, and pH.

By analyzing the amide I and amide II region of the FT-IR spectra, our findings show that the secondary structure of PrP is converted from mainly α-helical (bands at 1651 and 1550 cm^{-1}, respectively) to mainly β-sheet (bands at 1619 and 1540 cm^{-1}, respectively) at low pH (4.2) and at either 1–2 M GdnHCl or at sodium chloride concentrations of 0.8–2 M. In contrast, at the same concentrations of GdnHCl or sodium chloride at pH 7.0 such a conversion cannot be observed.

Light scattering measurements show a two phase growth of large PrP aggregates at pH 4.2 and 1 M GdnHCl via a temporarily stable oligomeric intermediate with a 16-fold mass of the monomeric PrP.