8 Summary

First of all, the aim of this study was to improve the sensitivity for the detection of PrP\textsuperscript{Sc}/PrP\textsubscript{27-30}, the biochemical marker for TSE-agents by Western-blotting. During this work it was possible by technical optimization of this method to increase the sensitivity by a factor of 200 fold allowing the detection of PrP\textsuperscript{Sc} from at least 6x10\textsuperscript{-6} g brain homogenate from terminally ill scrapie hamsters. By using new purification methods and introducing a collagenase-A digestion step it was possible to detect PrP\textsuperscript{Sc}/PrP\textsubscript{27-30} also from gut tissue by Western-Blot analysis. Subsequently by means of these improved purification and Western-blot methods the detection of PrP\textsuperscript{Sc}/PrP\textsubscript{27-30} in muscles of orally infected hamsters could be achieved already from animals from the preclinical phase of scrapie.

Besides the described technical advances it could be shown in this thesis that rectum biopsies can be used as a practical tool for TSE-diagnosis in living animals. However, this was only applicable in the terminal stage disease, since the amount of PrP\textsuperscript{Sc} in the rectum is in earlier stages not high enough for Western-blot detection. Hence, so far there is no significant advantage in comparison to other methods for an in vivo diagnosis of scrapie.

Furthermore, in this work a new PrP\textsuperscript{Sc} extracting method from faeces was established, facilitating a direct PrP\textsuperscript{Sc} detection in this tissue. By using the new method it could be shown that only 1-2 days after oral infection PrP\textsuperscript{Sc} is present in faeces. However, in samples from later time-points no PrP\textsuperscript{Sc} is detectable.

In contrast to earlier reports, where only the impact of a contact with possibly prion contaminated materials have been studied (Miller et al., 2004), in this work a more precise estimation for the risk of a transmission via faeces could be achieved.

Provided that the results in this study gained from a hamster model could be mirrored to natural hosts like sheep and deer, there is no justified evidence for an oral-faecal transmission of scrapie or chronic wasting disease in these animals.

The results from the in this work performed immunohistochemical examinations regarding the location of PrP\textsuperscript{Sc} within the gut wall are in good accordance with already published data and provide a spatial precise detection of the pathological prion protein in the small intestine. The intestinal PrP\textsuperscript{Sc} accumulation is localized predominantly apical in the mucosal epithelium with a relatively large distance to the epithelial cells of the gut lumen. By this observation it could be explained why no or only undetectable amounts of PrP\textsuperscript{Sc} from the gut wall are excrited together with the faeces.