

In Situ Prion Protein Structural Changes in Scrapie

Beamline: U10B

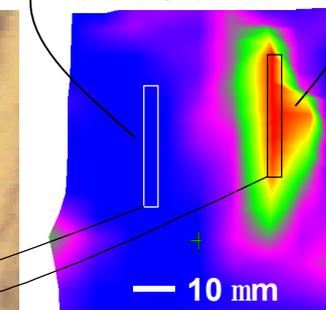
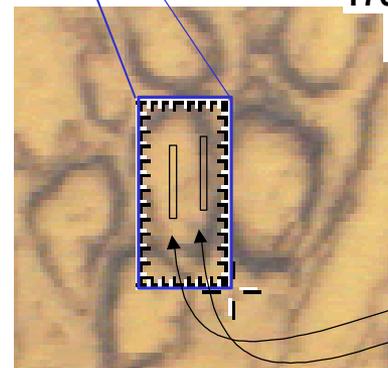
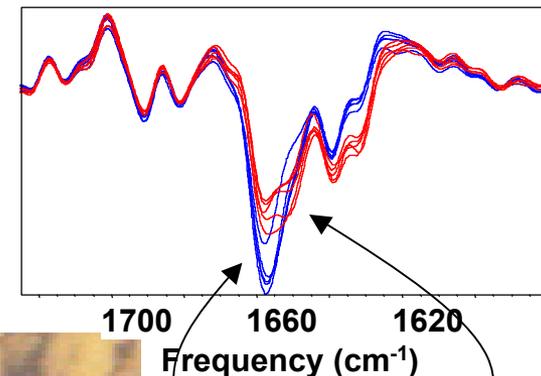
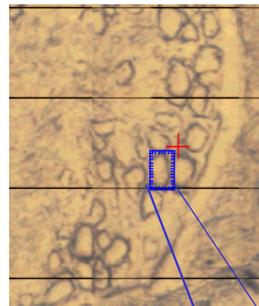
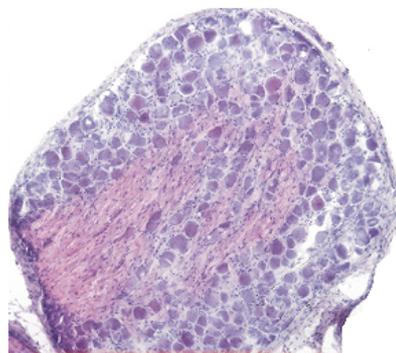
Technique: Infrared
microspectroscopy

Researchers:

L. Miller, Q. Wang (BNL)
J. Kneipp, A. Kretlow, P.
Lasch, M. Beekes, D.
Naumann (Robert Koch
Inst., Berlin)

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J. Kneipp, L.M. Miller, M.
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M. Beekes, D. Naumann.
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Motivation: Transmissible spongiform encephalopathies, such as scrapie, mad cow disease, and Creutzfeldt-Jakob disease, are a group of fatal neurodegenerative disorders characterized by the conversion of the normal prion protein into aggregates of its pathological conformer. To analyze the disease-related protein structural changes directly in the tissue environment, we have examined protein structure within the dorsal root ganglia in the 263K scrapie hamster model.

Results: Using synchrotron-based infrared microscopic imaging, individual neurons are scanned for the distribution of protein structure based on the infrared absorption of the protein backbone mode (Amide I: 1700–1600 cm^{-1}). The high brilliance of the synchrotron infrared light source permitted sub-cellular spatial resolution. We observe regions of increased β -sheet and decreased α -helical structure in and/or around scrapie-affected cells. No evidence of these structural changes is observed in normal neurons. Comparison of the infrared images with PrP^{Sc} immunostaining of the same tissue demonstrated that the elevated β -sheet regions correspond to the misfolded structure of PrP^{Sc} .

(Top left) Dorsal root ganglia of a hamster. Nerve fibers are pink; neurons are purple. (Top right) Unstained dorsal root ganglia illustrating the neuron imaged by IR microspectroscopy. Second derivative infrared spectra show increased β -sheet content near the membrane of infected cells.