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Prion Diseases in Animals

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central nervous system. Although multiple events, including ER stress caused by the accumulation of PrP^{Sc} aggregates, activated astrocytes and/or microglia or synaptic and dendritic alterations, have been suggested to be involved in neurodegeneration, its molecular mechanism is not fully understood yet. Neuronal cell lines used for analyses of the cellular mechanism of prion propagation have so far shown little cytopathic effect. Thus, a novel ex vivo experiment system, in which the generation of PrP^{Sc} in neurons and neurodegeneration can be reproduced, is required. Thus we analyzed prion infection in primary cortical neurons.

Materials and Methods. Mouse primary cortical neurons were obtained from 15-day mouse embryo. Four different prion strains, 22L, Chandler, Obihiro, and BSE-KUS, were used. PrP^{Sc}-specific staining was carried out using mAb132.

Results and Discussion. All the four prion strains could effectively produce PrP^{Sc} in primary cortical neurons, confirming the prion infection. Interestingly, the shape of PrP^{Sc}-staining observed confocal microscopy differed with strains; string shape staining was pronounced in cortical neurons infected with 22L or Chandler strains, whereas granular staining was mainly observed in Obihiro and BSE-KUS strain infection. A slight decrease in cell viability and in the expression of synaptic proteins such as PSD95 and N-cadherin was observed; however, double staining of PrP^{Sc} with tunnel-staining and cleaved caspase-3 did not reveal apoptosis of primary cortical neurons infected with prions. Efficient PrP^{Sc} generation in cortical neurons without neuronal cell death suggests that certain causes other than neurons, such as factors produced from activated astrocytes and/or microglia play a critical role in the neurodegeneration caused by prion infection. Analyses of neuron-glia interaction using prion-infected primary cortical neurons co-cultured with astrocytes or microglia may provide a clue to elucidate the neurodegenerative mechanisms of prion diseases.

P.131: Transmission of sheep-bovine spongiform encephalopathy in pigs

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Introduction. The transmissible spongiform encephalopathies (TSE) don´t occur in swine in natural conditions. However, the bovine spongiform encephalopathy (BSE) agent, inoculated by 3 simultaneous routes in pigs, is able to reproduce a neurological disease in these animals. On the other hand, the BSE agent after passage in sheep under experimental conditions (sheep-BSE) exhibits altered pathobiologic properties. This new agent is able to cross the cattle-pig transmission barrier more efficiently than BSE. The potential propagation of TSE in animals from the human food chain, including pigs, needs to be assessed regarding the risk for human infection by animals other than TSE-infected ruminants. The aim of this work was to determine the susceptibility of pigs to the Sheep-BSE agent and describe the pathological findings and PrP^{Sc} deposition in different tissues.

Material and Methods. Seven minipigs were challenged intracerebrally with sheep-BSE agent. Clinical observation and postmortem histopathology, immunohistochemistry (antibody 2G11) and Western blotting were performed on central nervous system (CNS), peripheral nervous system (PNS) and other tissues.

Results. One pig was culled in an early incubation stage, and remaining six were culled at the presence of clinical sings. Pigs developed a clinical disease with locomotor disorders in an average time of 23 months post inoculation, showing clinical findings in most of them earlier than those described in the BSE in pigs experimental infection. TSE wasn´t confirmed in the preclinical pig. In clinical pigs, the entire cerebral cortex showed severe neuropil vacuolation, extensive and severe vacuolar changes affecting the thalamus, hippocampus and cerebellum. PrP^{Sc} was found in CNS of all clinical pigs (6/6). Intracellular (intraneuronal and intraglial) and neuropil-associated PrP^{Sc} deposition was consistently observed in the brainstem, thalamus, and deeper layers of the cerebral cortex. Also, PrP^{Sc} was observed in PNS, mainly in the myenteric plexus and also in nerves belonging to the skeleton muscle. Moreover, the glycosylation profile showed a 3 band pattern with a predominant monoglycosylated band in positive pig samples. This features concern on the potential risk of utilization of meat and bound meal of small ruminants in feeding pigs.

P.132: Full-length PrP^{C} but not PrP-C1 is depleted in autolytic brainstem samples of cattle

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Introduction. In summers 2011 to 2013 in Switzerland, several brainstem samples from cattle in a severely autolytic stage were reactive with some of the BSE screening tests, but remained unconfirmed. In the Western immunoblot (WB), a truncated form of PrP^{res} type was detected after proteinase K (PK) digestion, with a profile distinct from either H-, L- or C-BSE. In order to investigate whether this particular PrP profile was related to the effects of severe autolysis, we compared the PrP species present in these autolytic samples to those in non-autolytic BSE negative samples and BSE positive samples.

Material and methods. Fallen stock autolytic brainstem samples that were initially reactive in the screening laboratory were selected. Freshly prepared control brains were collected at the slaughterhouse. All samples were analyzed with and without PK digestion and deglycosylation respectively using standard