Frist evidence of intracranial and peroral transmission of Chronic Wasting Disease (CWD) into Cynomolgus macaques: *a work in progress*

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This is a progress report of a project which started in 2009. 21 cynomolgus macaques were challenged with characterized CWD material from white-tailed deer (WTD) or elk by intracerebral (ic), oral, and skin exposure routes. Additional blood transfusion experiments are supposed to assess the CWD contamination risk of human blood product. Challenge materials originated from symptomatic cervids for ic, skin scarification and partially per oral routes (WTD brain). Challenge material for feeding of muscle derived from preclinical WTD and from preclinical macaques for blood transfusion experiments. We have confirmed that the CWD challenge material contained at least two different CWD agents (brain material) as well as CWD prions in muscle-associated nerves.

Here we present first data on a group of animals either challenged ic with steel wires or per orally and sacrificed with incubation times ranging from 4.5 to 6.9 years at postmortem. Three animals displayed signs of mild clinical disease, including anxiety, apathy, ataxia and/or tremor. In four animals wasting was observed, two of those had confirmed diabetes. All animals have variable signs of prion neuropathology in spinal cords and brains and by supersensitive IHC, reaction was detected in spinal cord segments of all animals. Protein misfolding cyclic amplification (PMCA), real-time quaking-induced conversion (RT-QuiC) and PET-blot assays to further substantiate these findings are on the way, as well as bioassays in bank voles and transgenic mice.

At present, a total of 10 animals are sacrificed and read-outs are ongoing. Preclinical incubation of the remaining macaques covers a range from 6.4 to 7.10 years. Based on the species barrier and an incubation time of > 5 years for BSE in macaques and about 10 years for scrapie in macaques, we expected an onset of clinical disease beyond 6 years post inoculation.