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SKIN PRION AND ITS IMPLICATIONS IN PRION DISEASES AND OTHER NEURODEGENERATIVE DISEASES

Zou WQ
Case Western Reserve University, USA

Prions (or PrP^{Sc}) are associated with a group of fatal transmissible prion diseases including sporadic Creutzfeldt-Jakob disease (sCJD, the most common human prion disease) in humans as well as scrapie, mad cow disease, and chronic wasting disease in animals. The currently incurable sCJD is transmissible, due to the contamination of abundant infectious prions in the brain through medical or surgical procedures. Some epidemiological studies have also associated sCJD risk with non-neurosurgeries, suggesting that prions may be present in other tissues such as skin. In addition, once disease onset has occurred, the brain becomes inevitably damaged. So, preclinical detection is key to providing the critical window for early treatments before irreversible brain damages occur once cures become available. Our recent study using the highly sensitive real-time quaking-induced conversion (RT-QuIC) assay and humanized transgenic (Tg) mice-based bioassay revealed that the skin of sCJD patients harbors infectious prions (Orrú et al., 2017). Moreover, our new preliminary results further indicate that skin PrPSc is detectable by RT-QuIC and serial protein misfolding cyclic amplification assays far ahead of neuropathological changes in prion-infected animal models. Our findings not only raise concerns about the potential for iatrogenic sCJD transmission via skin but also provide a basis for establishing alternative premortem and postmortem diagnostic assays for prion diseases. Moreover, they may improve our understanding of the role of other skin misfolded proteins in the diagnosis and pathogenesis of neurodegenerative diseases such as Alzheimer's and Parkinson's diseases in which disease-specific misfolded proteins have been detected in the skin of patients with these diseases. [Supported by the CJD Foundation, NIH (NS062787, NS087588 and NS096626), and CDC].

wxz6@case.edu