（別紙）研究成果の概要（英文）

Title of research project	In vitro approach to estimate the human transmission risk of prions
Research project number	1702
Research period	FY 2017– 2018
Name of principal research investigator (PI)	Yoshifumi Iwamaru

Abstract/Summary

Prion diseases are fatal neurodegenerative disorders in humans and animals. One of the characteristics of prion is the species barrier that limits the transmission between different species. Currently, bioassays using transgenic mice (Tg) overexpressing prion protein (PrP) of different species have become valuable tools for assessing cross species transmissibility of prions. Although Tg expressing human PrP have been used to model human susceptibility to animal prions, these experiments are costly and time-consuming. In addition, the results of bioassays are influenced by the lines of transgenic mice used and the lifespan of the challenged animals. These factors are needed to be taken into account when assessing the human risk of prions.

In attempt to develop the more time- and cost-saving method for assessment of the human transmission risk of prions, we optimized protein misfolding cyclic amplification (PMCA), one of the *in vitro* techniques used for disease associated PrP (PrPSc) amplification, by using brain homogenates (BH) of Tg expressing human PrP (TgHu) as the PrP substrate and TgHu affected with classical bovine spongiform encephalopathy (BSE) as PrPSc seed.

To investigate whether this optimized PMCA (PMCA/Hu) can be compatible with the bioassay using TgHu, we attempted to assess the human transmission risk of BSE prions *in vitro*. PMCA/Hu was seeded with PrPSc from classical BSE, atypical H-BSE or atypical L-BSE affected cattle. PMCA/Hu was able to amplify PrPSc from classical BSE and H-BSE, but not that from L-BSE. These findings were not consistent with the results of our previous bioassay demonstrating that TgHu were susceptible to classical BSE and L-BSE but not to H-BSE. Considering the inability of PMCA/Hu for amplifying PrPSc from TgHu affected with L-BSE, more optimization of PMCA/Hu is required to assess the human transmission risk of prions *in vitro*.

1. List of papers published on the basis of this research
2. List of presentations based on this research
   Iwamaru Y et al., In vitro approach to estimate the human transmission risk of prions., Prion2018, Santiago de Compostela, Spain, May 2018
3. The number and summary of patents and patent applications
4. Others　(awards, press releases, softw

are and database construction)