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Editorial Open Access

Recent Advances in the Immunity Research of Rabbits to Prion Diseases

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In Mar 2012 scientists showed that rabbits, which have been classified as TSE (transmissible spongiform encephalopathy, or prion disease) resistant for many decades, can also develop such infections [1].

The rabbit prions were developed using the protein misfolding cyclic amplification (PMCA) technique; rabbit brain homogenate, either unseeded or seeded in vitro with disease-related prions obtained from different species, was subjected to serial rounds of PMCA [1]. De novo rabbit prions produced in vitro from unseeded material were tested for infectivity in rabbits, with one of three intra-cerebrally challenged animals succumbing to disease at 766 d and displaying all of the characteristics of a TSE, thereby demonstrating that leporids are not resistant to prion infection [1]. Material from the brain of the clinically affected rabbit containing abnormal prion protein resulted in a 100% attack rate after its inoculation in transgenic mice over expressing rabbit PrP (RaPrP); transmissibility to rabbits (>470 d) has been confirmed in 2 of 10 rabbits after intracerebral challenge [1]. But at the end the authors declared despite rabbits no longer being able to be classified as resistant to TSEs, an outbreak of "mad rabbit disease" is unlikely [1].

In May 2013, the biochemical and biological properties of the new prions generated in vitro after seeding rabbit and dog brain homogenates with classical BSE (bovine spongiform encephalopathy) were studied [2]. Pathobiological features of the resultant prion strains were determined after their inoculation into transgenic mice expressing bovine and human cellular prion proteins (PrP^{C}); strain characteristics of the in vitro-adapted rabbit and dog BSE agent remained invariable with respect to the original cattle BSE prion, suggesting that the naturally low susceptibility of rabbits and dogs to prion infections should not alter their zoonotic potential if these animals became infected with BSE [2]. This study does not seem to support the opinion that "rabbits are not resistant to prion (TSE) infection" of [2].

In 2013, there are other researches on rabbits for diseased prions (PrP^{Sc}). Wang et al. (2013) aimed to investigate "potential mechanisms contributing to prion resistance or susceptibility by using the rabbit, a species unsusceptible to prion infection, as a model" [3] and investigated "the expression level and distribution of LRP/LR (laminin receptor precursor or laminin receptor) in rabbit tissues by real-time polymerase chain reaction and by immunochemical analysis with a monoclonal anti-67 kDa LR antibody" [3] and at last their findings confirmed the prion resistance in rabbits [3]. Sweeting et al. (2013) produced X-ray structures of mutants in the β2-α2 loop and reported that the helix-capping motif in the β2-α2 loop modulates β-state misfolding in RaPrP, and still acknowledged "rabbit PrP, a resistant species" [4].

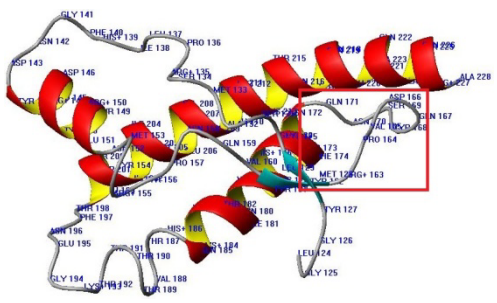

Figure 1: Molecular structure of rabbit prion protein ($RaPrP^{C}$), the β2-α2 loop is denoted in the circle.

Before [1], there are more than 160 research articles on rabbit prion protein listed in PubMed (ncbi.nlm.nih.gov/pubmed) all supporting the opinion that rabbits were apparently resistant to BSE as [2-4].

Thus, the opinion "Naturally prion resistant mammals: a utopia?" [5, 1] for rabbits should be furthermore studied and need to more evidences to support or refuse it.

Our research is focusing on the molecular structures and their structural dynamics of RaPrP and its mutants. A recent focus is on studies of the β2-α2 loop of the structure (Figure 1) [4, 6-26], which contributes to the conformational structural stability of RaPrP and to the resistant of rabbits to prion diseases.

We found that rabbit prion protein has a strong salt bridge ASP177-ARG163 (like a taut bow-string) keeping this loop linked [26-27].

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