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Mini Review

How Prion Particles are Lethal to Us?

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Abstract

Stanely B. Prussiner got Nobel prize in 1997 for the discovery of prion particles composed of only misfolded proteins which are devoid of any genetic materials. These are responsible to cause several life threatening neurodegenerative and brain diseases like bovine spongiform encephalopathy (BSE) and Creutzfeldt Jacob disease (CJD) in animals and humans respectively. Currently, it has also been noticed that these prion particles are able to cause cancer. The present paper is an attempt to summarize the recent informations on prions developing cancer in human.

Keywords: *Prions; Neurodegenerative Diseases; Cancer*

Introduction

Prion is an abnormal protein particle of a normally harmless protein usually found in the brains of human and animals. These abnormal protein particles are responsible to cause several neurodegenerative brain diseases in animals including human. They are all fatal diseases having no cure so far. Currently, it has also been reported that these prion and prion protein particles also cause to develop a variety of cancers in several parts of the human body as well. The present paper is an attempt to summarize the recent informations regarding the development of cancer due to abnormal protein particles. The paper also discusses the historical background, mechanism of cancer development and the transmission of diseases on the basis of recent researches done so far in the same field for the past 15 years.

Discussion

Prions are composed of misfolded forms of the prion protein (PrP) and are believed to be the cause of Transmissible Spongiform Encephalopathies (TSEs). They were identified as the causative agents of scrapie, TSEs and chronic wasting disease from sheep, cow and deer respectively [1]. In human, the disease is known as Creutzfeldt Jacob disease (CJD) with its variant as (vCJD), Gerstmann-Straussler-Shinker syndrome, fatal familial insomnia and kuru [2]. All known prion diseases affect the brain and neural tissues. In fact, the disease was first reported from Papua New Guinea as Kuru. The disease was transmitting as the brains were eaten by the people after death as a ritual. Kuru is a type of neurodegenerative disease in which brains become spongy due to the formation of holes. The disease is characterized by neurodegeneration, cerebral ataxia, tremors and trembling, loss of coordination, decreased muscle control, difficult walking and slurred speech, difficult swallowing, behavioral changes, random compulsive laughing or crying, moodiness, dementia and inability to grasp objects. Stanely Prussiner's discovery led to him being awarded the Nobel prize in 1997 [1,3]. Kuru has no cure and is progressively fatal within one year of contraction [2,3].

The prion proteins (PrP) are found even in healthy human and animals. It becomes pathogenic causing diseases only when its protein misfolded. However, the exact mechanism for the conversion is incompletely understood. PrP^C has been detected in the nucleus of colorectal and breast cancer cells and have played a key role in T-lymphocyte proliferations [4-8]. Antony., *et al.* [9] described the potential roles for prions and protein only inheritance in cancer. PrP^C plays an important role in cell adhesion, migration, proliferation, differentiation, ion homeostasis and signal transduction. All these functions implicated that it may be involved in tumorigenesis [8].

The human prion protein (PrP^C) is known to cause neurodegenerative diseases and has now been found to be up-regulated in multiple cancers. This is highly expressed at the protein level in several cancers and there are several lines of evidence that support the possible involvement of prions in cancer such as gastric cancer [8,10-13]; colorectal cancer [6,14-16]; pancreatic cancer [17-19]; prostate cancer [20]; glioblastoma [21]; breast cancer [22-24]; osteosarcoma [25] and melanoma [26]. In these cancers, PrP^C has been postulated to regulate apoptosis through various pathways. Inhibition of apoptosis is one of the hallmarks of cancer [9,12,27-29]. The most important fact is that the expression of PrP^C is not essential for life and it does not participate in some biological functions. But, this is not to be forgotten that PrP is upregulated in cancer cell lines and tumor tissues [8,30].

Conclusion

This review explores the possible role of prions developing cancer in human. It has been found that all known prion diseases are infectious and fatal regardless of their origin. The prion and prion proteins have always been found to be associated in the development of a variety of cancers in human. Some of them are as acute myeloid leukemias, myelodysplastic syndromes, gastric adenocarcinomas, anaplastic meningioma and astrocytomas [31]. Further, the buildup of mutant p53 aggregates already known for its involvement in cancer development in human like neuroblastoma, retinoblastoma, breast and colon cancers has also recently been shown to display prion like tendencies [9]. Lastly, a plethora of good informations have been gathered regarding the development of cancer due to prions, but unfortunately these results are conflicting in nature. And, it appears that these reported results are worth of serious re-evaluation.

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Conflict of Interest

The authors have declared no conflict of interest. They have approved the final version of the manuscript contributing equally.

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Bibliography

1. Prussiner SB. “Novel proteinaceous infectious particles cause scrapie”. *Science* 216.4542 (1982): 136-144.

2. Pocchiari M., *et al*. “Predictors of survival in sporadic Creutzfeldt- Jacob disease and other human transmissible spongiform encephalopathies”. *Brain* 127.10 (2004): 2348-2359.

3. Prussiner SB. “Prions”. *Proceedings of the National Academy of Sciences, U.S.A* 95.23 (1998): 13363-13383.

4. Cashman NR., *et al*. "Cellular isoform of the scrapie agent protein participates in lymphocyte". *Activation Cell* 61 (1990): 185-192.

5. Mironov AJr., *et al*. "Cytosolic prion protein in neurons". *The Journal of Neuroscience* 23 (2003): 7183-7193.

6. Morel E., *et al*. "The cellular prion protein PrP^{C} is involved in the proliferation of epithelial cells and in the distribution of Junction associated proteins". *PLoS One* 3 (2008): 3000.

7. Dery MA., *et al*. "Endoplasmic reticulum stress induces PRNP protein gene expression in breast cancer". *Breast Cancer Research* 15 (2013): 22.

8. Xiaowen Y., *et al*. "Prion protein and cancers". *Acta Biochimica et Biophysica Sinica (Shanghai)* 46.6 (2014): 431-440.

9. Antony H., *et al*. "Potential roles for prions and protein- only inheritance in cancer". *Cancer and Metastasis Reviews* 31.1-2 (2012): 1-19.

10. Du J., *et al*. "Overexpression and significance of prion protein in gastric cancer and multidrug-resistant gastric carcinoma cell line SGC7901/ADR". *International Journal of Cancer* 113 (2005): 213-220.

11. Konturek PC., *et al*. "Helicobacter pylori up-regulates prion protein expression in gastric mucosa: a possible link to prion disease". *World Journal of Gastroenterology* 11 (2005): 7651-7656.

12. Liang J., *et al*. "Overexpression of PrP^{c} and its antiapoptosis function in gastric cancer". *Tumor Biology* 27.2 (2006): 84-91.

13. Liang J., *et al*. "Function of PrP^{c} (1- OPRD) in biological activities of 4453- gastric cancer cell lines". *Journal of Cellular and Molecular Medicine* 13 (2009): 4464.

14. Antonacopoulou AG., *et al*. "POLR2F, ATP6VOA1 and PRNP expressions in colorectal cancer: new molecules with prognostic significance?" *Anticancer Research* 28.2B (2008): 1221-1227.

15. Antonacopoulou AG., *et al*. "Prion protein expression and the M129V polymorphism of the PRNP gene in patients with colorectal cancer". *Molecular Carcinogenesis* 49.7 (2010): 693-699.

16. De Wit M., *et al*. "Cell surface proteomics identifies glucose transporter type 1 and prion protein as candidate biomarkers for colorectal adenoma-to-carcinoma progression". *Gut* 61 (2012): 855-864.

17. Han H., *et al*. "Identification of differentially expressed genes in pancreatic cancer cells using CDNA microarray". *Cancer Research* 62 (2002): 2890-2896.

18. Li C., *et al*. "Binding of pro-prion to filamin A disrupts cytoskeleton and correlates with poor prognosis in pancreatic cancer". *Journal of Clinical Investigation* 119.9 (2009): 2725-2736.

19. Sy MS., *et al*. "The fatal attraction between pro-prion and filamen A: prion as a marker in human cancers". *Biomarkers in Medicine* 4.3 (2010): 453-464.

20. Sauer H., *et al*. "Redox regulation of intrinsic prion expression in multicellular prostate tumor spheroids". *Free Radical Biology and Medicine* 27.11-12 (1999): 1276-1283.

21. Mehrpour M and Codogno P. "Prion protein: From physiology to cancer biology". *Cancer Letters* 290.1 (2010): 1-23.

22. Diarra- Mehrpour M., *et al*. "Prion protein prevents human breast carcinoma cell line from tumor necrosis factor alpha-induced cell death". *Cancer Research* 64.2 (2004): 719-727.

23. Roucou X., *et al*. "Cellular prion protein inhibits proapoptotic Bax conformational change in human neurons and in breast carcinoma MCF- 7 cells". *Cell Death and Differentiation* 12 (2005): 783-795.

24. Meslin F., *et al*. "Efficacy of adjuvant chemotherapy according to prion protein expression in patients with estrogen receptor-negative breast cancer". *Annals of Oncology* 18 (2007): 1793-1798.

25. Sollazz V., *et al*. "Prion proteins (PRNP and PRND) are over-expressed in osteosarcoma". *Journal of Orthopaedic Research* 30 (2012): 1004-1012.

26. Li C., *et al*. "Pro-prion binds filamen A, facilitating interaction with integrin beta 1, and contributes to melanomagenesis". *Journal of Biological Chemistry* 285 (2010): 30328-30339.

27. Burkle A., *et al*. "Poly (ADP-ribose) immunostaining to detect apoptosis induced by a neurotoxic fragment of prion protein". *Journal of Histochemistry* 31 (1999): 711-716.

28. Liberski PP., *et al*. "Neuronal cell death in TSEs (prion diseases) revisited: from apoptosis to autophagy". *The International Journal of Biochemistry and Cell Biology* 36 (2004): 2473-2490.

29. Kovacs GG and Budka H. "Prion diseases: From protein to cell pathology". *The American Journal of Pathology* 172.3 (2008): 555-565.

30. Alvin D and Zou Wen-Quan. "Prions: beyond a single protein". *Clinical Microbiology Reviews* 29.3 (2016): 633-658.

31. Hinton C., *et al*. "Significance of prion and prion-like proteins in cancer development, progression and multi-drug resistance". *Current Cancer Drug Targets* 13.8 (2013): 895-904.

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