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Prion-chaperone interaction: parsimony and conceptual limitations

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Abstract

This study discusses the hypothesis of the appearance of prion diseases as an interaction of PRNP gene and chaperon gene, called X chap. It is believed that the hypothesis of the x protein of the connection of the chaperones with prionopathies has been neglected because scholars still do not know that there are a number of inheritance systems, a number of code types and a number of modules. These conceptual limitations are also accompanied by a violation of the parsimony principle.

Key words: prion, PRNP, xchap, parsimony, conceptual limitation.

Introduction

In the last two decades the Anfinsen (Anfisnen, 1973) dogma has been questioned, according to which the unique three-dimensional pattern of a protein has been coded in the sequence of amino acids it is composed of. The reasons that make the dogma a suspicious statement are two recent developments in molecular biology: prion and molecular chaperon (Zahn, 1996). It is widely accepted by the scholars that a prion is an infectious agent and more exactly a protein in a misfolded form. The term prion itself coined by S.B. Prusiner (1982) (protein and infection) shows that the misfolded proteins are infectious. This study discusses the problem whether a misfolded protein can be considered an infectious agent. The problem explained above is further justified when the prion is considered an infectious agent without nucleic acids.

On the other hand, various scientific material has been gathered, which shows the role of chaperons in the manifestation of prion diseases. Furthermore, the belief that chaperons play a key role in prion diseases is so strong that a number of scientists recommend them, such as hot schook proteins as strategies to treat some neurological diseases (Bagatell and Whitesell, 2004).

Also, today there are no doubts that prion diseases are genetic and infectious. This means that people and many mammals become victims of prion diseases when they inherit the respective gene or when they get infected. Another question arises here: what is the role of the pathogen or the kind of disease that causes to the living organism show such a behavioral pattern?

1.Prion diseases and parsimony

Transmissible spongiform encephalopathies (TSE), which are commonly known as prion diseases, causethe incurable degeneration and progressively fatal in men and mammals. From the biochemical perspective, the propagative mechanism relates to the conformational change of the prion cellular protein (PrP^{c}) in a prion pathogenic protein, or in short, in a prion (PrP^{sc}). The prion is considered as the main component of TSE and cause of a number of diseases in men.(Table1)

Table 1. Prion diseases in men (modified according to the V. Khaychuk, 2012)

Disease	**Source**
Kuru	Cannibalism
Sporadic Cretzfeldt-Jacob disease (sCJD)	Spontaneous mutations
IjatrogeneicCretzfeldt-Jacob disease (iCJD)	Acquired
IjatrogeneicCretzfeldt-Jacob disease variant (vCJD)	Acquired from animals
Gertsmann-Straussler-Scheinher syndrome (GSS)	PRNP mutation
Fatal Familial Insomnia (FFI)	PRNP mutation

As shown in Table 1, prion diseases in men occur because of PRNP gene mutations. In reality, it is known that PRN gene mutations are not the sole cause of prion diseases. The fact that prionopathities occur only when it forms copies of the pathogenic proteins (PrP^{sc}) from the conversion of the cellular protein (PrP^{c}) makes us think that the essence of these diseases is the connection between the mutations of PRNP gene and chaperone gene. Around twenty years ago, the hypothesis of the x protein was formulated, which states that the emergence of these diseases would depend on the interaction of the cellular prion protein (PrP^{c}) with the x protein. (Telling, et al., 1995). But, scientific opinion is still not engaged in this key knot of the prion phenomenon. In our opinion, this happens because scientists do not frequently apply the parsimony principle. According to the renowned philosopher Karl Poper, the scientist should prefer a simpler theory instead of more complicated one because the simple theory has a greater empirical content and it can be tested more easily. (Poper, 1992). In this case, a number of scientists make an analogy of DNA replication with the formation of PrP^{sc} copies instead of searching approximate examples from the biochemical reactions domain. As we know, the enzyme-substrate connection and the continuous formation of a product is analogous with the cellular prion protein with the x protein, which is thought to be a chaperone. Moreover, the connection of one of two allosteric centers of the enzyme and the production of a product or its termination is similar to the formation of PrP^{sc} in the presence of PrP^{c}. In conclusion, it is worth mentioning the statement that every chemical reaction is a recognition process (Rebek, 2009).

The fact that a substance in certain conditions is continuously formed with interruption, as it happens with PrP^{sc}, we come to the analogy of infection, or the analogy of propagative process of bacteria or viruses. The propagative process of microorganism is very different. The belief that the so-called prionic replication is similar to self-replication or infection of microorganisms, derives from the inability of scientists to overcome a number of conceptual limitations.

2.Essence of prionopathiesis the interaction between prion and chaperon

Previous studies (Bajrami, N., 2014; Bajrami, N. Bajarmi, Z., 2015) constructed the bimodularmodel of prion diseases and has come to the conclusion that genetic, sporadic and acquired forms of these diseases are determined by the presence of mutations in the PRNP gene and chaperone gene, called x chap. The genetic form of prion disease is characterized by the presence of mutations in both genes, PRNP gene and x chap gene, whereas the sporadic and acquired form from the presence of a mutation, respectively in the x chap gene and PRNP gene. (Bajrami, N., 2015). We think that our proposal is based on the principle of parsimony: chaperone is a protein and a gene (or some genes) is responsible for it and as every gene, mutations occur there. In our hypothesis, mutations in the x chap gene are responsible for the sporadic form, which constitute around 85 percent of all prion diseases. To support this hypothesis, there is the bi-modular model of the emergence of the acquired manifestation of the prion disease. The so-called infection occurs in a few individuals and this makes us believe that these individuals are affected by prion diseases only when they are in contact with contaminated materials with the pathogenic prion protein (PrP^{sc}).

Our model that in the main factor of the emergence of prionopathies is the chaperone protein, accepts the opinion that there is another information in addition to acid nucleic one. We think that not taking into consideration the steric information as molecular recognition, it is a conceptual limitation. This conceptual limitation explains that fact why the hypothesis of the x protein, although known for two decades, has been neglected as an unimportant hypothesis. In reality, the essence of the prion disease is the interaction between prion and chaperson, while the so-called infectious disease of prions, is the occurrence of the phenomenon. It is worth pointing out that if today many scholars study the occurrence of the prion phenomenon shown that they are inhibited by some concepts,

whose source must be searched in not recognizing a number of types of biological information. In favor of different types of biological information, there are a several hypotheses such as the presence of the four systems of inheritance (Jablonka and Lamp, 2005), of the various organic codes(Barbieri, M., 2008) or the four types of biological modules (Bajrami, Z., 2014).

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