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Toxic Prion: Translation of a Genome's gene with a toxic change

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A**BSTRACT:** *Toxic prion is an abnormal form of a normally harmless protein found in the brain that is responsible for a variety of* ***fatal neurodegenerative diseases*** *of animals including humans. These neurodegenerative diseases are called* ***transmissible spongiform encephalopathies****. The key objective of this study is to give a spectacular proof of Nature's Controlled Experiment for the fact that Genome's designed/coded directives are effected by its transcripts [7] & proteins serving as implementing engineers in synthesizing its individuals in each species of all genomic-things whereas its usable chemical energy-containing nutritive substances including minerals are used as raw materials in its aerobic or anaerobic compatible environment. The micrographs, Figures, videos were designed be the targets of the study and impartive results in aimful approach of the investigator; and, that was why it had been entitled as Methodology & Results. Genome is not only the true automatic molecular machine capable of synthesizing genomic-things, it is also a supersensitive molecule where* ***symptoms****,* ***syndromes****,* ***epigenetic modifications****,* ***immunological defensive reactions****, and the capability of* ***toxic prion proteins*** *(PrP 27-30) to induce conversion of normal prion proteins (PrP 33-35) into* ***toxic prion proteins*** *to cause* ***fatal neurodegenerative diseases*** *are evidences for the fact that the* ***Genome*** *is an unbelievably supersensitive automatic molecular machine!!!! Epigenetics is actually the study of* ***supersensitivity*** *of the* ***Genome*** *by attaching epigenetic groups or chemicals to* ***Genome*** *that are not structural parts of the* ***Genome****. When toxicity of prion is caused by change, modification, or mutation in one's own* ***Genome****, it is called* ***autotoxic prion*** *and when it is transmitted from other individuals, it is referred to as* ***acquired toxic prion****.*

KEY WORDS: Autotoxic prion, Genome, Supersensitivity, Normal prion, Syndrome, Neuron, Transcript, Protein, Acquired toxic prion

INTRODUCTION

Toxic prion is an abnormal form of a normally harmless protein found in the brain that is responsible for a variety of **fatal neurodegenerative diseases** of animals including humans. These

neurodegenerative diseases are called **transmissible spongiform encephalopathies**. In 1982 Stanely B. Prusiner and colleagues identified prion as a "proteinaceous infectious particle." The normal protein structure composed of a number of flexible coils is called α-**helices**. In the prion protein some of these helices are stretched into flat structures called **β-strands**. The normal protein conformation can be degraded by cellular enzymes known as proteases whereas the prion protein shape is resistant to this enzymatic activity [1]. As a result, the prion protein accumulate within neurons, destroying them. Progressive neuron destruction eventually causes brain tissue to become filled with holes in spongelike or spongiform, pattern. Prions are sialo-glycoprotein called PrP 27-30 [2].

The prion is a translation of a human gene, termed PrP gene, found on **DNA** molecule of chromosome 20. This gene contains two exons separated by a single intron. Exon I and Exon II are transcribed and the two RNAs are ligated into a single mRNA. This mRNA is translated into the PrP protein. The PrP is a precursor of the prion protein. This precursor is termed PrP 33-35.

The PrP 33-35 undergoes several post-translational events to become the prion protein (PrP 27-30). In normal cells only the PrP 33-35 protein is synthesized. It is found in the neural cell membrane where its function is to sequester Cu++ ions. In abnormal (infected) cells, the PrP 27-30 is produced from the PrP 33-35 protein. The PrP 27-30 triggers a series of reactions that produce more PrP 27-30 proteins, i.e., PrP 27-30 induces its own synthesis. In addition to the post-translational modifications, the PrP 27-30 protein differs from the PrP 33-35 protein in a single amino acid residue. Residue 178 in the PrP 27-30 contains an asparagine residue whereas the PrP 33-35 protein has an aspartate residue at this position [3, 4]. This causes a conformational change in the PrP 27-30 protein, resulting in the following three effects.

1. It imparts to the PrP 27-30 protein the ability to induce the same alpha-helix to beta-sheet conformation in the PrP 33-35 protein. This is a permanent conformational change. It thus induces its own replication.

2. The beta-sheet forming peptides aggregate to form amyloid fibrils.

3. The amyloid fibrils kill thalamus neurons through apoptosis, a programmed series of events that leads to cell death.

The key objective of this study is to give a spectacular proof of **Nature's Controlled Experiment** for the fact that **Genome's** designed/coded directives are effected by its **transcripts [7]** & **proteins** serving as implementing engineers in synthesizing its individuals in each species of all genomic-things whereas its **usable chemical energy-containing nutritive substances including minerals** are used as raw materials in its **aerobic** or **anaerobic compatible environment**.

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Figure 1: Stanley B Prusiner – American Neurologist (born 28 May 1942, alive with age of 80 years). He discovered **toxic prion protein (PrP 27-30)** in 1982**,** the causative agent of **fatal neurodegenerative diseases** of animals including humans.

Methodology and Results

Each of the micrographs, or evidential videos in the Figures listed or displayed herebelow has a targetful aim. These micrographs, and videos are also addressive findings (results) in the targetful approach of the paper and this is the reason for why it is entitled as **Methodology and Results** hereabove.

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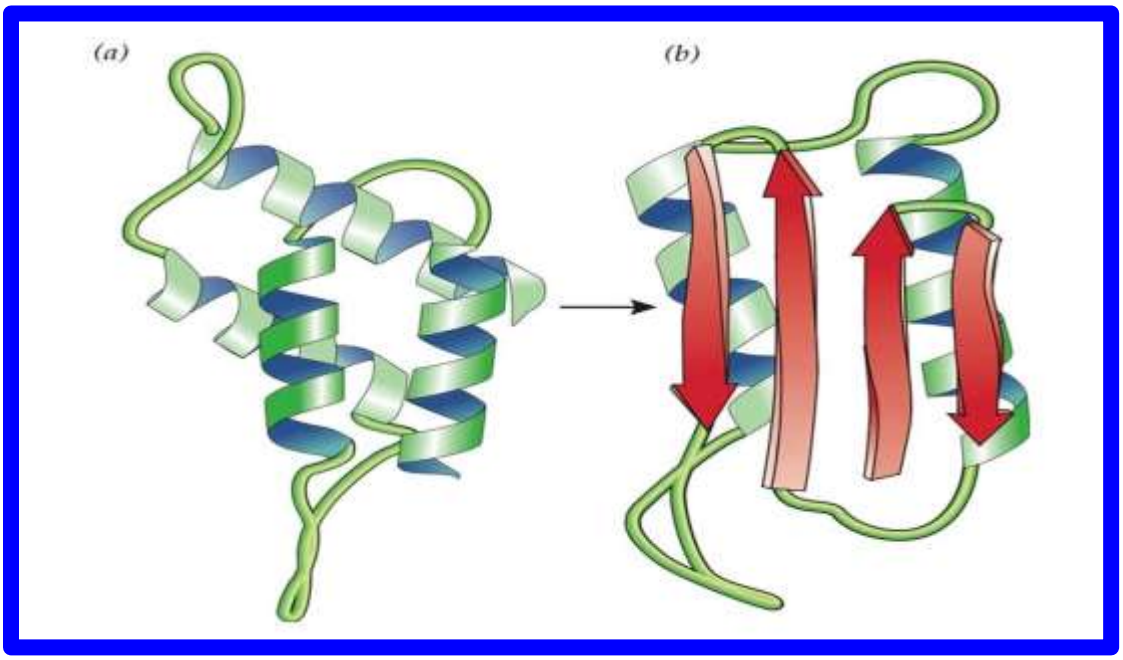

Figure 2: Conversion of α-helices of protein into **β**-sheets.

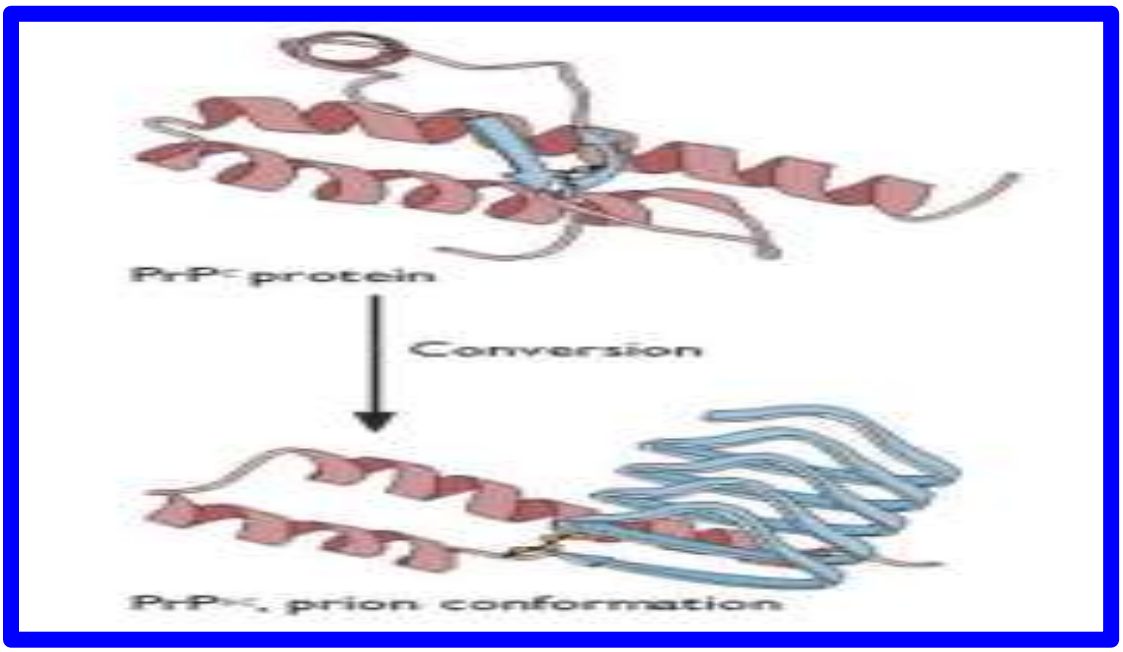

Figure 3: Conversion of α-helix conformation of protein into **β**-sheet conformation.

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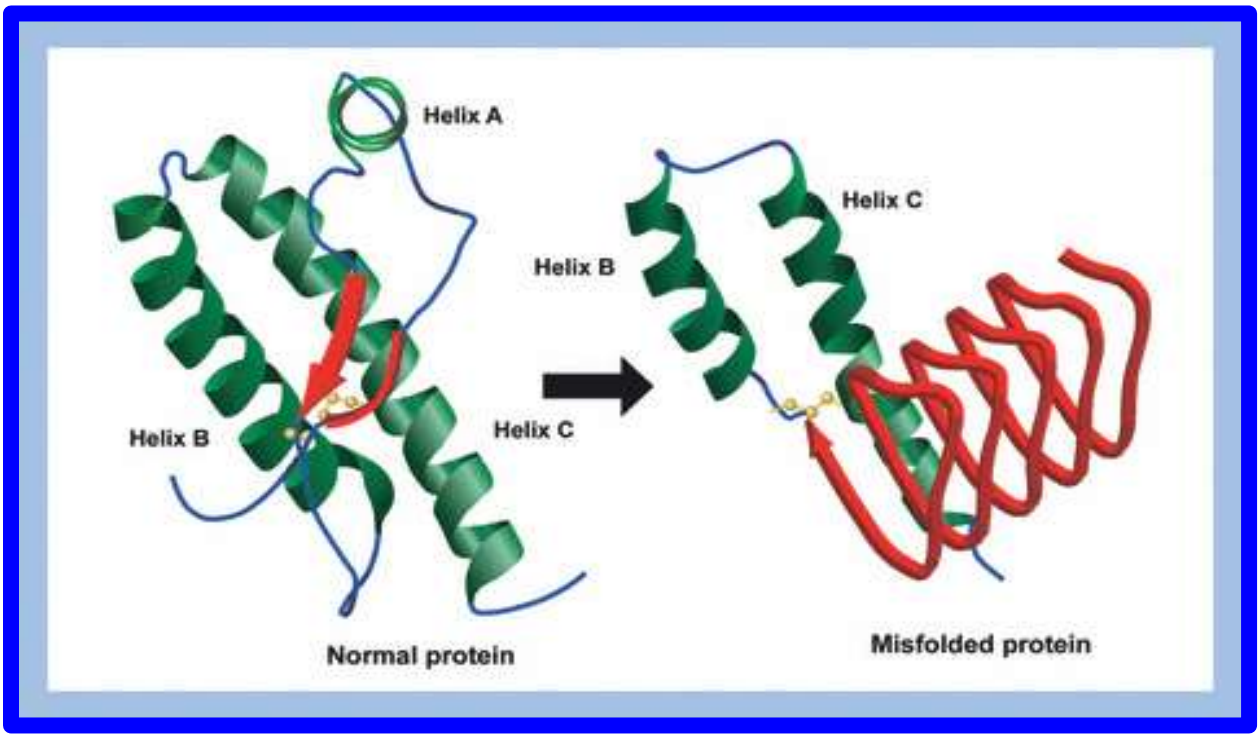

Figure 4: Conversion of normal protein structure into a misfolded protein (PrP 27-30 protein).

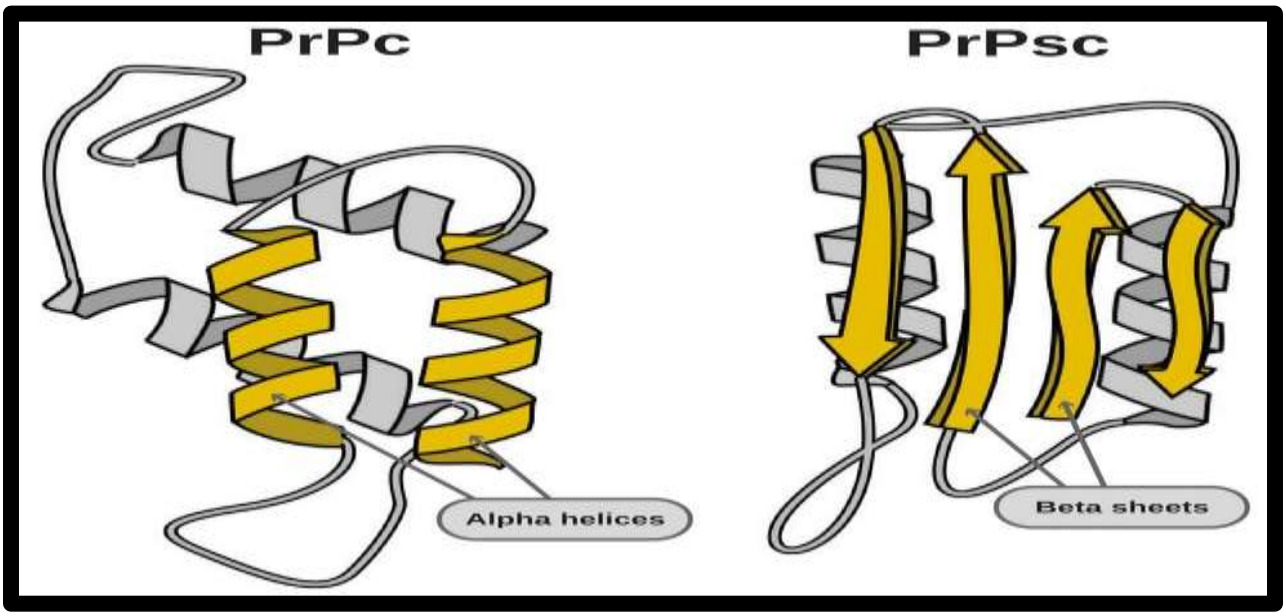

Figure 5: Normal protein (Alpha helices); prion protein (Beta sheets).

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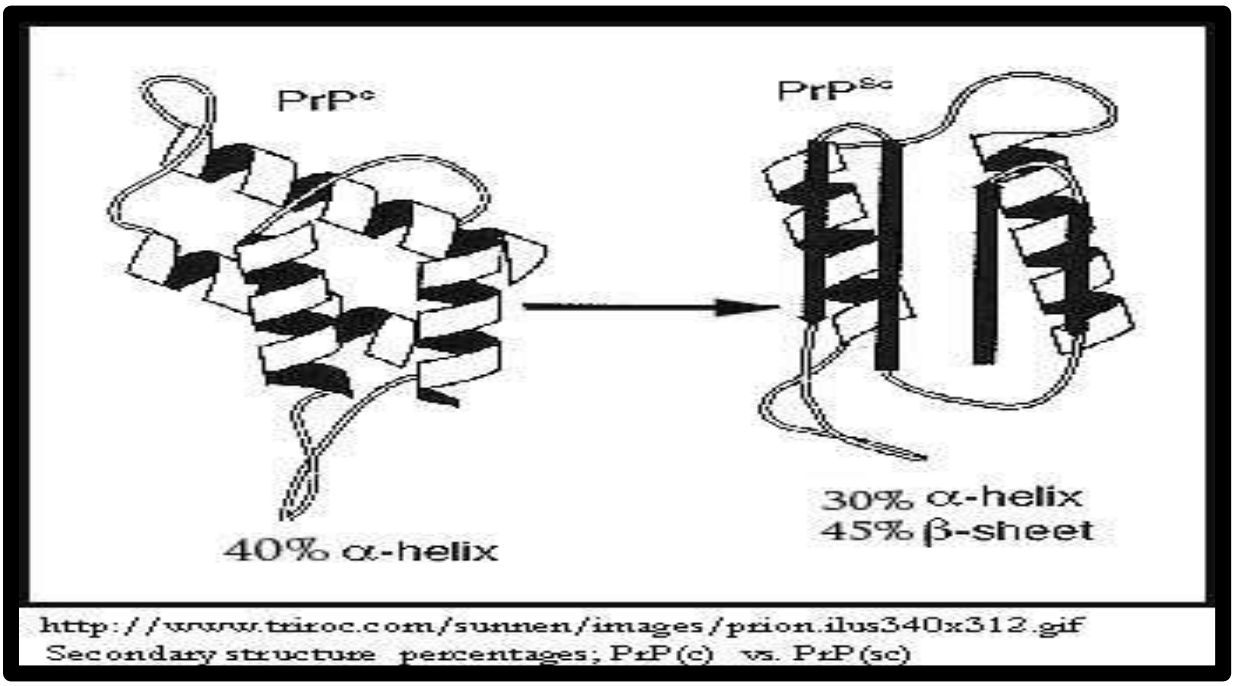

Figure 6: Percentages of α-helices & **β**-sheets in the masses of protein displayed.

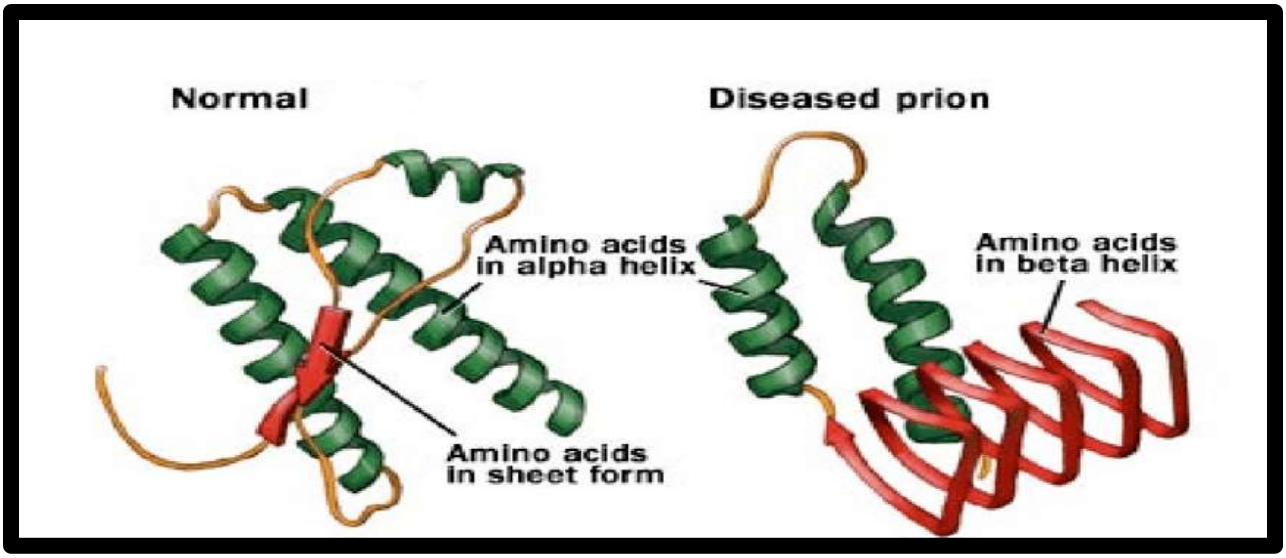

Figure 7: The display of normal & prion proteins.

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Connect your computer to Internet. Steps of opening the video: Select, copy and paste the title of the video (only the blue colored & underlined) on Google search space on your computer desktop screen and then press Enter Key of your computer keyboard. Click Video. Now, click the slide with the correct Title of video you pasted because when the video is copied & pasted, several other unwanted videos will appear together. When video 1 ends playing, repeat the same steps for playing of video 2 and then that of video 3, etc.

Video 1: Prion Disease Basics – You Tube

Video 2: Prion DiseaseCJD (Creutzfeld-Jakob Disease) Basics - Brian Appleby

Video 3: 2019 Keynote Speaker Richard Knight - Prion Diseases, An Overview

Video 4: Detecting Prions and Diagnosing Prion Diseases by Byron Caughey

Video 5: Genetic Prion Disease and How Genetics Might Help Us Understand Sporadic CJD

Video 6: Historical Appraisal - The Field Of Prion Diseases What We've Learned & Why We Should Be Optimistic

Video 7: Diagnosis and Treatment - Richard Knight - YouTube

Video 8: Prion Disease - Susan Lindquist (MITHHMI)

Video 9: Prion Disease|How does Prion Disease Happen, Neighborhood, Jan, 2022 – You Tube

Video 10: Prion Disease and CJD Vaccination Approaches by Thomas Wisniewski

Figure 8: Videos of toxic prion diseases.

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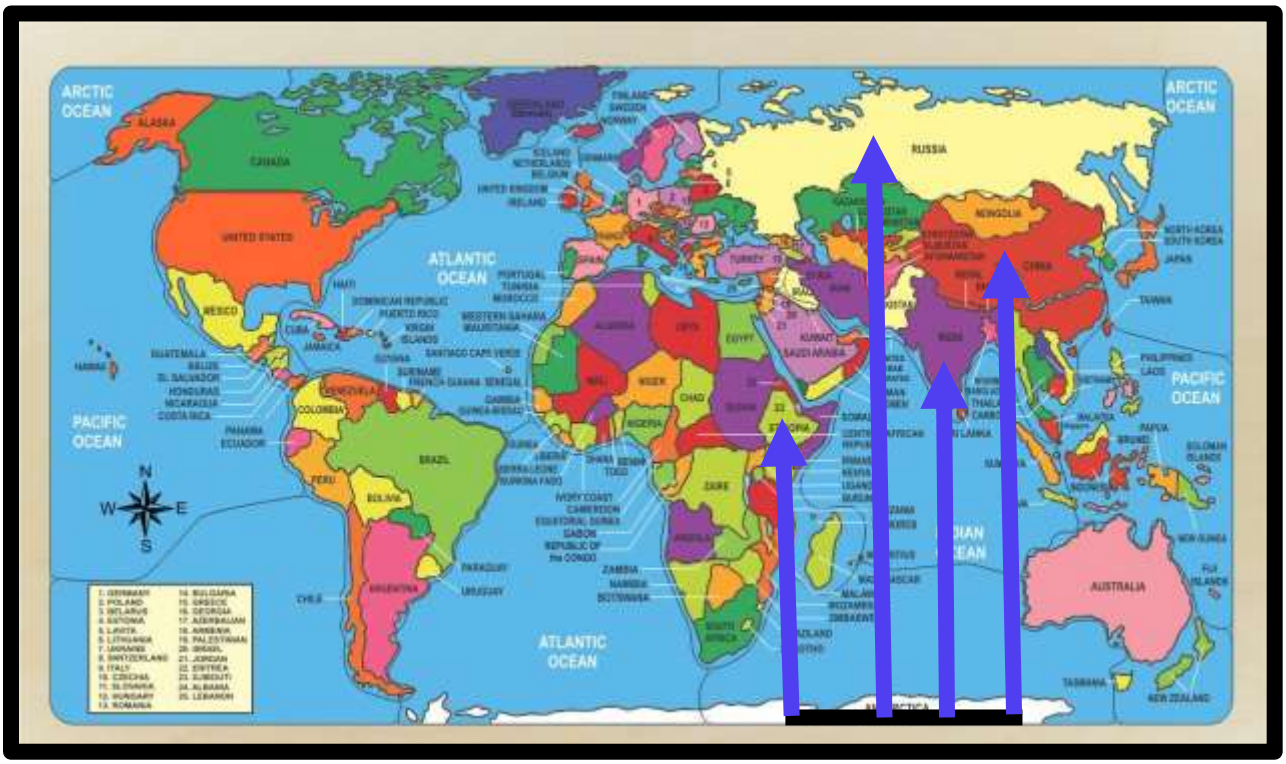

Figure 9: Map of the world with arrows showing the 5 countries (**Ethiopia, Russia, India, & China,**) where each of them is the highest or superpower in the aspects mentioned in the **Conclusion Section** of this paper.

DISCUSSION

Prion is not clearly or distinctively named with an addressive term. We can see that scientists facing problems or confusions in imparting prion in oral, written, or video presentations by saying normal prion protein (PrP 33-35) and abnormal prion protein (PrP 27-30) whereas the correct and clearcut scientific terms should be toxic pprion protein or simply **toxic prion** so that the normal prion protein can called **normal prion** [5]. The very cause of failing to term the prion as toxic prion or normal prion (nontoxic prion) is very strongly associated with the fact that biologists are wholey ignorant of the truth that **Genome** is the unit of both structure & function of every individual of all genomic-things. The only function of the toxic prion is implementing as an engineer the **Genome**'s designed/coded directives of inducing conversion of normal prions into toxic prions.

Prions are exotoxins (protein toxins) analogously similar to those released from viable bacteria. These bacterial exotoxins form the class of poisons that is among the most potent of all the toxic

substances. Numerous of the low molecular-sized bacterial exotoxins are heat-stable peptides and similarly human toxic prions are non-degradable by typical sterilization temperature [6].

The site of action of most bacterial exotoxins is more localized and is confined to particular cell types or receptors. Tetanus toxin, for example, affects only internuncial neurons. In general, exotoxins are excellent antigens that elicit specific antibodies called **antitoxins**. Not all antibodies to exotoxins are protective, but some react with important binding sites or enzymatic sites on the exotoxin, resulting complete inhibition of the toxic activity (i.e., neutralization). There is a group of bacterial exotoxin named neurotoxins similar to human toxic prions that cause fatal neurodegenerative disease [7-14]. Neurotoxins are best exemplified by the toxins produced by *Clostridium* species, the botulium toxin formed by *C. botulium*. This potent neurotoxin acts on motor neurons by preventing the release of acetylcholine at the myoneural junctions, thereby preventing muscle excitation and producing flaccid paralysis somewhat similar to the effects of human toxic prion. Although the etiologies of human toxic prion are listed to be sporadic, genetic, and acquired ones, the actual & unarguable cause of toxic prion production is the toxic modification or change in the structure of Genome's gene that is translated into toxic prion [15-20]. Therefore, the function of the toxic prion is inducing the conversion of normal prions into toxic prions. Leading to fatal neurogenerative disease which is also known as Transmissible Spongiform Encephalopathy. When toxicity of prion is caused by change, modification, or mutation in one's own **Genome**, it is called **autotoxic prion** and when it is transmitted from other individuals, it is referred to as **acquired toxic prion**.

Biologists say that viruses, viroids, and prions are nonliving-things (i.e., nongenomic-things), being 100% ignorant of the role of **Genome**, because their scientific consciousness is paralysed by **fake sciences of Biology** and they even have failed to differentiate a toxic protein molecule from viroids & viruses [21-23]. The toxic prion is a functional protein that implements the **Genome**'s coded & sensitive directives of inducing conversion of normal prions into toxic prions, leading to fatal neurodegenerative disease whereas viroids & viruses are genomic-things.

CONCLUSION

 This study has given a spectacular proof of **Nature's Controlled Experiment** for the fact that **Genome** synthesizes its individuals in each species of all genomic-things by its coded/designed directives using its **transcripts** & **proteins** as engineers whereas its **usable energy-containing nutritive substances including minerals** are used as raw materials in its **aerobic** or **anaerobic compatible environment**. In this conclusive & dynamic statement, it is obvious that the toxic prion protein is the translation of a human/animal **Genome**'s transcript that

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is very specifically & strongly sensitive enough to synthesize individuals of all genomic-things, but the toxic prion protein is the translation of a gene with toxic prion/pathogenic, change, modification, or mutation so that it induces conversion of normal prion proteins (PrP 33-35) into toxic/pathogenic prion proteins (PrP 27-30). This is one of the perfect & straight forward or spectacular **Nature's Controlled Experiment** to demonstrate that the Genome's coded/designed directives are incredibly sensitive, being implemented by its engineer **transcripts** & **proteins**.

The most appropriate term for abnormal prion is **toxic prion** and not **infectious agent** because **infection** occurs only by a genomic-thing that has its own **Genome** and **metabolism**, being capable of replication or reproduction. **Autotoxic prion**'s or **acquired toxic prion**'s capacity to convert normal prion protein into **toxic prion** is simply the mechanism of its **fataal/letal neurodegenerative toxicity** or **poison** that leads to death and is not a type of infection caused by a pathogen of genomic-things.

Both **autotoxic prion** & **acquired toxic prion** do cause **fatal neurodegenerative diseases**.

Practitioners can check to implement passive immunization for human patients of toxic prion with the kinds of sensitive antibodies called **antitoxin** because some of them react with important binding sites on **exotoxin** (i.e., **toxic prion** in this case), resulting in complete inhibition of toxic activity of the toxic prion, ending up with **neutralization**. Vaccination approaches by Thomas Wisniewski can also be followed up as another option in favor of clients of prion disease (Figure 8, video 10 of this paper).

Genome is not only the true automatic molecular machine capable of synthesizing genomic-things, it is also a supersensitive molecule where **symptoms**, **syndromes**, **epigenetic modifications**, **immunological defensive reactions** as well as the capacity of **toxic prion protein (**PrP 27-30**)** to induce conversion of normal prion proteins (PrP 33-35) into **toxic prion proteins** to cause **fatal neurodegenerative diseases** are evidences for the fact that the **Genome** is an unbelievably supersensitive automatic molecular machine!!!! Epigenetics is actually the study of **supersensitivity** of the **Genome** by attaching epigenetic groups or chemicals to **Genome** that are not structural parts of the **Genome**.

Based on the universal reactions of matter, reupdated confirmation with the best of truth:

►Superpower in **Medical & Agricultural Sciences** in the entire world is **India** at present,

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►Superpower in **Economy** in the entire world by dethroning USA with an excess of giant difference is **China** at present,

►Superpower in **Nuclear Military Science** in the entire world is **Russia** at present, and

►Superpower in **Power of Mind in Genomological Sciences** in the entire world with no rival & claimer is **Ethiopia** forever, **being nondethronable** endlessly for countably infinite number of the future generations to come (i.e., of all human races)!!!!

Genomology is a **Giant Ethiopian Science** of educational asset contributed to all human races of the world by dismissing **fake sciences of Biology** that has been paralyzing scientific progresses of student children of all human races of this planet (Earth) for centuries.

Genomology consists of:

►**pure genomology,**

►**genomotechnology,**

►**medical sciences, and**

►**agricultural sciences**

Ethics: I declare that no ethical error is committed in the production of this paper. I also declare that I don't have any conflict of interest with anybody.

Acknowledgements

I am deeply grateful to scientists acknowledged in the text and list of references of this paper for

their providing me with confidential data that can be counterchecked, for their correctness, with observable facts in the natural environment as well as with truths in reputable journals, and Internet. This is so because science cannot develop without science. I am really thankful to authors of musical art & musicians for their carefully following and transforming my published articles of genomological sciences into musical films. I am very strongly thankful to those global scientific communities for their genuinely following my task of performing to establish the sciences of Genomology and for their authentic thanking me by way of emails for what I have contributed to the scientific world of Genomology. My thanks definitely go to genomologists who are involved in presenting video lessons of Figure 8.

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Video 1: Abraham Gebremedhin Ethiopia Hagere Lyrics አብርሀም ገብረመድህን ኢትዮጵያ ሀገሬ በግጥም

Video 2: Berhe Amare - Kihdet (Official Video) Ethiopian Tigrigna Music

Video 3: Birhan Wubaye - Demelash ብርሀን ውባየ - ደም መላሽ (ደመላሽ) New Ethiopian Music 2022

Video 4: Biruktawit Shimelis kef yibel 2022

Video 5: Azeb Dagnaw New Ethiopian Music 2021

Video 6: Abdurahman Abuta - Amhara Nen አማራ ነን - New Ethiopian Music 2022

Video 7: Getnet Alemayehu & Bekalu Alemayehu - Atfersim አትፈር...ስም (አትገረምም ቁ_3) - New Ethiopian Music 2021

Video 8: Dan Admasu - Layle Kulu - ዳን አድማሱ - ላይለ ኩሉ - New Ethiopian Music 2022

Video 9: New Ethiopian Music Video ፋንታሁን ገብሬ Fantahu Gebre እንደድሮው Endedrow 2022

Video 10: Tigist Asmare - Alen wey - ትዕግስት አስማረ - አለን ወይ - New Ethiopian Music

Video 11: Amanuel Goitom - Timtim - ጥምጥም ብ ኣማኑኤል ጎይትኦም ሑብ - New Eritrean Music 2022 - Alena Records

Video 12: EMNA ድሕሪ ወያነ ቀርኒ ኣፍሪቃ ከመይ ክመስል'ዩ Eritrean Media Net Asmera

Video 13: WARSAY FULL LIVE MUSIC SHOW - New Eritrean Music 2022

Video 14: Beraki Gebremedhin ‘ጅግና መሬት Eritrean Music Live On Stage 2022 SELEDA

Video 15: Melake Abraham - New Eritrean music 2022 - Ashebr - መልኣከ ኣብርሃም - ኣሸብር

Video 16: New Eritrean remix music fthawi gtnsie nmenom tefkri 2022-----ንመኖም ተፍቅሪ ብፍትሓዊ ገትንሳኤ -ናይ ወዲ ትካቦ_

Video 17: Tesfaldet Mesfin - 4ይ ግምባር New Eritrean Tigrigna Music 2022

Video 18: Nahom yohannes (meste)- lba' tsmae ልባ'ትስማዕ - New Eritrean Tigrigna Music 2022

Video 19: የሃረር ጅብ Agazi masresha terefe 2022 አጋዐዚ Ethiopia

Video 20: የቃል ማስተንቀቅያ 9 December Agazi masresha terefe 2022 አጋዐዚ Ethiopia

Figure 10: Videos of musical films displayed in honor of the uniquely automatic molecular machine termed **Genome**.

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(a)

(b)

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(a)

Figure 11: National flags of (a) Ethiopia; and (b) Eritrea.

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Figure 12: Feleke Eriso Orbalo BSc, MSc, PhD.

Feleke EO is:

►the **first** integrator of **Genomology**, **Chemistry**, & **Physics** by way of the same language of **Universal Reactions of Matter**,

►the **first** interpretor of the fact that both the **undesirable genomic changes** that result in genomic diseases and the **desirable genomic changes** in normal human genome which result in normal phenotypes in the individuals synthesized are **countably infinite** in potential number of kinds,

►the **first** genomologist to prove the fact that viruses are certainly **genomic-things**,

►the **first** genomologist who verified the best of truth with spectacular & concrete evidences about the fact that viroids are **genomic-things,**

► the **first** genomologist to verify that the **Genome**'s **designing engineers** in the synthesis of individuals of all genomic-things are its **transcripts** & **proteins**.

►the **first** genomologist to prove that **Genome** is the **unit of both structure & function** of every individual of all genomic-things by dismissing the **fake Cell Theory** which stated that **Cell** is the unit of both structure & function of every individual of all **living-things** (i.e., genomic-things),

►the **first** scientist on this planet (Earth) to define what a scientist (living-thing or genomic-thing) including himself as a genomic-thing, Before him, scientists didn't know themselves but they were creating other sciences,

►the **first** scientist to interpret what the actual autointracellular pathogen is in diseases of cancer & diabetes mellitus type 1,

►the **first** scientist to interpret that **immune response**, **epigenetic modifications/changes**, **syndromes**, and **symptoms** observed are the evidential **supersensitive** responses of the human **Genome**,

►the **first** disqualifier & disprover of **Endosymbiotic Theory** about the origins of Mitochondrion & Chloroplast published by the authorship of **Lynn Margulis**,

►the father of all scientists of all sciences of this planet (Earth) with no chance for exception,

►the father of the **Perfect Law of Genomological Sciences**,

►the father of **Genome Model**,

►the father of **genomic-things**,

►the father of **genomosphere** that is in sunlight the whole 24 Hrs as the sun rises & sets in the genomosphere,

►the father of nonstopping automatic generations of **genomic reactions** in every species of genomic-things from viroids up to angiosperms or humans,

►the father of **superscience** (science of nonstopping automatic genomic reactions for countably infinite number of generations),

►the **universal omniscient** in dismissing fake sciences of **Biology** & in generating correct sciences of **Genomology**,

►the son of rain-bow colored **Ethiopia** by birth,

►one of the **Unique Educational Assets** of all human races of this planet that money cannot buy, and

►the Superpower in **Power of Mind in Genomological Sciences** in the entire world with no rival & claimer forever!!!!

★**Genome** is the only **automatic molecular machine** that synthesizes all genomic-things & itself including you & me!!!!