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CURLI FIBRES AND PRION STRUCTURAL REVERSIONS – IMPLICATIONS TO PHYSICAL BIOLOGY STUDIES

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ABSTRACT

New investigations in the field of protein structures, bacterial exudes and prion research; and related experimental indications derived suggest that when infectious forms of prion plaques placed in or with resistance – providing variant form(s) are irradiated with appropriate laser power; reversions of prion plaques into structures like coils, helices, etc. may hypothetically take place. These structures are less stable than the beta sheets, hence more susceptible to being biologically cleared off the plaque residues. This provides for a means to effectively cure or prevent prion – like amyloid plaque related diseases; with further implications for physical biology.

Key Words: Curli fibres, Prions, Amyloids, Protein structure - coils, Helices, Biofilms, etc

INTRODUCTION

Curli fibrils are proteins in the extracellular matrix secreted by *Enterobacteriaceae to make biofilms*; which aid primarily in adhesion to surfaces and invasion of host cells. They belong to the class of Amyloid fibre proteins which include the prion proteins. They are known to interact with various other proteins some of which lead to pathogenesis as in the case of bovine mastitis (1).

Curli fibres are considered functional amyloids as they possess many properties of amyloid proteins, but not as a consequence of their misfolded nature. Curli fibrils possess a cross-β structure which characterises protein amyloids. But solid state NMR studies indicated that the Curli structures are not based on in-register parallel β-sheet architecture, which is common to most human disease-associated amyloids and the yeast prion amyloids. (2).

Generally, the histopathological definition of amyloid is an extracellular, proteinaceous deposit with beta sheet structure. When stained with Congo red dye and seen under a polarized light they give an apple – green birefringence; which in general is commonly used to identify cross – beta type structures (3). Biophysically a polypeptide which polymerizes to form a cross-beta structure, *in vivo* or *in vitro,* may be called an amyloid. However, of late amyloid species have been observed in distinct intracellular locations as well (4); some of which, although demonstrably show cross-beta sheets in structure, actually do not have the classic histopathological characteristics such as the Congo-red birefringence (5).

Prions as transmissible agents causing lethal neurodegenerative diseases and are composed of assemblies of misfolded cellular Prion Protein (PrP) (6). All known prions can induce formation of amyloid folds, wherein proteins polymerise into aggregates consisting of tightly packed beta sheets. Amyloid aggregates are fibre - like growing from their ends and replicating when breakage causes two growing ends to become four growing ends (7).The PrP variant, G127V, under positive evolutionary selection during the epidemic of Kuru, has been reported to have provided strong protection against this disease in the heterozygous state (8).

Transgenic mice expressing both variant and wild type human PrP are completely resistant to both Kuru and classical CJD prions (which are closely similar) but can be infected with variant CJD prions. However, mice expressing only PrP V^{127} are completely resistant to all prion strains and demonstrates a different molecular mechanism to M129V providing for the relative protection against classical CJD and Kuru in the heterozygous state. A single amino acid substitution (G→V) at a residue invariant in vertebrate evolution is as protective as a deletion of the protein. Transgenic mice ex-

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pressing different ratios (either hetero or homo – zygous) of variant and wild type PrP revealed that PrP V^{127} is completely refractory to prion conversion besides acting as a potent dose-dependent inhibitor of wild type prion propagation (9); although the actual *modus operandi* of this phenomenon is yet to be found out.

Studies involving the N-terminally truncated form of the prion protein, PrP 27-30, and its corresponding recombinant protein, rPrP revealed that solubilising it in SDS caused transitions induced by changing the conditions from 0.2% SDS to physiological conditions; which are characterized by changes in solubility, resistance to proteolysis, secondary structure and multimerization. The alpha-helical structures of PrP can be transformed into beta-sheets within a minute consisting mainly of dimers. Large oligomers found after 20 minutes and larger multimers found several hours later exhibit resistance to proteolysis. Thus, monomeric alpha-helical conformations are stable in SDS or when attached to the membrane; but multimeric conformations of beta – sheet structures, forming at the state of lowest free energy, become stabilised at neutral pH in aqueous solution (10).

Crystals with beta – pleated sheets are one of the most stable secondary structures of proteins, a plausible reason for their pathogenesis in the formation of plaques in neuropathies like Alzheimer's disease. It is supposed that the beta-pleated-sheet crystals in the dry solid state are so stable that they do no melt upon been given heat energy alone. Peggy et al. demonstrated that the beta-pleated-sheet crystals can directly melt, changing from their solid states into random coils, helices, and turns. With fast scanning chip calorimetry performed at 2,000 K/s they reported the first thermally reversible melting of beta-pleated-sheet crystals of proteins (11). Their experiments using beta – pleated silk fibrin and synthetic polymers confirms the similarity of thermal melting behaviour of crystals of lamellar synthetic polymers with that of beta-pleated-sheet polypeptides.

Macedo et al. demonstrated that recombinant murine PrP and its C-terminal domain (90–231) can attain amyloid conformations inside bacteria. And the inclusion bodies formed by these two PrP proteins display conformational diversity, since they differ in fibril morphology, binding affinity to amyloid dyes, stability, resistance to proteinase K digestion and neurotoxicity (12).

Such indications can form the basis of new investigations; wherein infectious forms of the prion plaques placed in or with the resistance – providing variant forms get irradiated with appropriate laser power and are then checked for reversions into structures like coils, helices, etc. which are less stable than the beta sheets and therefore more susceptible to being biologically cleared off the plaque residues; hence providing for means to effectively cure or prevent prion – like amyloid plaque related diseases?

One must however take into consideration that "Energy loss due to the skin barrier for continuous HeNe (632nm) laser is 90%, for continuous GaAlAs (820 nm) and Nd:YAG (1064 nm) IR lasers, 80% and for GaAs (904 nm) infrared pulse laser, 50%" (13); these being the lasers commonly used on biological tissues, most of the time. In this scenario; there arises the problem of living tissue getting burnt with increasing laser powers; potentially restricting such advancements till the development of special techniques or systems only.

DISCUSSION

The implications of these advancements in studies of protein structure and their associated manifestations indicate the exciting possibilities of developing novel techniques to bioremediation. However, such techniques even if they were to be established in non – living systems, would require still higher efficiency for the focusing of high power lasers, etc. into microscopic cellular niches inside living bodies. This in turn calls for the development of better precision instruments for able accessorising of such technology. These technologies would find widespread applications in other varied fields as well; like cleaning of bacterial plaques instead of plasma cleaning and so and so forth.

CONCLUSION

Protein structures are directly correlated to the medium in which they fold. The chemical environment of protein folding is ultimately determined by the physical properties of the solution like density, specific gravity, etc.; which are in correspondence of the gravitational field and interplay of other fundamental forces and their manifestation(s) in the medium.

Applications at the interface of protein structure and high energy irradiations can lead to the development of useful techniques whereby translated proteins may be effectively dealt with for misfoldings and its related repercussions without genome editing; thus, providing for effective biomedical supplementary methods to cure and prevent till – date incurable diseases.

These indications encourage further interesting experiments wherein such biophysical interactions of protein – high power lasers are investigated as to how these work out in the natural environment of the biosphere of the Earth. It would also be interesting to study such experiments and look into their manifestations change over time on extra terrestrial Earth – analogue planetary surfaces like that of Mars where physical properties are variant. Surely, exciting implications relating ultimately to the evolution of molecular conformations into

living reactions and life forms shall be found.

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Conflict of Interest

The author declares that there is no conflict of interest.

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