

Critical Role Of Proline And Glycine Conservation With Repeats In Neurodegenerative Disorders

K A, S S, K V, C K, S A, K R

Citation

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Abstract

Progressive neurodegenerative diseases like Huntington's, Alzheimer's disease, Down's syndrome, Tay Sachs disease, spino cerebellar ataxia 2, Kennedy disease, Dentatorubral – pallidolusian atrophy and ALS have been gradually realized to be evolved from the common cellular and physiological pathways. The aim was to identify possible biases in the amino acid repeat patterns with respect to the repeats in other sequences responsible for neurodegenerative disorders, as this could be informative for specific constraints operating in the repetitive structures. Previous studies suggest the misfolding of the amyloid proteins as one of the most prominent causes. Our study reveals the critical role of proline and glycine conservation with Alanine, glycine, proline residue repeat polymorphism levels. Proline toxicities have been found involved in cardiac muscle disorder, neuro transmitter disorder, congestive heart failure and major depression found in most of the degenerative diseases worked on. We inspected the relative position 58 where proline conservation was seen in spino cerebellar ataxia 2 and Huntington giving rise to the common symptoms of the disease. Our study also suggests that Q repeats mostly fall in helical regions indicating responsible Proteins to be the surface proteins which cause different severe symptoms and effects.

INTRODUCTION

Neurological and psychiatric disorders taken together account for more chronic suffering than all other disorders combined¹. The sunset has been a prolonged one, as is usual in most neurodegenerative disorders, of which Huntington's and Alzheimer's are the prototype. All have an insidious onset, progress slowly over years, and death is usually due to an intercurrent illness and not directly due to the disease itself. The diseases will rise with increasing longevity. Much of the burden is also borne by carriers and relatives. Brain parenchyma is supposed to be the layer in brain where the illicit protein deposits take place and give rise to different neurodegenerative disorders². Previous studies reveal the role of proteins like amyloid which are rich in beta sheets to be involved in the toxicity and lethality of the progression of the disease. Our study suggests role of the alpha helical residues in toxicity and lethality of the diseases which are also supported with the conservation of proline and glycine residues. Previous animal trials by beta sheet breaker residues may have failed because of the of proline conservation in the neurodegenerative studies³. As per our study on proline repeats a suitable therapy for the treatment of the neurodegenerative disorders may be obtained. Proline-rich domain, along with a charged domain, is critical for

PQE-1 protein function. Analysis of ppe-1 suggests that proteins exist that specifically protect neurons from the toxic effects of expanded polyQ disease proteins⁴. Proline derivatives have affinity for the calcium channel alpha -2 delta subunit which is useful in the treatment of epilepsy, feats, hypokinesia, cranial disorders, neurodegenerative disorders, depression, anxiety, panic, pain, fibromyalgia, arthritis, neuropathological disorders, sleep disorders, visceral pain disorders and gastrointestinal disorders⁵. Glycine and proline residues are frequently found in turn and loop structures of proteins and are believed to play an important role during chain compaction early in folding⁶. The proteins worked out in our study have a good composition of proline repeats as well as conservation which may be worked out for the therapeutical aspects.

PROCEDURE

In silico analysis of the worked out proteins in the present study is concluded to be correlated with some proteins like titin, synapsin, natriuretic peptides, beta casein which causes different lethal conditions like Cardiac muscle disorder, neurotransmitter disorder, congestive heart failure, Parkinson's, major depression etc.

1. CONSERVATION OF PROLINE (P) AND GLYCINE (G) RESIDUES –

We found proline and glycine residues to be conserved in all the model neurodegenerative diseases. For this analysis, we used CLUSTAL W Boxshade (fig 1) and texshade (fig 2) which gave us the conservation pattern of proline and glycine.

FIG 1 (Green Color shows complete conservation)

Figure 1

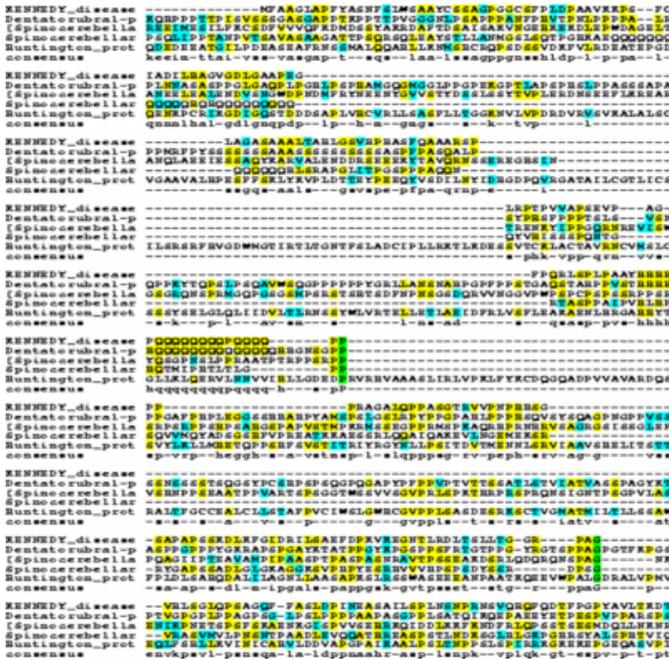
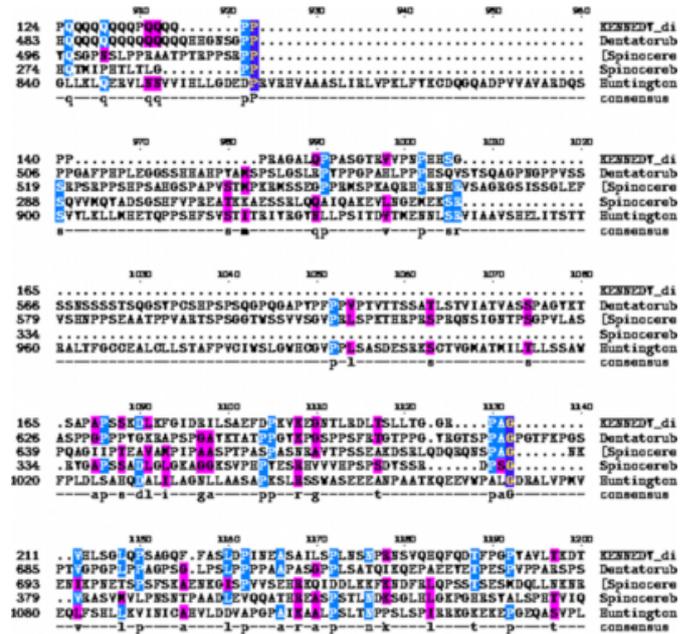


FIG 2 (Dark Blue color shows complete conservation)

Figure 2



2.FORMATION OF HELICES BY GLUTAMINE (Q) REPEATS-

Using PREDATOR it was found that repeats of glutamine form the helices, whereas a glutamine repeat can also be responsible for formation of strand.

3. GENE EXPRESSION LEVEL-

Gene card detected the expression of all the selected genes to be expressed in brain with a higher percentage.

1. HUNTINGTON DISEASE PROTEIN

>gil1170192|slp|P42858|HD_HUMAN Huntingtin (Huntington disease protein) (HD protein)

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1
MATLEKLMKAFESLKSFQQQQQQQQQQQQQQQQQQQQ
QQQQQPPPPPPPPPP 50
HHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHH
HH_____
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2.DENTATORUBRAL-PALLIDOLUYSIAN ATROPHY PROTEIN

>gil29429203|slp|P54259|ATN1_HUMAN Atrophin-1 (Dentatorubral-pallidolusian atrophy protein)

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101
PSEVPAGFPQRLSPLPAA YHHHPQQQQQQQQPQQQ
QPPPPPRAGALQPP 150
HHHHHH_____
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Author Information

Kumar A

Dept of Bioinformatics, BioAxis DNA Research CentreBioAxis DNA Research Centre

Srivastava S

Dept of Bioinformatics, BioAxis DNA Research Centre

Keshore V

Dept of Bioinformatics, BioAxis DNA Research Centre

Chengappa K

Dept of Bioinformatics, BioAxis DNA Research Centre

Sinha A

Dept of Bioinformatics, BioAxis DNA Research Centre

Kant R

Dept of Bioinformatics, BioAxis DNA Research Centre