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INTRACELLULAR FUNCTION OF UBIQUITIN SYSTEM

Dr. İbrahim PİRİM
Dr. Ahmet KIZILTUNÇ
Dr. N.Nuri ŞAHİN

SUMMARY:

In this article, we have searched the litarature to explain the ubiquitin system and its function within the cell, since the system appears to be important value to asses some neurodegenerative diseases in which ubiquitin is accumulated within the neuron.

UBIQUITIN

Ubiquitin (ub) is a small protein of 76 amino acid residues that is of high intracellular abundance in all eukaryotic cells. Its primary sequence shows extraordinary sequence conservation between species. there being only 3 amino acid differences between the human and yeast protein. With regard to structure ub has a highly packed globular structure, with 3 faces that may or may not interact with other proteins, one basic, one acidic and one hydrophobic (1,2). There is extensive hydrogen bonding between the molecule, thus suggesting that the protein has a firm rigid structure (fig.1). This structure may account for the remarkable thermal stability of ub associated with the heat shock response. The protein also shows resistance to a broad range of pH, and this may also be due to its internal structure (3-5). Catalysed by a family of enzymes, the C-terminus of ub, which protrudes from the globular core, can be attached via an isopeptide bond to the epsilon-amino groups of lysineresidues of target proteins (6-8).

Modifications of proteins by ub conjugation are thought to alter structure and modulate the function of protein substrates.

Atatürk Üniv. Tıp Fakültesi Biyokimya Anabilim Dalı

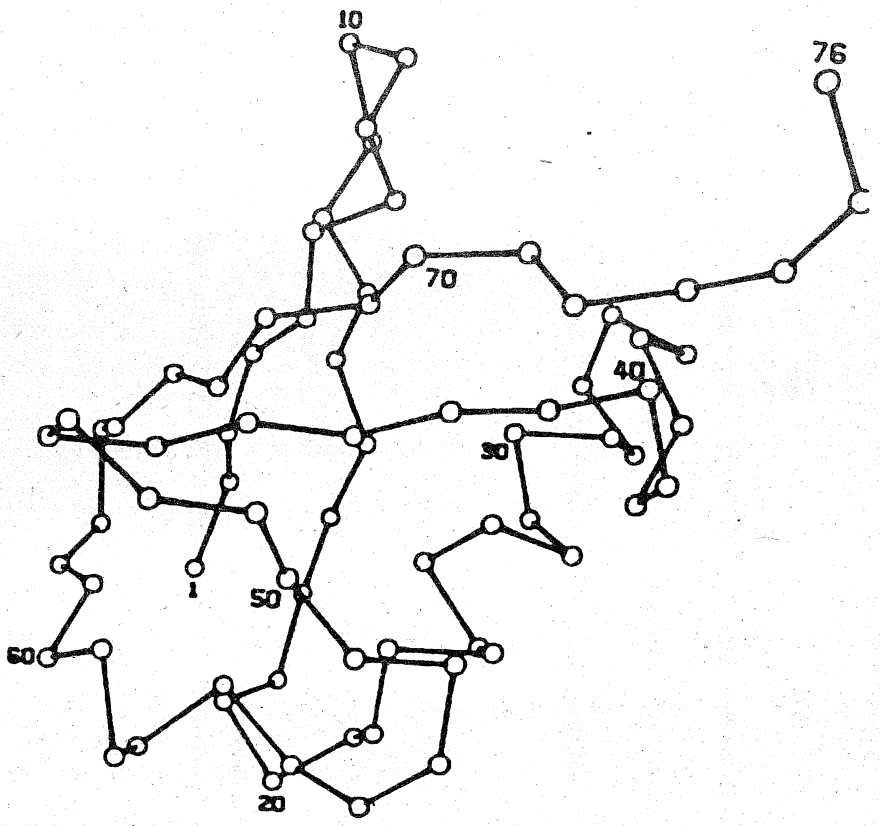

Fig.1:

GENES ENCODING UBIQUITIN

Three classes of ub genes have so far been identified in all eukaryotic cells. These three classes named I, II and III all code ub precursor molecules that have to be specifically processed by C-terminal hydrolase (9). Class I and Class II ub genes both code for fusion proteins. These consist of a ub molecule with extensions of 52 and 76 amino acid residues at the C-terminus respectively (10). Class III genes code for polyubiquitin proteins (11) (see fig. 2).

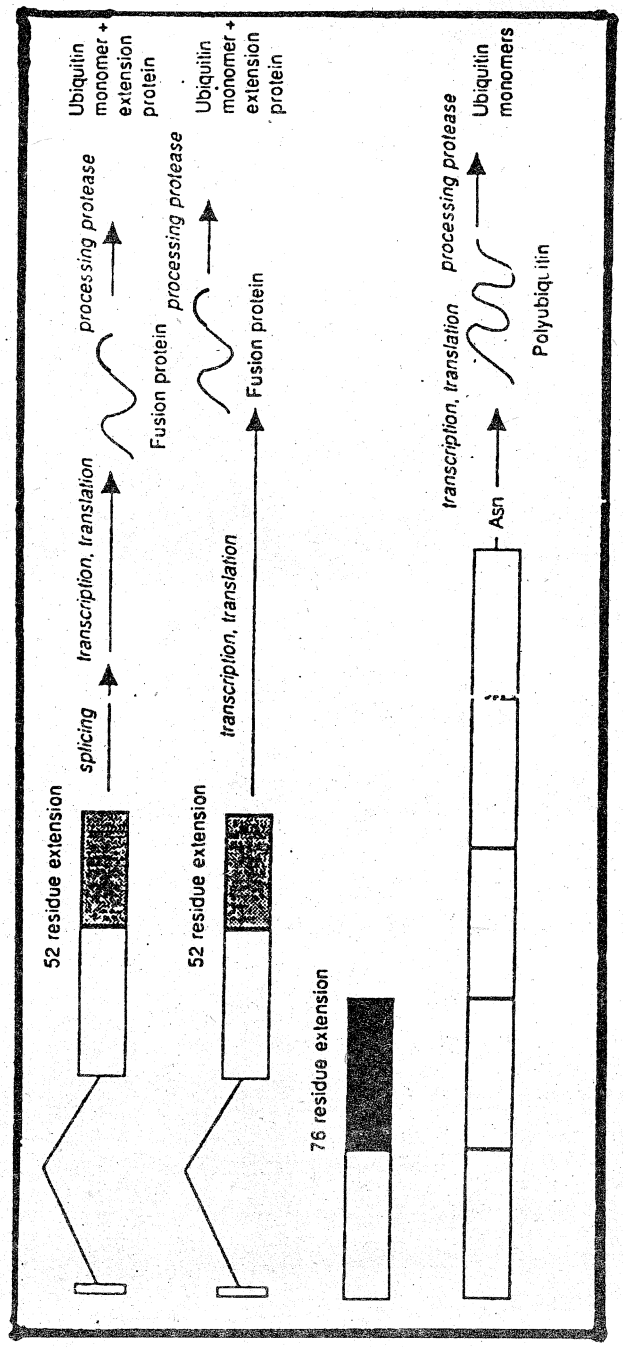
52 residue extension
splicing
transcription, translation
Fusion protein
processing protease
Ubiquitin monomer + extension protein
52 residue extension
transcription, translation
Fusion protein
processing protease
Ubiquitin monomer + extension protein
76 residue extension
transcription, translation
Asn
Polyubiquitin
processing protease
Ubiquitin monomers

Fig 2.

FUNCTIONS OF THE UBIQUITIN

In vivo, ub has been found conjugated to many proteins, including histones (12), actin (13), cell surface receptors (14) and the intracellular neurofibrillary tangles associated with many neurodegenerative diseases (15). The reasons for many proteins which are found conjugated to ub are destined for the ub dependant proteolytic pathway.

Ub plays an important role in the cell cycles involving in the degradation of cyclin.

The conjugation of ub to histone H2A, was first reported by Goldknopf in 1975 (16). This modification has also been identified in histone H2B. This suggests that ub may be important in the decondensation of chromosomes, as it is removed in the final stages of chromosome condensation and restored on post mitotic decondensation. There is no doubt that they are responsible for marking specific regions of the chromosome, but whether these tags are designed for DNA transcription or DNA repair is still unclear.

UBIQUITIN AND NEURODEGEN ERATIVE DISEASES

As the name indicates, neurodegenerative diseases are chracterised by degeneration and eventual death of nerve cells, many of which exhibit one of a variety of inclusion bodies. The current view is that most of these inclusions are composed of abnormal filaments and share epitopes with cytoskeletal proteins. Recently, many of these filaments have also been shown to have ub-conjugate immunoreactivity.

UBİQİTİN SİSTEMİNİN HÜCRE İÇİ FONKSİYONU

ÖZET

Ubiquitin 76 amino asitlik 8565 dalton moleküler ağırlığa sahib olan bir proteindir. Bu protein bütün ökaryotik hücrelerde mevcud olup türler arasında iyi korunmuştur. Bu proteninin en önemli özelliği, çeşitli sebebler ile ortaya çıkan nöronal harabiyet sonucu sinir hücresinde ubiquitin mevcudiyetinin aşırı bir şekilde artışının olmasıdır. Makalemizde bu protein hakkında daha geniş bilgi elde etmek için litaratür taraması yaptık ve ileride yapılabilecek önemli bir araştırma sahası olabileceğini vurgulamak istedik.

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