PRIONS AS PROTEINACEOUS GENETIC MATERIAL

M.D. Ter-Avanesyan, A.I. Alexandrov, V.V. Kushnirov
A.N. Bach Institute of Biochemistry of RAS, Russia, 119071 Moscow, Leninsky Ave, 33, bld. 2.
E-mail: mdter@inbi.ras.ru, Tel.: 8(495)954-40-97

Amyloids are fibrillar aggregates formed by proteins which are normally soluble. Amyloid formation is accompanied by the conformational rearrangement of proteins into a specific cross-β structure. Amyloids were discovered as causative agents for a large group of diseases of humans and animals, called amyloidoses a subclass of which, called prion diseases, are transmissible. However, many proteins, which do not form amyloids *in vivo*, have been shown to form fibrillar aggregates under some conditions *in vitro*, indicating that the ability to form the amyloid structure is a generic property of polypeptide chains. While negative selection may have made amyloidogenic proteins rare at present, in the past this property is likely to have been more common and may have played an important role(s) at early stages of evolution of living systems. Notably, living organisms can use amyloids for diverse and significant biological functions. Though the number of such examples is still not high, accumulating data demonstrate that some endogenous proteins can convert during normal physiological life cycle of the host organisms into amyloid fibrils that have functional rather than disease-associated properties. Perhaps the most remarkable of these properties lies in the ability of such amyloid structures to serve as transmissible genetic elements distinct from DNA genes. This phenomenon is related to a specific type of amyloids, called prions. While in mammals prions are infectious agents responsible for transmissible amyloidoses, in lower eukaryotes, e.g. in the yeast *Saccharomyces cerevisiae*, they underlie inheritance of phenotypic traits. In yeast a critical role in transformation of amyloids into genetic material is played by the chaperone machinery responsible for their replication and inheritance. The mechanism of yeast prion replication and their evolutionary origin are discussed.