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Amyloid-like aggregation of human transketolase

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Abstract

Human transketolase (TKT, EC 2.2.1.1) catalyzes transfers two-carbon units from ketoses (donor) to aldoses (acceptor). Abnormal activity of the enzyme in human tissues (hTKT) is associated with development of some severe pathological processes, including neurodegenerative and oncological diseases. There are some reasons to believe that these effects may be caused by aggregation of hTKT. In particular, the corresponding *E.coli* TKT is quite prone to aggregation [Jahromi R., 2011]. Crystal structure of hTKT demonstrates high content of β-structure [Mitschke L. 2010], which is known to be a key element of amyloid fibrils. The objective of this study was to investigate the propensities of hTKT for aggregation and factors affecting this process. Previously hTKT with N-terminal (His)6-tag was expressed in *E.coli* and isolated from cytoplasm fraction using Ni-agarose affinity chromatography [Meshalkina L., 2013]. However, most of the protein was found in the inclusion bodies (IBs). Preparations of hTKT solubilized from IBs using 1% SDS were highly stable. At the same time, dissolution of IBs in 8 M urea results in formation of SDS-resistant sediment upon incubation for 24 hours at 8°C. Analysis of the corresponding supernatant in SDS-polyacrylamide gel showed the presence of high molecular weight aggregates, located at the start of gel. These aggregates demonstrate the ability to bind specifically Congo red (CR) dye. Both SDS-resistance and CR binding indicate the amyloid nature of aggregates formed. With the purpose to identify potentially amyloidogenic sites within hTKT structure several well-known amyloid prediction software packages (FoldAmyl, Aggrescan, etc.) were used. The most pronounced sites were identified in the regions of 45-55, 145-185, 350-395, 460-490, 570-590 aa. In conclusion, the results obtained allowed one to suggest, that hTKT is prone to amyloid-like aggregation, the presence of urea being the triggering factor. The aggregation of hTKT may be of biological significance *in vivo*.

Biography

Nadejda Davydova is Senior Research Scientist at A.N. Nesmeyanov Institute of Organoelement Compounds Russian Academy of Sciences (INEOS RAS) in Moscow with the following research interests: organic chemistry; biotechnology; research in bioactive polymers; drug design; search for new drugs. Nadejda Davydova graduated from the Moscow Institute of Fine Chemical Technology and obtained her PhD in Organic Chemistry from the All-Union Chemical Pharmaceutical Research Institute in Moscow. Dr. Nadejda Davydova is the author of many inventions, e.g., discovery of original chemical substances for Russian antiarrhythmic drugs: Nibentan and Niferidyl (Refralon).

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