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International Journal of Bioinformatics Research
ISSN: 0975–3087, E-ISSN: 0975–9115, Vol. 3, Issue 2, 2011, pp-200-201
Available online at http://www.bioinfo.in/contents.php?id=21

HIGHER CARBON CONTENT IN ALANINE AMINOTRANSFERASE

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Received: May 10, 2011; Accepted: July 25, 2011

Abstract- Alanine aminotransferase (ALT) is an enzymatic protein involved in catabolism of amino acids. The carbon distribution study on this clinically important protein is carried out here. The study reveals that the carbon content is generally higher than the expected values of 31.45%. The alteration in carbon content other than the active site might improve the activity of this enzymatic protein. Particularly the reduction at the carboxyl end of the sequence is more appropriate. Carbon distribution analysis clearly locates the active site of ALT protein, which is reported here.
Keywords: carbon distribution, ALT, alanine transaminase, alanine aminotransferase, carbon content, Carbana, jaundice, ALAT, enzyme.

Introduction

Alanine transaminase or ALT is a transaminase enzyme, found in serum and various bodily tissues, but is most commonly associated with liver [1]. It catalyzes the transfer of an amine group from alanine to a-ketoglutarate. It is often a case for jaundice patient in clinical laboratories. Other proteins such as aspartate aminotransferase (AST) and gamma-glutamyltransferase (GGT) are also clinically important and concern but ALT is taken as a case study here. Alanine transaminase is a sensitive predictor of liver diseases. The risk of liver disease is higher in diabetics [2]. It is reported that the ALT elevation is 3–4 times higher in patients with either type 1 or type 2 diabetes than normal. The ALT levels in relation to the clinical, biochemical and histological characteristics of patients with hepatitis C is investigated [3]. It reports that in patients with hepatitis C virus the elevation of ALT is associated with viral load and duration of disease.

Carbon distribution in proteins is the factor which determines protein stability and function (4 &5). In this line of study the carbon distribution analysis on ALT is important step in understanding the nature of this protein and understands its role in human and its relevance to diseases. This study is carried out on ALT of human and compared with other related species including bovine, mouse and rat.

Materials and Methodology

Alanine amino-transferase sequences of human, bovine, mouse and rat are taken from Swissprot database. The carbon distribution profile was obtained from Carbana software which is available online (www.rajasekaran.net.in/tools/carbana.html). The principle, methodology and procedures are given in reference [6]. The Carbana program reads the protein sequence in fasta format and converts into atomic sequence which then statistically analysed for carbon content. The length for carbon averaging is taken as 500 atoms. The step interval is taken as 17 here. The outputs obtained from Carbana are plotted for visualisation of carbon content along the sequence and discussion. Though there are several ALT sequences of different species are studied, only 4 are given here for discussio.

Results and Discussion

The carbon distribution profile obtained from Carbana tool is shown in fig.1. The figure shows the percentage of carbon along the sequence. Normally protein prefers to have 31.45% of carbon all along the sequence but other than active site. The region along the sequence have above 31.45% is considered to be higher carbon content or hydrophobic regions. As can be seen in the figure, most of the portions are above this value. That is to say alanine aminotransferase contain more than sufficient carbon content.

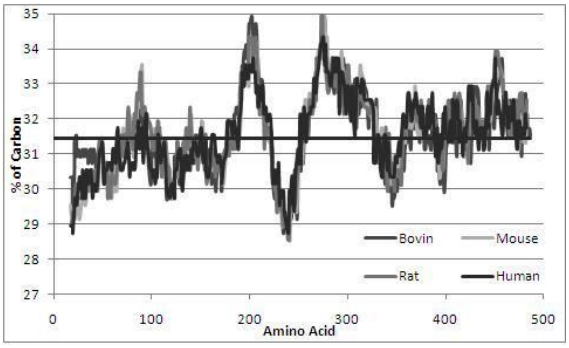

Fig. 1-Carbon distribution in alanine aminotransferase of different species

Generally, protein accumulate higher amount of carbon at

active site. This increase in carbon content at active site reduces carbon content in the flanking regions. ALT has the active site at 175 - 375. As seen in the figure that this region is identical in all four species including in human, bovine, mouse and rat. Apart from this active site, the other regions show up with variations in carbon contents. This confirms the mutations that are accepted during evolution in these regions. But otherwise the mutation is not tolerated at active site. ALT sequences of several other species are studied but results are not shown. A variation in carbon distribution pattern is noticed in the other species.

As alanine transaminase is a sensitive predictor of liver diseases and its elevation is associated with diabetics and hepatitis virus infection, the higher carbon content reported here might give clue on alteration in liver cell. Alteration in carbon content in the C-terminal (after amino acid 350) is suggested. A program for mutational study based on carbon content is underway. For stabilization or activation of this ALT protein can studied using this program.

Conclusion

A carbon distribution study on alanine aminotransferase is reported here. Generally this enzymatic protein contain greater amount of carbon. Reduction of excess carbon will improve the activity of this enzyme. Particularly the reduction at the carboxyl end of the sequence is more appropriate. The carbon distribution in active site is remarkably same in all 4 species studied here. The carbon distribution analysis on ALT is another proof of active site identification from computational point of view. Further to improve these clinically important enzymatic proteins one can do a detailed study to see its relevance in its mRNA sequences to fix the hydrophobicity that would be the permanent and passed on to the next generation.

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