CHAPTER 5

CARBON DISTRIBUTION STUDIES ON ALANINE AMINOTRANSFERASE

5.1. INTRODUCTION

Alanine aminotransferase or ALT is a transaminase enzyme, found in serum and various bodily tissues, but is most commonly associated with liver (Bakthavathsalam, 1984). It catalyzes the transfer of an amine group from alanine to aketoglutarate. 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 aminotransferase is a sensitive predictor of liver diseases. The risk of liver disease is higher in diabetics (West et al., 2006). 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 was investigated (Akkaya et al., 2007). 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 was the factor which determines protein stability and function (Suhanya et al., 2008; Rajasekaran et al., 2009). In this line of study the carbon distribution analysis on ALT is important step in understanding the nature of this protein 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.

5.2. METHODOLOGY

Alanine aminotransferase sequences of human, bovine, mouse and rat are taken from SWISSPROT database. The carbon distribution profile was obtained from
CARBANA software is available at www.rajasekaran.net.in/tools/carbana.html. The principle, methodology and procedures are given in reference (Rajasekaran and Vijayasarathy, 2011). 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 was taken as 500 atoms. The step interval was taken as 17 here. The outputs obtained from CARBANA were plotted for visualisation of carbon content along the sequence and discussed.

5.2.1. DATASETS

Alanine aminotransferase sequences of human, bovine, mouse and rat are taken from SWISSPROT database.

5.3. RESULTS AND DISCUSSION

The carbon distribution profile was obtained from CARBANA tool. The figures 5.1, 5.2, 5.3 and 5.4 showed the percentage of carbon along the protein 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 figures 5.1, 5.2, 5.3 and 5.4 most of the portions are above this value. That is to say alanine aminotransferase contain more than sufficient carbon content. 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 – 275 as shown in the figures 5.1, 5.2, 5.3 and 5.4 that this region showed identical in all four species human, bovine, mouse and rat. Apart from this active site, the other regions showed up with variations in carbon contents. This confirms the mutations that are accepted during evolution in these regions. But otherwise the mutation was not tolerated at active site. ALT sequences of several other species were studied but the results were not shown. However, a variation in carbon distribution pattern was noticed in the other species.
Figure 5.1. Carbon distribution in alanine aminotransferase of human using CARBANA.
Figure 5.2. Carbon distribution in alanine aminotransferase of rat using CARBANA.
**Figure 5.3.** Carbon distribution in alanine aminotransferase of bovin using CARBANA.
Figure 5.4. Carbon distribution in alanine aminotransferase of mouse using CARBANA.
As alanine aminotransferase is a sensitive predictor of liver diseases and its elevation was associated with diabetics and hepatitis virus infection. The higher carbon content reported here gave clue on alteration in liver cell. An alteration in carbon content in the C-terminal (after amino acid 350) is suggested.

5.4. 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 was remarkably same in all 4 species studied here. The carbon distribution analysis on ALT was another proof of active site identification from computational point of view. Further to improve these clinically important enzymatic proteins one can have detailed study and its relevance in its mRNA sequences to fix the hydrophobicity that would be the permanent and passed on to the next generation.