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Detection of C-terminal Betatrophin Peptide in Human Plasma and Rodent Liver

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Summary: The present study using immunohistochemistry and Western blot analysis shows the intact betatrophin as well as C-terminal fragment peptides in the human plasma and rat liver. By using affinity purification, HPLC and MALDI-TOF, the C-terminal betatrophin fragments have been further identified to be betatrophin (118-198) and betatrophin (133-198). Radioimmunoassay (RIA) and enzyme immunoassay (EIA) also confirm the presence of intact betatrophin and a portion of C-terminal peptide in human plasma. In addition, the present study confirms the plasma betatrophin levels increased after re-feeding. A similar increased C-terminal betatrophin level in plasma was observed. In conclusion, the methods developed here were able to detect betatrophin protein and its C-terminal betatrophin. Our studies also show that both the intact betatrophin and C-terminal betatrophin peptide are present in human plasma and rat liver.
Keywords: betatrophin, plasma protein, liver, MALDI-TOF

Introduction

Betatrophin, a circulating hormone discovered in insulin-resistant states, has been shown to increase pancreatic β cell proliferation [1] and lipid regulation [2]. Although there is some evidence showing a cause-and-effect relationship in the ability of betatrophin to play a physiological role in obesity, diabetes and cardiovascular diseases, the circulating level of betatrophin has not been quantified in the health and diseased state. The major goal of this study was to detect and quantify plasma betatrophin and its fragments in normal and diabetes individuals. In additional, the previous report of Quagliarini et. al. [2], found that the plasma betatrophin level increased after re-feeding from the Western blot analysis. This issue was re-examined using similar observation was made by EIA or RIA.

Based on previous bioinformatics evidence of the presence of protease cleavage sites in betatrophin sequence, proteomic study has found two peptide fragments of betatrophin (TIELLGQEVSR and SAWLGPAYR) from the human plasma and urine samples [3]. We have focused on the antibody against C-terminal betatrophin and to explore the possibility of the presence of this C-terminal betatrophin. We hypothesized that both the full length betatrophin and the C-terminal betatrophin are present in the human blood plasma and rat liver and that the plasma level varies in response to refeeding.