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Post Transcriptional Regulation of Gene Expression

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Abstract: *Post transcriptional regulation by means of RNA editing is a very powerful gene regulation mechanism which aimed to control gene expression at translational level. However this regulation mechanism could result in genetic mutations causing gene products to function abnormally or rendered them completely non-functional depending on the length of the mutated protein*

Keywords: *mRNA; Familial hypobetalipoproteinemia; RNA editing*

1. Introduction

RNA editing is a post transcriptional modification mechanism of premature mRNA. Non-coding regions such as in trons are removed from the premature mRNA so the resulting RNA sequence only contains the coding sequences of a gene. Evidences were gathered to show that RNA editing contributes in mRNA stability and this mechanism is quiet common in unicellular and multi cellular eukaryotic organisms such as in mammals, plants, nematodes, viruses, fungi, protozoa, marsupials, fruit fly, slime molds etc [1]. Besides contributing in mRNA stability, RNA editing is responsible for producing novel or mutated proteins. This post transcriptional regulation of gene expression could result in phenotypic effects that could be beneficial or deleterious [2].

2. Apolipoprotein B mRNA Editing

Apolipoprotein B (APOB) gene is responsible for coding two apolipoprotein B proteins. A 48 amino acid short B-48 and a 100 amino acid long B-100apolipoprotein. These lipoprotein functions in transport of cholesterol and lipids in the blood. Chylomicrons is formed by B-48 apolipoprotein in the intestine which transport cholesterol and fats into the blood circulation. Chylomicrons are also required for the absorption of fat-soluble vitamins A and E.B-100 apolipoprotein on the other hand is produced in the liver and is a constituent of VLDLs (very low-density lipoproteins), IDLs (intermediate-density lipoproteins) and LDLs (low-density lipoproteins) which also act as cholesterol transporters [4]. B-100 lipoprotein permits cholesterol or fats molecules to adhere to explicit receptors present on the surface of the liver cells which transfer low-density lipoproteins into the cell to release cholesterol which is then utilized by the cell. Post transcriptional editing of apolipoprotein B mRNA involves deamination of cytidine to uridine at nucleotide position 6666. As a result glutamine codon (CAA)is altered to a stop codon (UAA) that terminates translation producing two lipoproteins which differs in their amino acids counts [5] (Figure 1).

3. Mutations in Apolipoprotein B Gene

Familial hypobetalipoproteinemia is caused by >90 mutations occurring in Apolipoprotein B (APOB) gene. It is a type of genetic disorder in which the body fails to absorb and transport cholesterol [6]. Mutations in apolipoprotein B gene produces either a B-48 lipoproteins that is shorter than apolipoprotein B-100.Severity of the disorder depends on the length of the polypeptide. Even in these scenarios, normal length B-48 lipoprotein is still produced in the intestine which forms chylomicron

but the mutated B-100 made in the hepatic cells is less likely to be a part of lipoproteins. In extreme cases mutation produces a protein that is even shorter than B-48 and B-100apolipoprotein. As a result no normal length apolipoprotein B protein is produced [7, 8]. This extremely short protein is unable to form lipoproteins in the intestine or even in the liver. The resultant symptoms of the disorder are extremely severe due to the non-functionality of the mutated protein in the transportation of dietary fats and cholesterol. As a result affecting absorbtion of fats and fat-soluble vitamins from the diet leading to familial hypobetalipoproteinemia [9] (Figure 2).

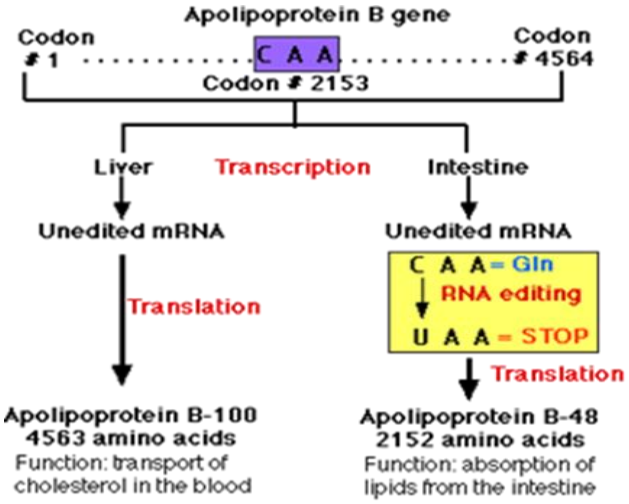

Fig1. *Editing of apolipoprotein B mRNA [5]*

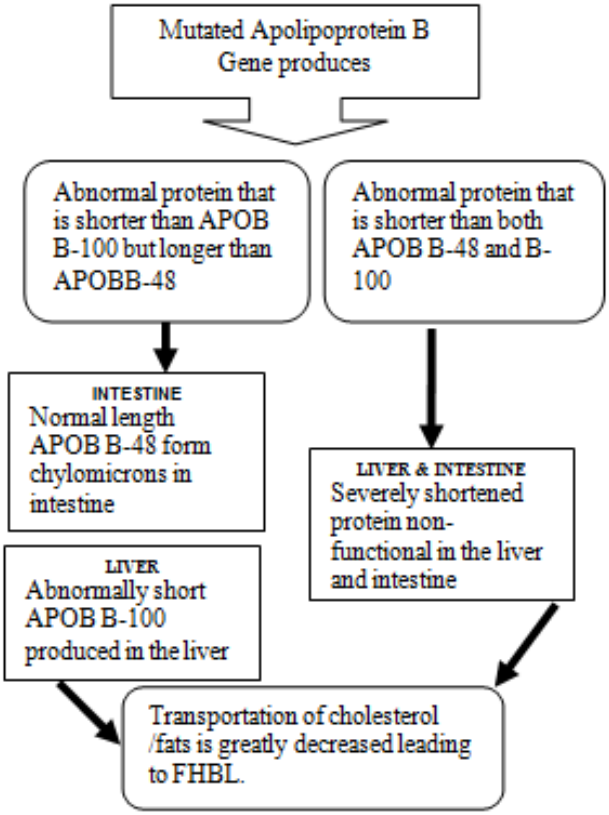

Fig2. *Mutations in the Apolipoprotein B Gene*

Familial defective apolipoprotein B-100 is produce by a minimum of five mutations in the APOB gene .Abnormal level of cholesterol is detected in the blood of the affected ones leading to an elevated risk of developing heart diseases. The transformed protein prevents adhesion of lipoproteins to their respectivereceptors. As a result affecting normal cholesterol levels in the blood. Abnormalcholesterol present in the blood is deposited in different tissues such as skin, tendons, and walls of coronary arteries causing heartstrokes [10, 11, 12].

4. CONCLUSION

Thus an effective yet a major cause of genetic disorders such as familial hypobetalipoproteinemia and inherited hypercholesterolemia.

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