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Abstract

The genetic and epigenetic basis of unconjugated hyperbilirubinemia

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Abstract:

The present study investigated three enzymes involved in the bilirubin metabolism. The first one; the is enzyme 1A1 of UDP-glucuronosyltransferase (UGT1A1) is implicated in hepatic glucuronidation of water-insoluble bilirubin. The two others called SLCOB1 and SLCO1A2 are proteins implicated in the hepatic bilirubin transport. The deficiency in these kinds of proteins leads to the unconjugated hyperbilirubinemia (UCB) and subsequent to cholelithiasis. UCB is a feature of the Gilbert's syndrome (GS) and Criglar-Najjar's syndrome (CNS), which are two hereditary defects in bilirubin metabolism. These defects are caused by mutations in the UGT1A1 gene leading in reduction or absence of UGT1A1 enzymatic activity. UCB is also observed among patients with chronic hemolysis such as sickle cell disease (SCD). Herein, we reported the molecular basis of the UGT1A1 gene in patients presenting with unconjugated hyperbilirubinemia. Also, we investigated the rs4149000 of SLCO1A2 and the rs4149056 of SLCO1B1.395 subjects are enrolled in this study divided into 102 SCA patients, 76 β thalassemia patients, 76 patients with cholelithiasis and 141 controls. The molecular analysis was performed by DNA Sanger sequencing. Several bioinformatic tools were used to explore the effect of the novel mutations. Fifteen different UGT1A1 variations were identified, among which four are described for the first time. Regarding the MicroRNA prediction of UGT1A1 variations, 15 novel MicroRNAs were detected to target the mutated sequence of the mutation c.*90C>T and 5 novel MicroRNAs were identified to target the mutated sequence of the mutation c.*388C>T. As for SLCO1A2, our results show that UCB is associated with rs4149000.

Biography:

Leila Chaouch is an Associate Professor at the Faculty of Medicine of Sousse, Tunisia. She is also a researcher at the Laboratory of Molecular and Cellular Hematology, Pasteur Institute of Tunis, Tunisia. She has published more than 20 papers in reputed journals.

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