DIFFERENTIAL PROTEOMICS STUDY OF HEMATOLOGICAL DISORDERS

ABSTRACT

HbEβ-thalassemia has been characterized by interaction of HbE (β-26 Glu ➔ Lys) with β thalassemia. The variant (HbE) is innocuous in its homozygous states. The primary clinical importance of HbE trait arises when the βE allele interacts with other β-thalassaemia leading to a moderate to severe anemia known as HbEβ-thalassaemia. Our objective was to do a proteomics study of the body fluids such as plasma and urine. To complete our total knowledge we have also done a lipidomics study of plasma, erythrocytes and erythrocyte membranes.

From our proteomic study of two different body fluids (plasma and urine) we have seen that proteins which play a significant role in homeostasis were altered. The levels of proteins participating in cholesterol metabolism (apolipoprotein A I and IV), iron transport (transferrin), coagulation (adenylate kinase 1), hemoglobin scavenging (haptoglobin) and redox regulation (glutathione S transferase A2) were differentially regulated. These processes are inter-related and triggering one of them leads to the successive initiation of the other processes.

Our lipidomics study shows that the lipids also play a role in the disease. The changes observed clearly indicate that the erythrocytes are under oxidative stress and are in a proapoptotic condition in the diseased samples. Lipids such as phosphatidylycholines (PC) and ethers of PC, ceramides, sphingomyelins and lysophospholipids show a change in their levels which might be due to the presence of oxidative stress. The changes in the processes such as cholesterol trafficking, coagulation and antioxidant machinery are also reflected in our lipidomics study.

The changes in the lipidome combined with our knowledge of the changes observed in the plasma and urine proteome as well as the erythrocytes may help us discover new insights so as to prolong the survival of the diseased erythrocytes. A detailed quantitative study of these changes might enable a “fingerprinting” approach towards a better understanding of the disease. This area has a huge potential in the therapeutic level as well as diagnostic level of this disease. We believe our study augments the knowledge already available.