Label-free intrinsic imaging capillary zone electrophoresis analysis to detect homocysteine from blood serum for the detection of genetic metabolic disorders in new-born babies in Qatar

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Over 14,000 babies are born in Qatar each year, and it is the State’s intention to provide each with a health screen at birth for the timely diagnosis of inborn errors of metabolism. And since the population is characterized by a high consanguinity (estimates vary between 25–70%) from first-cousin marriages, congenital and genetic disorders are responsible for a major proportion of infant mortality, morbidity, and handicap birth defects and are relatively common among the population. Accurate and reliable quantification of amino acid (AA), generally in a plasma sample, allows early diagnosis of disorders such as phenylketonuria, tyrosinemia, maple syrup urinary disease, hyperornithinemia and citrullinemia. A deficiency of cystathionine B-synthase (CBS) can cause an autosomal recessive disorder of methionine and homocysteine (Hcy) metabolism known as homocystinuria which results in elevated concentrations of Hcy in plasma and urine. Clinical symptoms in untreated patients include progressive myopia and lens dislocation, thromboembolism, epilepsy, and mental retardation. Hcy is implicated as a wide variety of natal and other disorders – including Alzheimer’s. The aim of this study is to develop novel screens for AA levels – and in particular Hcy - in the blood using novel approaches in capillary zone electrophoresis (CZE). In order to quantify relevant amino acids it is necessary to deplete proteins from a complex biological sample such as plasma. In this investigation two protein depletion protocols were investigated on human plasma containing Hcy by label-free intrinsic imaging in the UV using CZE. As with a majority of amino acids, Hcy has very little or no UV absorption and for this reason analysis of samples were performed on an advanced high performance capillary electrophoresis (HPCE) platform, by multiple-pixel multiple-imaging indirect UV measurements. Two complementary analysis workflows were deployed to take advantage of the time-development of the AAs in the analysis allowing accurate quantification and minimum inherent bias.

Studies have been made with pure AAs and also with samples spiked in known quantities in blood which offer real clinical advantages. We have also developed methodologies for the simultaneous detection of several amino acids in plasma samples and limits of detection (LOD) and limits of quantification (LOQ) will be presented. These have been shown to be greatly improved with a pre-concentration technique known as ‘stacking.’ Work has been undertaken in our labs in Qatar Science & Technology Park and in collaboration with Hamad Medical Center.