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Interference of immunoglobulin paraproteins with chemistry assays

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Immunoglobulin paraprotein present in patient serum samples can interference with various chemistry methods causing erroneous results. The mechanisms of the interference have not been clearly elucidated or understood. Using samples containing various types of paraproteins, we studied the interference of paraprotein with the direct bilirubin, creatinine and total protein assays on the Beckman Coulter AU5400/2700 platforms. Repetitive testing of some of the samples exhibiting interference revealed a pattern of fluctuation in test results. Protein precipitation was observed when the reactions were scaled up 10 fold in a test tube. Aggregates of paraprotein can scatter light resulting in altered absorbance. Furthermore, removal of paraproteins by ultra filtration can eliminate the interference providing evidence that paraprotein precipitation being the cause of the interference with chemistry tests. We performed experiments at various pH and ionic strength to demonstrate that at extremely high (pH 12-13) or low ionic strength as that in the creatinine assay, an IgM paraprotein formed large aggregates. After testing additional samples containing immunoglobulin paraproteins from different patients, we can show that different paraproteins behaved differently in response to changes in pH and ionic strength possibly due to the individual set point determined by amino acid compositions of each monoclonal paraprotein. We conclude that pH and ionic strength are the key factors that contribute to protein aggregation and precipitation which interfere with the measurements of creatinine assay. Therefore, one should consider the possibility of paraprotein interference if the results are irreproducible. Understanding the mechanisms of interference by paraproteins and be able to recognize such interferences can help clinicians to troubleshoot the problem with chemistry tests.

Biography

Lu Song is the Associate Director for Clinical Chemistry at UCLA Medical Center since joining the Department of Pathology and Laboratory Medicine at UCLA School of Medicine in 2012. Dr. Song obtained her B.S. in analytical chemistry from the University of Science and Technology of China in 1982, and her PhD in Physical Chemistry from University of Washington in 1989. She completed postdoctoral training in cell and molecular biology at the Lawrence Berkeley Laboratory in 1991, and clinical chemistry training at the Mayo Clinic in 1998. Dr. Song has held technical director positions in both hospital and reference clinical laboratories. In the six years before joining the Department of Pathology and Laboratory Medicine at UCLA School of Medicine, Dr. Song was a scientific director for the Department of Chemistry and the Department of Immunoassay at Quest Diagnostics Nichols Institute in Chantilly, Virginia. Her research activities are focused on clinical utilization of biomarkers in the detection and/or monitoring of heart disease, cancer, endocrine disorders and other diseases.

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