Serum autoantibodies in breast cancer show strong binding with peroxynitrated-albumin

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Numerous studies have pointed out that inflammation, which ultimately enhances stress level, is associated with cancer development. The relationship between inflammation and cancer may be traced back to 1963. Oxidative stress induces cellular redox imbalance; a feature reported in several cancers. Under proinflammatory conditions, simultaneous production of superoxide and nitric oxide may occur, causing an increase in the formation of peroxynitrite by 1,000,000 fold. Peroxynitrite, a potent oxidizing and nitrating agent, when produced in excess, can modify variety of biomolecules including human serum albumin. In this study, albumin was modified by peroxynitrite and structural changes have been studied by UV, fluorescence, CD and thioflavin T binding. Biochemical analysis of modified-albumin demonstrated increased levels of carbonyl, 3-nitrotyrosine and dityrosine. Thiol content was significantly decreased in peroxynitrated-albumin. Scanning electron microscopy confirmed the formation of aggregates in peroxynitrated-albumin. Gross structural changes in albumin may change its antigenic properties; subsequent processing of peroxynitrited-albumin by immune cells may generate autoantibodies. Thus, peroxynitrited-albumin was used as antigen for testing autoantibodies in breast cancer sera by ELISA. Peroxynitrited-albumin showed strong binding with autoantibodies in breast cancer. The study demonstrates that peroxynitration of albumin may generate immunologically active neo-epitopes on albumin, and may result in the induction of autoantibodies in cancer**.**

Biography

I, Dr. Zarina Arif, completed my M.Phil. and Ph.D. in Medical Biochemistry from the Faculty of Medicine, Aligarh Muslim University, Aligarh in 1990 and 1993, respectively. I have worked as post Ph.D. Research Assistant for 15 years at the College of Applied Medical Sciences, King Saud University, Riyadh, Saudi Arabia and subsequently as Research Associate at the Department of Biochemistry, Faculty of Medicine, Aligarh Muslim University, Aligarh. I have also worked as a Postdoctoral Fellow of the University Grants Commission, New Delhi at the Rajiv Gandhi Centre for Diabetes and Endocrinology, AMU. Since July 2015 I am working as an Assistant Professor in the Department of Biochemistry, Faculty of Medicine, AMU. I have been involved in active research and teaching for the past 26 years and published 44 research papers in journals of International repute. I have attended numerous International/National symposia and conferences and presented my research.

Importance of Research and Development

Cancer is a complex group of diseases with many possible causes. Scientists believe that it is the interaction of many factors together that produces cancer. These factors may be genetic, environmental, or constitutional characteristics of the individual. It is believed that many cancers

arise due to inflammation in addition to other factors. It is well established that inflammation alters redox state. In vivo, peroxynitrite generation represents a crucial pathogenic mechanism in conditions such as cancer, stroke, myocardial infarction, chronic heart failure, diabetes, circulatory shock, chronic inflammatory diseases and neurodegenerative disorders. Peroxynitrite has multiple damaging effects on biomolecules including human serum albumin and may confer immunogenicity on it. Therefore, it has been hypothesized that circulating human serum albumin may be irreversibly modified by excessively formed peroxynitrite. The modified-albumin may be used for the detection of autoantibodies in cancer patients in early stage of the disease.

About the University

Aligarh Muslim University (AMU) is situated at a distance of 130 Km South-East of Delhi. It was established in 1920 and evolved out of the Muhammadan Anglo-Oriental College (MAO College) which was first set up in 1877 by the great visionary and social reformer, Sir Syed Ahmad Khan. It draws students from all states of India and from different countries. The university is open to all irrespective of caste, creed, religion and gender. AMU offers more than 300 courses in the traditional and modern branches of education. It has more than 30000 students, 1400 teachers and 6000 non-teaching staff. The university comprises of a wide spectrum of academic disciplines and now has 13 faculties comprising 107 departments of studies, 7 colleges, 19 centers, 3 institutes, 2 polytechnics, 10 schools and 3 off campus centers. A special feature of the university is its residential character with most of the students residing within the campus.There is 19 hall of residence for students with 80 hostels. AMU has regularly been ranked among top Indian Universities in recent years.

Recent Publications

1. Tarannum, A., **Arif, Z.,** Moinuddin Alam, K. and Tajalli Ilm Chandel. (2022). Biochemical and microscopy evidence on adverse effects of nitroxidized human serum albumin. **Indian J. Biochem. Biophys. 59: 23-32.** (Impact factor JCR =1.918).

2. Tarannum, A., **Arif, Z.,** Musafa, M., Qais, FA., Habib, S. Moinuddin and Alam, K. (2021). Studies on the synergestic action of methylglyoxal and peroxynitrite on structure and function of human serum albumin. **J. Biomol. Struc. Dyn.** DOI: **https://doi.org/10.1080/07391102.2021.2003865** (Impact factor =3.392).

3. Islam, S.N., **Arif, Z.,** Moinuddin and Alam K. (2021) Biophysical, biochemical and microscopic studies on whole histone glycated by deoxyribose. **Applied Biol. Res.** 23, 196-208.

4. Badar, A., **Arif, Z.,** Qais, F.A. Islam, S.N. and Alam, K. (2020) Carbamylation of human serum albumin generates high-molecular weight aggregates: fine characterization by multi-spectroscopic methods and electron microscopy. **Int. J. Biol. Macromol. 164: 2380–2388**. (Impact factor = 6.95).

5. Tarannum, A., **Arif, Z.,** Alam, K. and Moinuddin (2020) Glycation, nitro-oxidation, glycol-nitro-oxidation of human serum albumin: A physico-chemical study. **J. Mol. Struc. 1210, 127991** (Impact factor =2.46).

6. **Arif, Z.,** Tarannum, A., Arfat, M. Y., Arif, B., Shahab, S., Arif, M., Nelofar, Km., Badar, A., Islam, S.N., Zaman, A., Ahmad, S., Iqubal M.A., Gupta, A., Aggarwal, A. and Alam, K.(2020) Impact of endogenous stress on albumin structure in systemic lupus erythematosus (SLE) patients. **Int. J. Biol. Macromol. 151: 891–900**. (Impact factor =6.95).

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4. Pacher P, Beckman JS, Liaudet L. Nitric oxide and peroxynitrite in health and disease. Physiol. Rev. 2007; 87: 315-422.
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