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Autoantibodies in rheumatoid arthritis may arise from immunogenicity of peroxynitrite-modified IgG

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Peroxynitrite (PON) is a potent oxidizing and nitrating agent with a biological half-life of approximately 10 ms. It is produced in vivo by diffusion-controlled reaction of nitric oxide and superoxide anion. It can oxidize and/or nitrate many amino acids causing changes in protein structure and function. The changes may lead to the pathogenesis of several inflammatory diseases including Rheumatoid Arthritis (RA). In this study, IgG was isolated from healthy subjects' sera on protein A-agarose affinity column and PON was synthesized by rapid quenched flow method. PON-modified IgG (PON-IgG) was prepared by incubating IgG with PON at 37°C for 30 min and maintaining pH at 10-11. Physicochemical alterations in PON-modified IgG were monitored by UV, fluorescence, CD and FT-IR spectroscopy, and SDS-PAGE. Oxidation and aggregation were assessed as free thiols, protein carbonyls, and thioflavin T and congo red binding. Nitrotyrosine, dityrosine and nitrotryptophan were also quantified. Formation of 3-nitrotyrosine was verified by LC-MS and HPLC, and attachment of PON to IgG was elucidated by MALDI-TOF mass spectrometry. PON-modified IgG exhibited hyperchromicity at 278 nm along with bathochromic shift and appearance of a new peak at 420 nm, decrease of tryptophan and tyrosine fluorescence, loss in β-sheet and appearance of new peak in FT-IR, compared to native IgG. SDS-PAGE results revealed concentration dependent decrease in the band intensity of PON-IgG compared to native IgG. Experimentally induced antibodies against PON-IgG showed high titre antibodies and specific binding may be due to generation of highly immunogenic neo-epitopes on PON-IgG. PON-IgG binding with circulating autoantibodies of RA patients were compared with the experimentally induced antibodies against PON-IgG and its significance was analysed using biostatistical tools. The results so far suggest likely involvement of PON-IgG as an autoantigen in the induction and/or progression of RA.

Biography

Mir Yasir Arfat is pursuing his PhD in Biochemistry at Aligarh Muslim University, India. He has been working to understand the role of AGE-IgG and its peroxynitrite-modified counterpart in the induction and/or progression of rheumatoid arthritis. He is a recipient of doctoral fellowship award on the basis of qualifying national level competitions. He has participated in several national and international conferences including one held at Budapest, Hungary. He is a member of the "World Society Interdisciplinary Anti-Aging Medicine (WOSIAM)" France.

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