

25th International Conference on
HUMAN METABOLIC HEALTH- DIABETES, OBESITY & METABOLISM
&
2nd World Congress on
NUTRITION AND OBESITY PREVENTION
March 21-22, 2019 Dubai, UAE



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Glycoxidative modification of proteins in diabetes results in generation of neo-antigenic epitopes

Structural rearrangements and condensations of proteins under glycoxidative stress have been implicated in various pathological disorders. Novel immunological epitopes upon glycoxidatively modified proteins have been discovered and multi-specific natural antibodies against them have been identified. In this study, we have probed the glycoxidation of Human Serum Albumin (HSA) and human IgG in diabetes type-2. Glycoxidation was found to perturb the structural integrity of HSA and IgG. It affected their aromatic micro-environment and caused the generation of Advanced Glycation End products (AGEs) and aggregate adducts. Generation of N-epsilon-Carboxy Methyl Lysine (CML) was observed under HPLC and LCMS studies. The modified proteins showed altered secondary and tertiary structure that would also affect their function. Glycoxidation caused disordered or amorphous type aggregation in the modified proteins, as confirmed by electron microscopy. It enhanced carbonyl content and reduced the free lysine and arginine content. Modified HSA and IgG presented novel antigenic determinants that lead to an aggressive immune response in the immunized rabbits as was evaluated by ELISA studies. The antibodies had high affinity towards the immunogens. Auto-antibodies derived from T2DM patients exhibited strong affinity towards the modified HSA and IgG in comparison to the respective unmodified proteins. Specificity of serum antibodies from T2DM patients was further confirmed by competitive-inhibition ELISA and gel retardation assays. The study shows that the neo-antigenic determinants on glycoxidatively modified proteins generate specific immune response in diabetes type-2, which may possibly lead to the biomarker development for the disease.

Biography

Moinuddin has completed his MPhil and PhD in Biochemistry from the Faculty of Medicine of the Aligarh Muslim University, India. His research interest includes nucleic acid immunology, autoimmunity and free radical biology. He has published over 90 papers in reputed international journals, *Seminars In Cancer Biology*, *FEBS Letters*, *ABB*, *BBRC*, *Rheumatology*, *PLoS One*, *IUBMB Life*, etc. He is the recipient of Commonwealth Academic Fellowship to work in UK. He is a Life Member of Society for Free Radical Research (SFRR) and Indian Academy of Biomedical Sciences (IABS).

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