

Abstract

Natural autoantibodies (NAA) are autoantibodies that are present in the sera of healthy individuals. NAA can belong to the IgA, IgG and IgM isotypes. They exhibit high degrees of polyreactivity and connectivity but low affinity to self antigens. The main function of NAA in healthy people is probably to clear the catabolic waste and ageing cells.

In this study, an indirect Enzyme-linked Immunosorbent Assay (ELISA) method was used to detect NAA against hormones, namely adreno-cortical (hydrocortisone, aldosterone, androstenedione), adreno-medullary (adrenaline, noradrenaline) and other related steroid hormones (progesterone, testosterone, β -estradiol).

In eleven normal human serum (NHS), IgG anti-cortisol were detected in all and IgG anti-aldosterone in ten of the sera. For natural IgM, 6 and 8 of the 11 NHS reacted with cortisol and aldosterone respectively. All the 11 sera contained natural IgA to aldosterone. There was no detectable natural antibody of any isotype to the adrenal androgen, androstenedione and hydrocortisone.

For adrenal medullary catecholamines, natural antibodies appear to bind selectively to noradrenaline (NADR) compared with adrenaline (ADR). IgG was reactive in 9 and only 2 of the eleven NHS to NADR and ADR respectively. No natural IgM to ADR was found but two sera had natural IgM to NADR. IgA natural anti-NADR was present in 10 and IgA anti-ADR in only one of the 11 NHS. No antibodies of any isotypes was detected to acetylcholine.

The presence of these natural antibodies to cortisol, aldosterone and noradrenaline is of interest as these adrenal hormones are related to blood pressure control; cortisol (vascular sensitivity), aldosterone (sodium/ECF volume), noradrenaline (vascular reactivity).

Perhaps there is as yet an undefined immunophysiologic role of these natural antibodies in mean arterial pressure regulation by modulating the biologic activity of these hormones in the circulation.

The natural antibodies binding to epitopes of apolipoprotein E was also tested. For apolipoprotein E, 13-mer peptides covering the entire amino acid sequence were synthesized and epitope mapping was analyzed using peptidylated Pin ELISA. In NHS, natural IgA and IgG strongly recognized peptides 23 and 35, IgA and IgM recognized peptides 41 (QIRLQAEAFQARL), while IgG and IgM share one common epitope of apo E at peptide 33 (ATVGSLAGQLQE).

In atherosclerotic patient's sera, IgA recognized 5 different epitopes, IgG 10 different epitopes and IgM 7 different epitopes, except peptide 11. Peptide 11 (WVQTLSEQVQEEL) is the common for all the antibody isotypes. Similar to natural antibodies, IgA and IgM in the patient's sera recognized peptide 41 (QIRLQAEAFQARL) while IgG and IgM share one common epitope at peptide 43 (SWFEPLVEDMQRQ).

Although there were similar epitopes for antibodies in NHS and patient sera, dissimilar regions bound by NHS and atherosclerotic sera were also identified. Whether and how this differential reactivity to apo E regions is related to the function of natural and autoimmune antibodies remain to be determined.