THE STRUCTURE AND FUNCTION OF HUMAN IgA SUBCLASSES

Summary

An unusual structural feature of human immunoglobulin A (IgA) is the heterogeneity of the molecular forms, with a characteristic distribution in various body fluids. Serum IgA is largely monomeric, but in external secretions it exists as S-IgA — a dimer consisting of two IgA molecules bound together by J chain and attached to secretory piece (SC). Both in serum and secretions IgA occurs in two isotypic forms, IgA_1 and IgA_2. IgA_2 exists as two known allotypes, namely $IgA_2m(1)$ and $IgA_2m(2)$, with a form $IgA_2(n)$ possibly representing a third allotype. The major difference between the IgA subclasses is an absence of 13-amino acid segment in the hinge region of IgA_2 that is found in IgA_1 molecules. This truncated hinge region in IgA_2 molecules renders them resistant to at least two families of IgA_1-specific bacterial proteases, which presumably is advantageous to IgA_2 antibody function at mucosal surfaces. Further and profound structural difference between the $\alpha 1$ and $\alpha 2$ chains concerns the distribution and composition of the oligosaccharide side chains. The IgA_1 contains two *N*-linked glycosylation sites (Asn^{263} in the CH_2 domain and Asn^{459} in the tail piece) as well as nine potential *O*-linked glycosylation sites in the hinge region. All three IgA_2 variants lack these *O*-linked sugars, but they have two extra *N*-linked glycosylation sites (Asn^{166} in the CH_1 and Asn^{337} in the CH_2). The $IgA_2m(2)$ and $IgA_2(n)$ allotypes have a fifth potential *N*-linked side in the CH_1 (Asn^{211}) domain. The variations in the glycosylation structure of the different form of IgA play a significant role in determining antibodies conformation and assembly, receptors (TCR, ASGP-R) binding and $t_{1/2}$. Here we review current knowledge concerning the relationship of the structure of human IgA_1 to the IgA_2 isotype, the polymeric IgA and secretory IgA structures, and IgA function.