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Structures and receptor recognition mechanism of immune inhibitory HLA-G molecules

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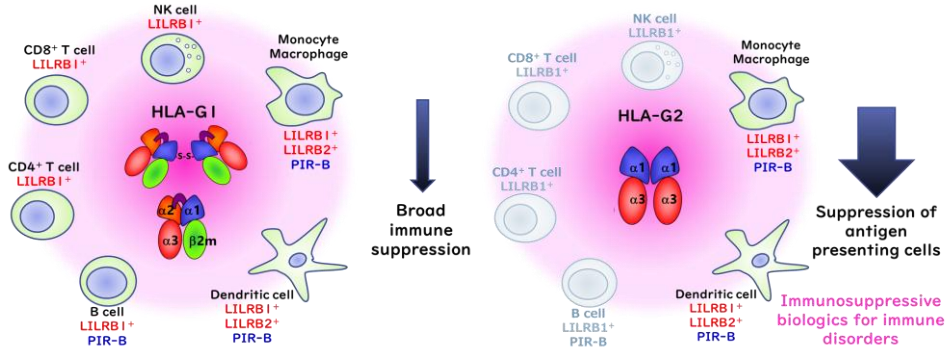
HLA-G is one of the non-classical HLA class I molecules expressed in the placenta, thymus, and tumor cells. In the placenta, HLA-G is expressed by fetal cells and contributes to the establishment of pregnancy by suppressing maternal immune responses. HLA-G is a non-polymorphic gene but is expressed in various forms, including dimeric forms and splicing isoforms lacking domains. In particular, the HLA-G2 isoform has been reported fully complements the function of the major isoform, HLA-G1 consists of the heavy chain, beta-2-microglobulin and a peptide.
We have elucidated the molecular recognition mechanism of various HLA-G molecules with the receptors LILRB1 and LILRB2. HLA-G1 showed a higher binding affinity to the receptors, signaling ability, and in vivo anti-inflammatory effect through dimerization than the monomer. On the other hand, the HLA-G2 isoform exists as a homodimer consisting of a single polypeptide chain. HLA-G2 showed anti-inflammatory effects in a mouse model of rheumatoid arthritis at lower doses than the HLA-G1 homodimer. Interestingly, HLA-G2 receptor specificity is different from that of HLA-G1. In terms of the cellular distribution of the receptors, the HLA-G2 isoform specific to LILRB2 expressed in antigen presenting cells is possibly expected as a novel biologic candidate with fewer side effects.



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[Field of research] Structural immunology, Human genetics