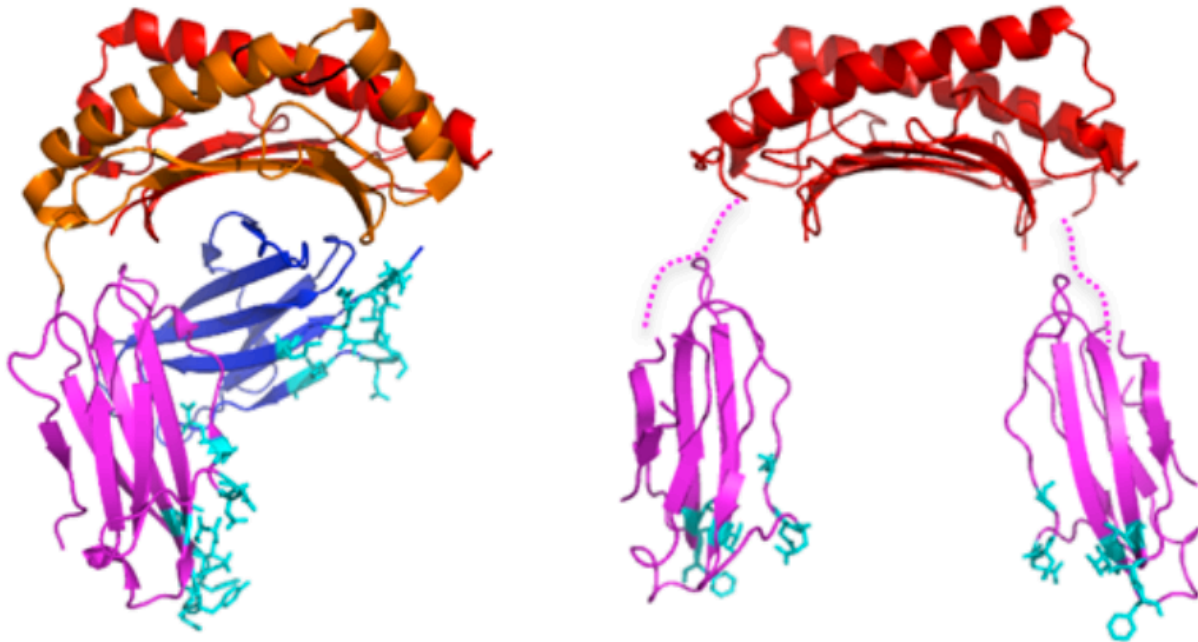


Deciphering an embryo-protecting protein

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Comparison of a HLA-G1 protein (left) and a HLA-G2 protein (right), showing significant structural difference. The HLA-G2 protein shown here is in a pair form called homodimer. Credit: Kuroki K. et al., *The Journal of Immunology*, March 27, 2017

Revelations about a protein expressed in fetal cells could provide novel insights into its function and future immunosuppressive therapies.

Researchers at Hokkaido University together with colleagues in Japan have uncovered the structure of a protein that protects embryos from

being attacked by their mothers' immune system. Further understanding of this protein could give rise to [immunosuppressive therapies](#).

Trophoblasts are [cells](#) found in the outer layer of the developing embryo that form part of the placenta. They express a type of protein called human leukocyte antigens-G (HLA-G) which interacts with receptors on the maternal cells to suppress immune responses to the embryo during pregnancy.

The structures of HLA-G1, the major form of HLA-G, are well understood. Interestingly, individuals whose cells lack HLA-G1 could be born and healthy. Researchers believe this is because they can express another form, HLA-G2, which should compensate for the loss of the former's function. But the structure of HLA-G2 has been largely unknown.

In a study published in the *Journal of Immunology*, the team investigated the structure of HLA-G2 by a single particle electron microscopy.

Surprisingly, the structure of HLA-G2 was completely different from HLA-G1, but was similar to another class of human leukocyte antigens called HLA class II. This suggests that the HLA-G gene evolved from the same ancestral gene as HLA class II.

They also found that HLA-G2 make pairs called homodimers which strengthen the binding to the receptors. HLA-G1 is also known to form homodimers but in a different manner. Furthermore, their biochemical analysis revealed that HLA-G2 bound strongly to a leukocyte immunoglobulin-like receptor B2 (LILRB2), but not to LILRB1. By contrast, HLA-G1 binds strongly to both [receptors](#).

Previous research by the Hokkaido University team showed that, in addition to its protective role during pregnancy, the HLA-G2 [protein](#) had

an anti-inflammatory effect when injected into collagen-induced arthritis mice.

"A narrower target specificity of HLA-G2 could be advantageous in developing [immunosuppressive drugs](#) with less side-effects. We suggest further investigations to elucidate the [structure](#) of the HLA-receptor complex for a more precise understanding of this interaction," says Katumi Maenaka, the corresponding author at Hokkaido University.

More information: Kimiko Kuroki et al. Cutting Edge: Class II–like Structural Features and Strong Receptor Binding of the Nonclassical HLA-G2 Isoform Homodimer, *The Journal of Immunology* (2017). [DOI: 10.4049/jimmunol.1601296](https://doi.org/10.4049/jimmunol.1601296)

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