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CONNECTIVE TISSUE DISEASES

ApoER2 linked to pregnancy complications in APS

"Our work revealed for the first time that apoER2 is required for the adverse effect of antiphospholipid antibodies on pregnancy outcomes in a mouse model of antiphospholipid syndrome," summarizes Jane Salmon, one of the corresponding authors of a paper now published in *Arthritis & Rheumatology*.

> "...lack of one or both alleles of the gene encoding apoER2 conferred protection against aPL-induced fetal loss..."

Antiphospholipid syndrome (APS) is associated with serious complications such as fetal loss, preterm birth and intrauterine growth restriction (IUGR). Alteration of trophoblast function is known to contribute to pregnancy complications in APS but, until now, the exact mechanisms were incompletely understood. Previous research has shown that interaction of glycoprotein-bound antiphospholipid antibodies (aPL) with endothelial apolipoprotein E receptor 2 (apoER2) induces a signalling pathway that promotes leukocyte adhesion and thrombosis. Here, Salmon and colleagues investigated the possible involvement of apoER2 in eliciting cell dysfunctions responsible for the adverse effect of aPL on pregnancy outcomes in APS.

First, the investigators demonstrated abundant apoER2 expression in trophoblasts from human and mouse placentas by immunohistochemistry and immunoblotting techniques. They then showed that interaction with apoER2 is necessary for aPL-induced inhibition of trophoblast proliferation and migration in further experiments using cell cultures treated with IgG from healthy individuals, aPL isolated from patients with APS, and aPL with addition of a soluble binding domain of apoER2.

Next, the authors determined the involvement of apoER2 in aPL-induced pregnancy complications in a mouse model of APS. By passive transfer of aPL, the researchers established that lack of one or both alleles of the gene encoding apoER2 conferred protection against aPL-induced fetal loss and IUGR.

Currently available treatments are limited to anticoagulant therapy, which does not always prevent adverse events. Future research efforts of this group will be focused on the development of an antibody inhibiting aPL actions that could ultimately prevent thrombosis and fetal loss.

"Identification of apoER2 as a linchpin for aPL actions both in trophoblasts and endothelial cells provides a strong basis for development of interventions that target the molecular pathway related to apoER2," explains Chieko Mineo, the co-corresponding author.

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Original article Ulrich, V. *et al.* ApoE receptor 2 mediates trophoblast dysfunction and pregnancy complications induced by antiphospholipid antibodies in mice. *Arthritis Rheumatol.* doi:10.1002/art.39453