Is there a place for autoimmunity-thrombophilia testing in infertility patients?

There is controversy over several aspects of thrombophilia and autoimmunity´s implications in human reproduction. Routine screening for all infertile couples is not advised and a tailored approach is needed for some subsets of patients.
The relative inefficiency of human reproduction is reflected in a high prevalence of pre-implantation embryo losses, early and clinical miscarriages. More than 10% of clinical pregnancies end in miscarriage. Since the prevalence of recurrent miscarriage (RM) is higher than what would be expected by probability alone, it is likely to indicate specific etiologies in affected patients. Fetal genetic abnormalities, uterine abnormalities, antiphospholipid syndrome and thrombophilic disorders are a known cause of reproductive failure. However, in more than 50% of cases, no cause is identified.

Could we explain some factors included as unknown etiologies?

The successful maternal adaptation to the semi-allogeneic fetus is a complicate process. Insufficient invasion of the uterine lining by trophoblast and vascular conversion in decidua are thought to be the primary defect on disorders as RM, preeclampsia and fetal growth restriction (FGR). Current clinical interest is focused on the role of uterine natural killer (uNK) cells. Spiral arteries are remodeled by extravillous trophoblast cells (EVT) and uNK, as a result of interaction between maternal Killer immunoglobulin-like receptors (KIRs) expressed by uNK and their ligands, HLA-C molecules, expressed by invading trophoblast cells (EVT).
Pregnancies have an increased risk of RM, preeclampsia or FGR in mothers´ homozygous KIR AA with HLA-C2 fetus and this effect has been described on medically unassisted pregnancies.
IVF cycles usually included single or double embryo per transfer and the oocyte, sperm or embryo donation are often used during the assisted reproductive treatment (ART).

In patients with recurrent miscarriages (RM) and recurrent implantation failure (RIF), does the maternal KIR haplotype have an impact on pregnancy, miscarriage, and live birth rates per cycle after single or double embryo transfer (DET), with the patient's own or donated oocytes?

We observed (retrospectively studied 291 woman with RIF and RM after ART and 1304 cycles) a higher miscarriage rate after DET and their own oocytes, in mothers´ KIR AA haplotype. A significantly decreased live birth rate have been observed after donor oocyte cycle with DET in mothers´ homozygous KIR AA compared with KIR AB and KIR BB haplotypes.
In human populations, the pregnancy disorders are predicted to reduce the frequency of group A KIR, HLA- C2 or both and this selection has originated during the humans evolution. This human genetic adaptation is not taken into consideration nowadays during the ART.
In conclusion, tailoring ART in RIF and RM patients could help to prevent pregnancy disorders and improve live birth rate. These ART individualized protocols could include control of thrombophilic and autoimmune disorders (subsets of patients), selection of SET, oocyte and/or sperm donor by HLA-C in patients with RM and RIF and KIR AA haplotype since HLA-C1/C1 donors are predicted to be safer and, C2/C2 males or oocyte donors may be "dangerous" identified by epidemiological studies.