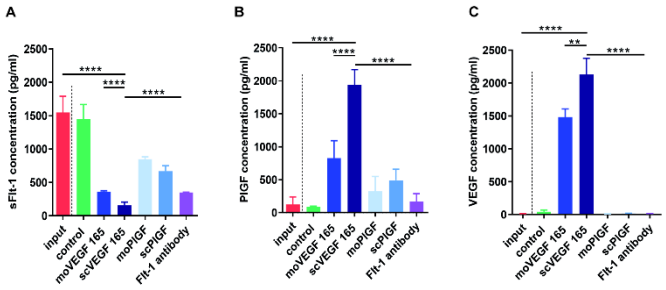
D-VLAP

VEGF-multimer based apheresis to treat preeclampsia

Invention

Preeclampsia is a potentially life-threatening multisystem disease affecting 4% to 8% of pregnant women after the 20th week of gestation (EGA). Around 20% of affected pregnancies have to be terminated before the 34th EGA. An excess of placental expressed anti-angiogenic soluble VEGF-receptor 1 (sFlt-1) scavenges VEGF and PlGF, causing generalized endothelial dysfunction. Interventions to restore the angiogenic balance in preeclamptic pregnancies are intensively studied and improve maternal and neonatal outcomes. Especially extracorporeal strategies to remove sFlt-1 are promising in human pregnancy. However, available apheresis systems adsorb sFlt-1 unspecifically and with low efficiency. Affinity enhanced ligands are needed to improve performance and compatibility of apheresis treatments.



Characteristics of sFLT-1 capturing molecules employing patient samples. A) Apheresis of sFlt-1 on columns with VEGF and PlGF variants as well as sFlt-1 specific antibody; B) Apheresis of sFlt-1 with VEGF and PlGF columns releases PlGF; C) VEGF release is only present in apheresis columns containing VEGF variants. For details, see relevant publication.

Researchers of the University Hospital Cologne have developed VEGF-based sFlt-1 capturing molecules (scVEGF165) characterized by higher affinity for sFlt-1 as compared to competing products and the ability to displace complexed endogenous VEGF and PlGF from its binding to sFlt-1 in patient blood. Thus restoring the angiogenic balance in double action, which will result in shorter treatment duration and more efficient sFlt-1 removal at low sFlt-1 plasma levels. For ex vivo characterization, ligands were immobilized to biocompatible agarose matrix routinely used in medical aphersis systems.

Commercial Opportunities

There is strong interest in novel approaches with regard to extracorporeal therapies for preeclampsia. So far only one company is in the process of developing an antibody-based approach of sFlt-1 apheresis, which is less efficient as compared to this VEGF-based apheresis system. Specifically, the efficient liberation of endogenous VEGF and PlGF is an advantage of this novel approach.

Current Status

Before rolling out to clinical studies in pregnancies with preeclampsia, toxicity and compatibility, e.g. the safety of endogenous VEGF- and PlGF-release for mother and fetus, has to be tested *in vivo*. Finally, pivotal clinical trials comparing this novel strategy to the state-of-the-art at this future time point will be needed before approval of this novel medical device.

Relevant Publications

Matin, M., et al. (2020) Affinity-Enhanced Multimeric VEGF (Vascular Endothelial Growth Factor) and PlGF (Placental Growth Factor) Variants for Specific Adsorption of sFlt-1 to Restore Angiogenic Balance in Preeclampsia. Hypertension
doi: 10.1161/HYPERTENSIONAHA.120.14974

An invention of the University Hospital Cologne.

Competitive Advantages

- Higher affinity for sFlt-1 as compared to competing products
- Displace complexed endogenous VEGF and PlGF from its binding to sFlt-1
- Thus restoring the angiogenic balance in double action

Technology Readiness Level

1 2 3 4 **5** 6 7 8

Technology validated in relevant environment

Industries

- Medical engineering
- Pharmaceutical industry gynecology

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