2nd Work Progress Presentation

Investigation of therapeutic potential of candidate recombinant proteins in trophoblast differentiation and placenta spiral artery remodeling in murine models of pre-eclampsia

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Guide: Dr. Taruna Madan Gupta
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10th April, Friday from 04.00 pm to 05.00 pm
Venue: Dr. Shanta Rao Auditorium

Meeting Link: https://zoom.us/j/91854066851?pwd=6va0jtsTZ1owYNBkMcbAbLXoDPtMur.1
Meeting ID: 918 5406 6851
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Abstract

Preeclampsia (PE) is a pregnancy-specific hypertensive disorder characterized by the onset of hypertension, proteinuria, and exaggerated edema after 20th week of gestation, as a result of abnormal placentation. Physiologically, the condition is characterized by an imbalance of pro- and antiangiogenic factors, pro- and anti-inflammatory cytokines, and immune cell activation-tolerance. Various therapies proposed and tried for PE have yielded satisfactory outcomes with/without toxicity concerns.

Surfactant Protein D (SP-D), a collectin in the family of PRRs, modulates and regulates the inflammatory response, which is a critical etiological factor of PE. Data from SP-D KO mice show that sustained SP-D levels are critical during implantation and placentation. Moreover, significantly downregulated serum levels of SP-D are associated with the development of severe PE. The proposed work, hence, aims to assess the potential of recombinant SP-D (rfhSP-D) to induce angiogenic differentiation in trophoblast cells, thereby promoting uterine spiral artery remodeling to rescue pre-eclampsia in mouse models.

The objectives set for the proposed work are: (1) To study the effect and mechanism of recombinant proteins on the angiogenic differentiation of human trophoblast cells in vitro; (2) To evaluate the effect of exogenous recombinant proteins mediated preventive therapy in murine models of preeclampsia (PE). The study design follows a range of *in vitro*, *ex vivo* and *in vivo* experiments to evaluate the therapeutic effects of rfhSP-D in an induced model of PE.

To summarise the study progress, we have observed that rfhSP-D produces a significant pro-angiogenic, pro-migratory & pro-invasive, and anti-inflammatory response in HTR8/SVneo cells. rfhSP-D treatment also induces the expression of pseudo-endothelial markers on HTR8 cells. Additionally, we have been able to induce and mimic PE in an *in vitro* setting on HTR8/SV neo cells by ultra-low dose LPS stimulation, which is evident by an imbalance of pro- and anti-angiogenic markers, inflammatory cytokines, and oxidative stress markers. In tandem with our *in vitro* study, we have also developed and characterized an LPS-induced early onset model of PE (EOPE) in mice and performed immunophenotyping of mice placentae. We have also procured the transgenic STOX1 PE mice model. STOX1 is a transcription factor that drives angiogenesis, invasion, and inflammatory signalling. A normal FVB dam develops PE when mated to a male STOX1 mouse, thereby specifically overexpressing STOX1A in the placenta. Further, we have also characterised this transgenic STOX1 PE mice model. The detailed experimental methods followed, and the results obtained for each will be discussed in the presentation.