SRF VACATION SCHOLARSHIP REPORT 2021

The form below should be completed by the student, then forwarded to the supervisor for approval and submission to srf@conferencecollective.co.uk within 8 weeks of completing the project. Please submit the form as a Word document.

A maximum of one figure (with legend of less than 100 words) may be appended if required.

Please note: excerpts from this form may be published on the SRF website, so please ensure content is suitable for website publication, and does not compromise future dissemination of data in peer-reviewed papers etc. The SRF reserves the right to edit responses to ensure suitability for publication on the website, newsletter or in promotional material.

Student's Name:	Nusaiba Masnurah	**Student's Institution/University:**	St Georges University of London
Degree Title and year of study:	Biomedical Sciences 2nd year		
Supervisor's Name:	Guy Whitley	**Supervisor's Department and Institution:**	Molecular and Clinical Sciences
Project Title:	The Role of MMP-10 in Spiral Artery Remodelling		

Briefly outline the background and aims of the project *(max 200 words)*

The maintenance of a healthy pregnancy is determined by the correct remodelling of maternal spiral arteries (SpA). This ensures the foetus gets enough oxygen and nutrients. Failure to remodel the SpA adequately can lead to common pregnancy disorders such as pre-eclampsia and foetal growth restriction.

The underlying mechanisms behind poor remodelling are not fully understood but poor trophoblast invasion may play a role. Using a vascular spheroidal model of the vessel wall stimulated with trophoblast conditioned media (TCM) it was possible to identify a number of genes that were either up- or down- regulated. One of these genes was matrix metalloproteinase 10 (MMP-10) which was up-regulated in endothelial but not vascular smooth muscle cells. In other systems MMP-10 expression can facilitate invasion by degrading the extracellular matrix but can also regulate apoptosis and cell growth.

Project aims:

1) To produce an endothelial cell line with knock-down expression of MMP-10 using shRNA
2) To use ELISA assays and zymography to determine whether MMP-10 knockdown reduced MMP-10 secretion or activity
3) To use western blotting to determine whether there is a difference in the expression of MMP-10 in both first trimester placental and decidual tissue from normal pregnancies and those at increased risk of pregnancy complications

Did the project change from that proposed in the application? If so, what changes were made and why? *(max 100 words)*

The aims of the project didn't change but as the transfected cells failed to respond in the way we hoped we were unable to do the functional studies planned.

What were the main results/findings of the project? *(max 300 words)*

1) We used lentiviral infection to knockdown MMP-10 gene expression in endothelial cells and selected using puromycin. Non-targeting sequences were used a control. The transfection worked well as we got high levels of puromycin resistance.

2) We stimulated the puromycin resistant control and shRNA MMP-10 cells with interleukin-1β or TCM and measured the secretion of MMP-10 by ELISA. There was no difference in the secretion of MMP-10 from the control cells. We also stimulated the cells with phorbol-12-myristate 13-acetate (PMA) which also stimulates MMP-10 in these cells and both the control and MMP-10 knock-down cells produced significant amounts of MMP-10 which also suggested the knock-down had not worked. Using zymography we were able to say that the MMP-10 produced was active.

3) Tissue from 8 normal and 8 high risk patients were analysed using western blotting. This data showed that there was a significant difference in the levels of MMP-10 expressed in decidual tissues between the pre and post 11 weeks gestation, with more MMP-10 being produced in the high-risk category after 11 weeks. There was no significant difference in the expression of MMP-10 in the placental tissue.

What do you conclude from your findings? *(max 150 words)*

The findings demonstrate that the MMP-10 produced by the endothelial cells in culture was enzymatically active. I have also showed that there were differences in the level of expression of MMP-10 from normal and high-risk pregnancies however, further experiments should be done to establish whether this varies in patients in the high and low risk groups at other gestational ages. The difference in MMP-10 levels seen among the cohorts suggests that this protein could play a part in establishing proper remodelling as levels of expression varies in the different risk groups. The reason behind these differences needs to be investigated further to discover why they exist and how they impact SpA remodelling as well as other physiological processes in the first trimester.

How has this experience influenced your thinking regarding your future/ongoing studies, and/or career choice? *(max 150 words)*

This has been an enlightening experience that demonstrated the significance medical research plays in establishing better methods of diagnosis and treatments and showed me the vast difference between laboratory projects conducted during undergraduate courses, and original research as you have the ability to choose what particular area you would like to work in and delve into it deeper. The structure of working in a lab has also been extremely enjoyable as I was able to work as part of a team to solve problems, but everyone also has their own research interests. This experience has made me want to pursue a career in research alongside medicine and strengthened my interest in reproductive sciences and I would love to combine these by working in women's reproductive health as a clinician, as well as a researcher. I have also really enjoyed the wider reading into obstetric disorders for this project and it has helped with my reproduction module at university.

Please use the space below to add any other comments/thoughts about the SRF Vacation Scholarship *(max 100 words)*

Student: This project has been absolutely wonderful and has improved my confidence in working in the lab and ignited an interest in reproductive research. Thank you to Professor Whitley, Zoe Tryfonos (in particular) and Alexa Bishop for their support and guidance. I have learned a great deal from working with them.

Supervisor: This studentship has given Nusaiba the opportunity to experience the highs and lows of laboratory research. Although she has had to deal with unexpected challenges she has become proficient in a number of important techniques. In addition, Nusaiba has obtained some interesting preliminary results which will be taken forward.