



## Project: Primary Human Enteroids: A Translational Research Tool to Study Therapeutic Implications of Modulating TGF $\beta$ Signalling in Inflammatory Bowel Disease.

*'Being awarded the Falk/Core Student Bursary means a huge amount to me, primarily because it recognises the importance of research into Crohn's disease, a disease that I feel passionately about. It also gives the opportunity to raise awareness and give something back to the patients whose lives change significantly after diagnosis. I feel greatly honoured to be chosen for the award and it will give me the confidence and aspiration to engage in research throughout my career in medicine.'*

*Rosie Simson is currently undertaking a Master of Research (MRes) at the Institute of Cellular Medicine at Newcastle University. She will be returning to her medical studies next academic year.*

'Crohn's Disease (CD) is a disease of the digestive system affecting anywhere from the mouth to anus. It causes ulceration, pain and diarrhea and often presents in young adults,' says Ms Simson.

'A healthy gut lining (epithelium) relies on a precise balance between proteins (cytokines) that cause inflammation and those that reduce inflammation. These cytokines influence the barrier function of the gut epithelium and control the passage of certain cells into the epithelium, which cause the inflammatory reaction needed to fight off infection. If this balance is disturbed, long-term inflammation may occur.

'I became interested in Crohn's even before the project for a couple of reasons. Firstly because with aspirations to be a general surgeon, I have seen many operations on Crohn's patients that have completely changed their lives. Overall what is a devastating illness can be made manageable with a range of treatments which is truly remarkable. Secondly, it being a disease manifesting in younger generations, I have close friends who suffered from the condition, giving me a personal reason to do whatever I can do to help others.

'My research project aims to demonstrate how TGF $\beta$  modification influences the barrier function of the gut epithelium by investigating changes in epithelial integrity.

Using this information, I aim to investigate the possible short and long-term beneficial or deleterious effects that therapeutic modification of TGF $\beta$  signaling may hold in CD.

'I am interested in a particular cytokine (TGF $\beta$ ), which is found at lower levels in patients with CD as compared to healthy individuals. Recent clinical trial data suggests that indirectly increasing the levels of TGF $\beta$  in the gut may help to resolve inflammation in CD.

'Unlike other tissues in the body such as the kidney, I have shown TGF $\beta$  does not harm the barrier function of the gut. This has been demonstrated by looking at cells exposed to TGF $\beta$  using electron microscopy and immunofluorescence, a method to stain for certain proteins that make up the junctions. My data provides evidence that the cell junctions, normally broken down, are still present.'

Ms Simson's supervisor states:

'Rosie has for some time shown great interest in translational gastroenterology and the current MRes has provided a perfect opportunity to develop both her clinical and academic skills in inflammatory bowel disease.

'She has shown great drive and determination in her MRes studies so far undertaking a 6-month modular programme in immunology where she achieved highly. Rosie has now begun her laboratory placement with great enthusiasm, has shown real flare in scientific technique and has been fully involved in the development of the above hypotheses and methodologies.

'I consider Rosie to be an exceptional undergraduate student whom it has been a pleasure to work with so far. I have been consistently impressed with her level of commitment to this project and wholeheartedly endorse her application for this bursary.'