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## Dr Falk/Guts UK Awards 2022

### MEDICAL STUDENT PRIZE WINNER: Ms Amber Orr

#### PROJECT: Bile Acid Metabolism as a Therapeutic Target for Metabolic Disorders



*Ms Orr is undertaking this research project whilst intercalating for her BSc in Biomedical Sciences (Physiology) in the Rowett Institute at the University of Aberdeen. In August she will return to her fifth year of studies at the University of Aberdeen School of Medicine.*

#### Ms Orr explains:

'The prevalence of metabolic disease and its associated healthcare costs have increased rapidly. However, effective pharmacological interventions remain limited, driving the need to further our understanding of the complex underlying pathophysiology.

'Bile acids are instrumental in the process of lipid digestion and may provide an interesting target for modulating metabolic disorders. Bile acids undergo a series of biotransformations initiated by Bile Salt Hydrolase (BSH) which is an enzyme produced by bacterial components of the gut microbiome. Inhibition of this protein may elicit changes in the bile acid pool and this altered signalling has been linked to reduced rates of obesity in mouse models. Therefore, identifying compounds that can safely achieve these effects may produce novel anti-obesogenic agents.

'This project aimed to overexpress and purify BSH from three known intestinal Lactobacilli strains including acidophilus, plantarum and salivarius. Thereafter, the effects of potential inhibitors on enzymatic BSH activity were measured to test their credibility as future therapeutics.

'We found that BSH differed across species in terms of levels of expression and activity. A catalytically active BSH protein could only be derived from Lactobacillus salivarius. Cyanidin, a natural anthocyanin compound, was found to be the most potent inhibitor with 65.1% inhibition at a concentration of 0.5 mM.

Another interesting finding from our results was the contrasting inhibitory activity between different types of blueberry extract (BBE) wherein BBE (D) (from the James Hutton Institute, Dundee) and BBE (V) (from Vitablue, Futureceuticals) produced respective inhibitions of 11.1% and -2.80%.

'Overall, these results suggest differing biological functions of BSH between bacterial species and support work that has suggested a role for natural plant chemicals, or phytochemicals, in manipulating the gut microbiome thus addressing rising metabolic disease. Insight to these mechanisms could be significant in addressing the rising problem of obesity and its associated conditions.'

#### Ms Orr's Project Supervisor Dr Andreas Kolb, Senior Research Fellow at the Rowett Institute, University of Aberdeen wcomments:

'Amber Orr spent 3 months in my lab as an Honours student (studying for an intercalated degree in Medical Sciences). This was her first stint in experimental lab work, but she familiarised herself quickly with the methodology and was able to carry out the experiments independently.

'From the start Amber demonstrated an excellent combination of inquisitiveness and maturity in her approach to science. She was very skilful in documenting and analysing the datasets and she presented the results very well, both in her oral thesis presentation and her thesis write-up.'

#### Ms Orr states:

'I am passionate about gut health and I chose this thesis topic due to my keen interest in the gut microbiome and its fascinating interactions throughout the body. This project challenged me to learn new laboratory skills and explore how the gut microbiome is closely involved in our bile acid metabolism.

'I am truly honoured to receive the Dr Falk / Guts UK Medical Student Prize. Receiving this has encouraged me to continue going outside my comfort zone and hopefully work more in researching gut health and metabolic disease in the future!'



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