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MEET THE AWARD WINNER

Taking equine research across the Atlantic

How the Steve Bishop Award helped Isabelle Smith develop new skills and international collaborations.



“The award has shaped my personal development as a scientist…”

— Isabelle Smith

Isabelle Smith
University of Edinburgh
PhD Researcher

4 weeks
Specialist training at UCLA

3D
Tumour culture research

USA
International collaboration

" This award has fundamentally shifted my career outlook from national to international "

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I am currently an Integrative Physiology PhD student at the University of Edinburgh entering the final stages of my study. My project centres around identifying the drivers of pituitary tumourigenesis, using horses as my primary research model due to the high frequency of intermediate lobe pituitary adenomas in aged equids with equine Cushing's disease. This research is highly collaborative between physiologists and equine veterinarians- integrating classical molecular biology techniques with bioinformatics, clinical veterinary medicine and now with developing advanced tissue culturing techniques thanks to the Steve Bishop Award.

The pituitary, a small gland at the base of the brain, produces hormones which regulate reproduction, metabolism and stress. In over 20% of older horses, this gland undergoes abnormal changes that lead to a common hormonal disorder called equine Cushing's disease (EC). This condition is characterised by tumours formed of a specialised type of pituitary cells called melanotrophs. These cells become hyperactive and release excessive hormones, causing significant health and welfare problems. Despite its prevalence, the triggers of these changes and the mechanisms that sustain these tumours remain unknown.

By analysing pituitary tissue from horses with different stages of disease, my work has identified genes which may contribute to tumour development. However, studying these processes is very challenging and has ethical issues in live animals, making it essential to develop ways to study tumour cells in a dish. Currently, there are no effective models to study EC: no suitable laboratory animal models exist, and immortalised cell lines poorly represent equine or tumour biology minimising their translational relevance. An ability to take postmortem tissue, freeze and then restore the cells forming the tumour for culture in the laboratory would transform studies of the disease and test potential treatments.



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Dr Heaney's lab (based in the David Geffen School of Medicine, University College Los Angeles) have established a method for storage and culture of human pituitary tumour tissue, providing the type of model we require in horses. This method allows storage of tumour cells, which can then be thawed and grown in a dish in functional cell clusters, which behave like the real tissue with sustained hormone secretion and growth potential. Over the duration of 4-weeks in the Heaney lab, I received intensive training in the cryopreservation and 3D culture process- covering optimal conditions for 1) initial tissue collection- methods of how to effectively break the tissue into individual cells and process this to remove blood cells (cells that can interfere in cell cultures). 2) The culturing processes themselves- how to plate the cells, the clustering behaviours of cells in different types of plates and gel scaffolds used, and optimal cell media components for long-term growth. 3) Cryopreservation- how to best freeze down the cell clusters for later use.

I am now in the process of transferring the technology learnt from the Heaney lab to our group in Edinburgh, using both human and horse tumours to establish the methodology. We will then test the response of the tumour cells grown in a dish to factors currently used to treat pituitary tumours in the clinic (both human and horse), as well as some novel targets that we have identified.

The future development of this research relies on sustaining collaboration with the Heaney lab to refine both our human- and equine-specific protocols. My immediate research priority is finalising the optimisation of the 3D pituitary organoid protocol in Edinburgh on tissue from humans. Once this is robustly developed, this will assist in overcoming the challenges of sporadic tissue availability and generate a biobank of patient-derived tumouroids as we optimise longitudinal imaging and handling techniques alongside conducting hormonal assays before we move to validating the equine culture.

Once the equine pituitary culture is established, the long-term aim of this model is to functionally validate the candidate tumourigenic genes identified in my previous work and whether they drive abnormal melanotroph growth and secretion. Specifically, I plan to integrate multi-omic approaches (transcriptomics and secretomics) to map how cellular activity evolves in disease progression and in response to therapeutic interventions. This will culminate in a novel functional characterisation of equine pituitary adenomas, revealing how pathogenic drivers dictate malignant cellular behaviour. Preliminary data will be used to support applications for further funding from UKRI and industry.

The Steve Bishop award has been transformative for my development as an early career researcher by fostering new transatlantic collaboration that bridges our laboratories in Edinburgh and the US. Beyond advancing my specific project, the exchange provided invaluable exposure to a distinct research culture. The Heaney lab's clinically orientated environment offered a unique opportunity to broaden my wider pituitary tumour understanding as I gained critical insight into human pituitary tumour presentation, diagnostic workflows and therapeutic options- which are key to application of the technology to comparative medicine. Furthermore, integrating into a new clinically focused team strengthened my ability to translate complex equine research for an audience of patient facing clinicians, significantly sharpening my scientific communication skills as I adapted my presentations to resonate with specialists unfamiliar with veterinary contexts. This experience has solidified my confidence in my own technical and interpersonal abilities, preparing me to engage in future collaborative research initiatives.



This award has fundamentally shifted my career outlook from national to international, allowing me to be immersed in the research culture of the States and establish a vital international partnership that will continue long after my PhD. It has equipped me with a unique dual-perspective of pituitary research (equine and human), with the technical mastery and cross-disciplinary communication skills gained during this exchange making me a more competitive candidate for post-doctoral fellowships in translational medicine. Perhaps most importantly, the award has provided the platform and confidence necessary to begin to transition into a more independent research career focusing on bettering our understanding of pituitary tumours.

This project will deliver the first 3D organoid model of equine pituitary tumours, providing the animal science community with a critical tool to advance the understanding and treatment of EC disease. It is anticipated that the methodology will be applicable to study of tumours in other domestic animals, such as cats and dogs, where pituitary tumours are relatively common. This approach strongly supports the 3Rs of animal research by providing a biologically relevant culture system replacing the need for live-animal experiment. The ability to expand and cryopreserve organoids allows for repeated experiments from a single clinical sample, drastically reducing the number of animals needed for meaningful data. This ultimately translates to improving animal welfare through enhanced diagnostic accuracy, the identification of biomarkers and potential development of more effective therapeutic options.

For industry and academia, this model when developed for high-throughput screening, will provide a cost-effective platform for equine-targeted drug screening as these equine derived organoids will retain species-specific physiological characteristics. This may lead to the development of more targeted treatments for the equine market.

The key barrier is identification and communication with potential industry partners at the early stage of a project involving transformative technology, such as that used in the project here. Whilst it is not expected that immediate support should be provided by potential industry partners, a pathway to informal discussions would benefit translational aspects. Industry input would also help focus the research and expand its application through identification of other diseases that could benefit from the technology. Whilst this is likely following publication of our research, earlier interactions with industry would be beneficial.

I would like to thank BISAS and Innovate UK Business Connect for their generous support with this project. With their support, my PhD research has been innovated with the addition of a novel culture system- both for our lab at the University of Edinburgh but also for the new culturing of equine pituitary tissue. The Steve Bishop award has shaped my personal development as a scientist, recognising my early career work and giving me the confidence to pursue research possibilities across national contexts.