A research update from the UCD School of Veterinary Medicine

The team at University College Dublin's School of Veterinary Medicine present an update on the new research developments taking place within the School

New research within the University College Dublin's (UCD) School of Veterinary Medicine is built upon a strong existing research framework within the School, as well as collaborative networks with other areas of the university and centres within Ireland and overseas. This has resulted in a diverse array of research topics encompassing basic science, translational medicine, clinical practice, and education. This article will provide an overview of some of the ongoing research within the School, with emphasis on some of the new and exciting projects undertaken by junior or recent members of staff.

ONE HEALTH AND TRANSLATIONAL MEDICINE

Under the broad theme of one health and translational medicine, Dr Clodagh Kearney is pursuing research that aims to further the development of novel therapeutics for arthritis. Arthritis in humans is ranked in the top 10 causes of disability worldwide, and reduces the quality of life of patients, by severe joint pain and stiffness and loss of mobility. As in humans, arthritis is a major welfare and economic concern in the horse causing an estimated 60% of all lameness. Currently, there is no disease-modifying treatment for arthritis in any species; therapies are symptomatic, designed to relieve pain and discomfort. In humans these show limited effectiveness, and come with adverse effects, for example osteoporosis and insulin resistance. In horses, long-term use of oral anti-inflammatories can lead to gastric ulcers and repeated intra-articular injections of corticosteroids show limited efficacy and can damage cartilage metabolism. Finding better therapies for controlling joint inflammation, the hallmark of arthritis in both horses and humans, is the goal of this research.

Utilising existing strong collaborations within the School of Veterinary Medicine between clinical specialists and researchers in inflammation, drug delivery and medical devices, and by building new international collaborations with basic research groups developing new cell-based therapies in the Netherlands, the group aim to develop treatments that target interruption of the inflammatory cascade within the joint before disease progression enters a state of no return. In particular, the safety and efficacy of nanomedicines and cell-based therapies are being explored using an equine model of synovitis. This research may have future application for humans since the horse is an accepted pre-clinical animal model for arthritis in humans. Therefore, resultant novel therapeutics may improve the quality of life of affected horses and potentially human patients.

Also within the theme of translational research, Dr Robert Shiel is investigating potential causes of

Figure 1.

greyhound meningoencephalitis, a breed-associated neuroinflammatory disorder that has been seen exclusively in young greyhounds in Ireland (see Figure 1).

The disease occurs in multiple related littermates, which raises the likelihood that there is an underlying genetic or infectious cause. No common infectious agents have been identified. A collaborative project with researchers at the Wellcome Trust Centre for Human Genetics (University of Oxford) and Maynooth University, sponsored by the American Kennel Club and the UCD Seed Funding initiative, is designed to explore potential underlying mechanisms of disease using a combination of exome sequencing, genome sequencing and mass spectrometry. This 'multi-omics' approach is hoped to shed new light on pathways driving neuroinflammation in this well-defined disease, which could increase understanding of neuroinflammatory mechanisms in other diseases and species.

COLLABORATIVE INVESTIGATIONS INTO CANINE SEIZURES

Canine congenital portosystemic shunts are frequently encountered in small animal practice and represent abnormal vascular communications between the principal portal vein or one of its tributaries and a systemic vein, allowing portal blood, destined for the liver, to bypass and enter directly into the systemic circulation. Shunting of portal blood around the liver results in myriad clinical signs affecting the gastrointestinal, urinary and central nervous systems. Surgical correction of these abnormal vessels is the recommended treatment, with those undergoing surgery experiencing improved survival and quality of life. Development of severe refractory seizures following closure of these vessels is a well-recognised complication

with often devastating consequences. Dr Ronan Mullins' research involves investigating, in collaboration with 12 other veterinary teaching hospitals and private referral practices worldwide, the possible protective effects of pre-treatment of dogs undergoing surgery with the anti-epileptic drug levetiracetam against development of these often fatal seizures. Further aspects of research involve investigating prognostic factors for short-term survival of dogs that develop post-attenuation seizures and investigation of possible risk factors for development of these seizures. The findings of this research will help optimise pre-operative medical management of dogs undergoing portosystemic shunt attenuation, identify dogs that may have a more favourable prognosis following development of post-attenuation seizures, and identify risk factors for development of these seizures, which could help reduce their occurrence in the future.

ENGINEERING AND VETERINARY MEDICINE PROJECT

A collaborative project between the UCD Schools of Veterinary Medicine and Engineering aims to bring together expertise in materials science and development and medical device design with the knowledge and experience of veterinary clinicians, anatomists and radiologists to create high-fidelity, anatomically accurate simulated models for teaching veterinary clinical skills led by Dr Niamh O'Donoghue. Using the facilities and expertise available within the UCD Veterinary Hospital, computed tomography (CT) data will be used to capture the anatomical detail of the area of interest (urogenital tract of a female dog). Using specialist software, the veterinary radiologist and materials engineer will translate the DICOM file from the CT scan into the relevant printable data. 3D printing directly onto flexible materials, which is particularly desirable for simulated models, is currently under development by the UCD materials engineering team. In collaboration with the end users of the printed components (veterinary surgeons and nurses), the textures and properties of printed products will be optimised to produce a high-fidelity simulation. Validation of simulated models produced will take place in the School of Veterinary Medicine's Clinical Skills Centre in line with accepted validation protocols. Through collaborations such as this, the final products will greater represent the system or animal part being simulated. This optimisation can also have benefits to parallel developments in materials science with medical applications for development of therapeutic devices, or surgical implants in the field of veterinary medicine and potentially relevant for human medicine.
The production of anatomically correct simulated models for use in the field of veterinary medicine allows for ex vivo training in skills that otherwise rely on access to cadavers or live animals. The development of such reduces the numbers of cadavers required to train to competency, andalso reduces the stress on students and live patients while mastering these techniques. A high-fidelity model for teaching ultrasound is planned as a lead on from this project.

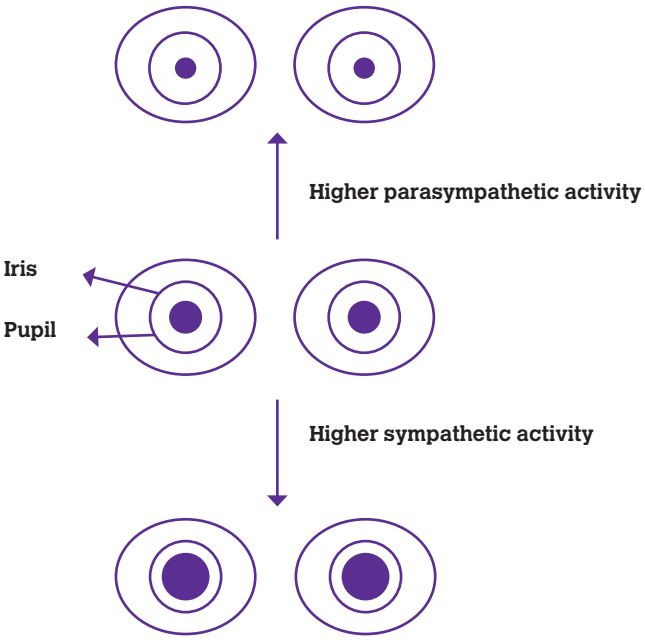

Figure 2.

ANIMAL WELFARE AND STRESS AWARENESS

Measuring and ensuring animal welfare is of paramount importance while working with clinical, experimental and laboratory animals. However, most of the measures of animal welfare are subjective or invasive and often fail to detect vary early signs of stress. To address this challenge, the research work of Dr Arun Kumar and Dr David Kilroy looks at the potential of pupillary diameter as an objective measure of early phase of stress.
As pupillary diameter is exclusively regulated by the autonomic nervous system, the assessment of pupil size (pupillometry) provides an indirect measure of sympathetic nervous system activity and hence an estimation of the degree of stress in the patient. Rise in the levels of sympathetic neurotransmitters is the early sign of stress, which is often beyond the detection limit of currently, used bioassays. However, the muscles regulating pupillary diameter are sensitive to the low threshold of sympathetic neurotransmitters. The long-distance digital photography of the eye and the image analysis to measure iris-pupillary diameter ratio offers a non-invasive and objective measure of elevated sympathetic activity and hence stress in a wide array of species (see Figure 2). The research work done so far has evaluated the feasibility of iris-pupillary diameter ratio to identify dogs and cats with borderline hypertension, chickens raised under stress conditions (high ammonia levels) and stress levels in captive primates. A database of species-specific pupillometry is planned to develop a smartphone-based app for point of care measure of animal welfare as an outcome of this research.

DAIRYTECH RESEARCH PROJECT

On the farm-animal front, research is being carried out by Dr Joris Somers as part of the DairyTech research project based in UCD Lyons Research Facility.
DairyTech, funded by Enterprise Ireland, unites colleagues

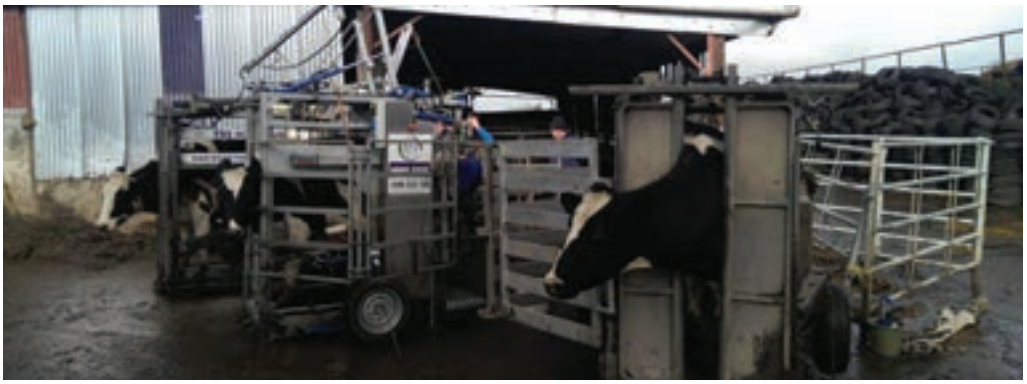

Figure 3.

from UCD School of Veterinary Medicine, UCD School of Agriculture and Irish dairy industry stakeholders, to conduct novel research in five interrelated work packages to address some of the most significant challenges to growth faced by the Irish dairy industry including: (i) genetic and bioeconomic modelling of dairy production systems; (ii) evaluating control strategies for low milk fat percentage in Irish dairy herds; (iii) monitoring lameness in dairy cows using remote sensor technology; (iv) nutritional manipulation to improve the microbiological and processability characteristics of late lactation spring milk and (v) development of a grassland-management protocol for higher input/output dairy systems to support production expansion with constrained land holding availability. Based on his track record in dairy cow lameness, Joris is the primary investigator in the work package aiming to advance the application of sensor technology in dairy farming for the use of lameness monitoring. The objective is to record cow activity and lameness in a dairy herd and examine the relationship between the activity data gathered and lameness with the ambition of facilitating lameness prediction and the identification of algorithms using data-mining techniques. Over the first 12 months of this pilot project, daily activity data were collected from 140 cows in the Lyons dairy herd using readily available technology. Simultaneously, these cows were subject to regular locomotion scoring and clinical diagnosis and treatment of lameness. At present, all energy is focused on the data mining and algorithm identification based on the large data set generated. This will allow exploration of the relationship between the various activity patterns and all the animal health data collected. Ultimately, DairyTech will produce new knowledge and skills for use in the creation of new products, processes and services in dairy production.

CALF-PNEUMONIA STUDY

Pneumonia is one of the largest causes of morbidity, mortality and antimicrobial usage in dairy calves. Causative pathogens are largely ubiquitous among dairy herds and the disease is precipitated by various stressors. The housing systems used in modern dairy farms play a fundamental role in the development of pneumonia, however, minimal literature is available regarding the particular environmental conditions that predispose to the establishment of pneumonia. Supported by an SFI-HRB-Wellcome Trust Biomedical Research Partnership grant, Dr Conor McAloon is investigating the role of the environment in the development of calf pneumonia. The study involves the development of an integrated, real-time monitoring system in commercial calf sheds, capturing data on environmental conditions (temperature, humidity, CO_2 concentration), milk intake and feeding behaviour, weight measurement and tympanic membrane temperature. This work will help to inform optimum shed design(see Figure 3) and aid in the development of new automatic detection methods for calf pneumonia.

LEPTOSPIROSIS INVESTIGATIONS AND IMPACT

In the wildlife field, Dr Hanne Jahns from veterinary pathology is involved in the investigation of leptospirosis in the pygmy shrew. Leptospirosis is one of the most widespread zoonosis in the world and can affect a large variety of different species. Latently-infected carriers, among wildlife mainly rodents, contribute to the maintenance of pathogenic leptospires in the environment posing a risk of exposure to humans and livestock. In 2013, a novel pathogenic leptospira serovar Room22 related to *Leptospira astonii* previously only reported in Asia was isolated from the greater white-tooth shrew (*Crocidura russula*) in Ireland. This invasive mammalian species belonging to the order *Eulipotyphla* and family of *Soriocidae* was first reported in Ireland in 2007. Since then the population has expanded rapidly with a detrimental effect on the only native shrew species, the pygmy shrew (*Sorex minutus*). As part of a large project on the impact of the greater white-tooth shrew on the broader Irish ecosystem led by Dr Allan McDevitt, University of Salford, UK the prevalence of this new leptospira serovar in the invasive and native shrew is being investigated. The study may further shed some light on the pathogenesis of the isolate and if the greater white tooth shrew brought the serovar Room22 to Ireland or acquired it in Ireland. This project also involves collaboration with the UCD School of Agriculture and Food Science, UCD School of Biology and Environmental Science, UCD Earth Institute and the Infectious Bacterial Diseases Research Unit, National Animal Disease Center, Ames, Iowa, US.

The above research projects are just some of many currently underway within the School. With continued support, the research drive within the school will continue to grow in the years to come.