Royal Veterinary College
University of London

Minutes: AWERB SUMMARY MINUTES

Status: Chair approved

Meeting held: 2 October 2018 at 3pm in Camden Council Room VIDEOLINKED to F82 Hawkshead

Attendees: 10 members, 5 in attendance, 2 by invitation, 6 apologies

1 MINUTES OF PREVIOUS MEETING

The minutes of the meeting held on 30 August 2018 were confirmed as an accurate record of the meeting.

2 NEW PROJECT LICENCE APPLICATION

The project licence holder was welcomed to the meeting. It was explained that the applicant had recently joined the RVC as a new lecturer and was wanting to transfer the work that she has been doing at her previous institute to the RVC so was applying for a new project licence. There was also a scientist in attendance who had been involved in reviewing the application to provide comments from a scientist's perspective.

The project licence holder explained that she had been awarded a grant that would fund the proposed work in the project licence. She had theoretical and technical knowledge of several animal models of cardiovascular disease in rodents (rats and mice) and also in zebrafish, which was work that she was proposing to continue at the College. She was also very experienced in carrying out the protocols listed in the project licence from her work at the previous institution.

An overview of the proposed work was given. Coronary artery disease was a major global cause of adult mortality and chronic ill-health. The two main components leading to the occlusion of coronary and cerebral arteries were atherosclerosis and thrombosis. The typical atherosclerotic lesion (plaque) develops as a result of initial damage to the endothelium and subsequent endothelial dysfunction, followed by the accumulation of lipid and foamy, cholesterol-rich macrophage cells, vascular smooth muscle cell (VSMC) proliferation and migration, accumulation of T-lymphocytes, and deposition of connective tissue matrix and cholesterol to form complex plaques, which were the underlying primary cause of almost all cardiovascular disease (ischaemic heart and peripheral disease, and stroke). Endothelial cell damage and the proliferation, migration and apoptosis of VSMC were also pivotal in cardiovascular proliferative disorders such as vessel stenosis following coronary artery angioplasty/stenting and after bypass surgery, the two main procedures used to treat ischaemic heart and peripheral disease. Vascular endothelial growth factor (VEGF) was essential for endothelial cell differentiation (vasculogenesis) and angiogenesis during development and was a key mediator of neovascularisation in several common human diseases, particularly cancer and eye disease. The central importance of inhibiting VEGF as a therapeutic target in human neovascular disease had been highlighted by the now widespread use of the VEGF inhibitory antibodies, Avastin and Lucentis, for treatment of some cancers and the eye disease, wet age-related macular degeneration.

In the work proposed under this licence application the aim was to continue the current work in animal models of angiogenesis and cardiovascular diseases, including genetically-altered and wild-type mouse and zebrafish models. Protective effects of VEGF- genes, receptors, and components of signalling pathways already identified in cell culture studies as candidate mediators of important VEGF-regulated endothelial functions, or of important PDGF-regulated VSMC functions in established models of mouse endovascular injury, and zebrafish heart and fin regeneration would be investigated. Given the key role of VEGF pathways in angiogenesis and the important role this plays in common human diseases such as cancer, the effects of VEGF-regulated genes, VEGF receptors, and components of VEGF signalling pathways in established animal models of angiogenesis and tumour growth dependent on neovascularisation (mouse and zebrafish) would also be investigated.

There were 6 protocols listed in the licence. Two of them related to breeding and maintenance of genetically modified mice and zebrafish.

The following queries/comments were raised:

- Were there any anticipated adverse effects from the zebrafish model? It was explained that generally there was a 90% recovery rate, with one in 10 of the fish not surviving. This was generally because those fishes were smaller and slender. Where possible larger fishes were therefore used for these studies. Once the procedure had been undertaken the fish would be observed in their tanks. Any that were in distressed would be culled.

  It was pointed out that 1:10 fish was still quite a high number and that there was potential of exceeding the project licence severity level. How were these distressed fish identified before the situation becomes severe? It was explained that this was done by observing their gills. Water would be pipetted onto the gills for a couple of minutes. If there was no spontaneous movement after 5 minutes then they would be scheduled 1. Clear humane end points needed to be incorporated into the project licence to ensure that severities were not breached. These would cover what they were and what actions would be taken so that the Home Office Inspector was able to see that there was a clear plan and guidelines of what steps should be taken.
- Fin regeneration would be undertaken to evaluate the regenerative outgrowth. This would be done by undertaking caudal fin amputation after lightly anaesthetising the fish. Analgesia would be used if appropriate.
- For protocol 2, how would the intramuscular injection into the hindlimb muscle of the mouse be done? There would be an application of pluronic gel around the injury. This was a liquid when cold but when placed on a warm body would turn into a gel and stay there.
- Given that vascular smooth muscle proliferation was one of the steps involved in atherosclerosis development, how much of the science could be done in vitro using cells from the knockout mice?' The project licence holder explained that she had done a lot of in vitro work and would do more to look at the role of her proteins of interest but that ultimately she needed to run the in vivo models proposed to study the complex interplay between multiple different cells and mediators that occurred in vivo. The committee suggested that more of the in vitro work should be included in the licence application as background.
- The NVS suggested that instead of injecting the mice with tamoxifen, that it be mixed with peanut oil and fed to the mice as that would be less stressful to the mice. There were groups that have had success in feeding the mice non-invasively as they liked the peanut oil and so were happy to come to the syringe and lick it. The project licence holder queried whether putting the tamoxifen into the food would be problematic as it would not then be possible to determine the exact dose that the mice have had. The relevant literature would be forwarded to the project licence holder so she could look into it further.

- It was noted that the licence stated that suturing would be replaced if necessary under analgesia. It was recommended that a limit of how many times the suturing could be replaced should be included in the licence.
- It was noted that pilot studies had been done. It was recommended that for the numbers of animals to be used, a justification be provided about why those numbers were needed. There was concern that a high number of animals had been included – estimates should be refined based on power calculations given that pilot studies had now been performed.
- A query was raised whether any ischaemia differences between mice strains had been noticed. The project licence holder advised that she had not observed any differences in the severity of the ischaemia induced. She used the black 6 strain and the mice always walked fine afterwards. She would also discuss with another scientist who had experience of this area of work and had found strain differences
- The project licence would be amended to include what would happen if the animals showed signs of dermatitis.

The project licence holder was thanked for attending the meeting and was advised that she would be informed of AWERB's decision following the meeting.

After the project licence holder had left, it was agreed that although there was still a lot of work to be done on the project licence, doing the work seemed to be justified. AWERB also confirmed that they were happy with the general principles of the licence and the need to use these animals for this type of work. Integration of *in vitro* work needed to be included though as there was a lot that could be done this way to study these mechanisms. Specific comments on the project licence would be sent to the project licence holder directly.

3 WORKING GROUP

3.1 Environmental Enrichment Working Group

The group had discussed the following:

- BSc students: There were two BSc students signed up to do environmental enrichment projects on research animals. Exact details (such as species and enrichment) needed to be determined and discussions would be held with BSU staff and the students. The results of the enrichment audit would be used to help identify areas of need.

- Environmental Enrichment Audit: An audit had been undertaken in 2017. The intention for 2018 was to review appendix 3 of the report (which provided a summary of the information obtained) to see what has since changed. In 2019, a more in depth audit would be undertaken again to see what progress has been made.

- Animal Research Showcase Event: one of the aims of this could be to stimulate balanced thought in (initially internal) visitors to help recruit more volunteers for things like dog walking and refinement projects as well as help stimulate more people to innovate in 3Rs areas now or in their future careers.

- Enrichment competition: students would be asked for suggestions to design better enrichments for our animals in Camden that were kept in the yard. The top 4 would be chosen and tried out with the animals for a week to see if the animals enjoyed them. Different groups would be approached for seed funding.

4 MATTERS ARISING FROM THE MINUTES

4.1 Lab Animal Workshop plus poster for the workshop (Item 4.1 – August 2018 meeting/item 3.5 July 2018 meeting)

This workshop has been scheduled for March 2019. Two nominees from our AWERB would be put forward. The workshop was intended to help people who have no formal training in Experimental Design of Data Analysis but would be required to appraise those elements of PPL applications as well as their direct welfare implications.

The top 3 responses in relation to topics for the poster had been identified. People were suggested to lead working parties to take forward putting the panels together for the poster:

- Dog socialisation and rehoming programme
- Tissue Sharing project
- Environmental enrichment project

Members of AWERB would be asked to sign up for the working group that most interested them.

4.2 Rehoming (Item 9.1 – August 2018 meeting)

The technicians had set up a working party to look at harmonizing the rehoming approach. This included both Camden and Hawkshead technicians. They would be invited to a future AWERB to give an update on their work so far.

4.3 2018-19 CPD Programme (Item 10 – August 2018 meeting)

5 places had been allocated to animal technicians.

4.4 Stockpiling of animals (Item 16 – August 2018 meeting)

Although had been some movement with users reducing the size of their colonies, the problem of project licence holders building up a stockpile of animals was a recurrent issue. Animal technicians were ensuing that they regularly notified project licence holders when this was happening.

4.5 Attending other AWERB meetings (Item 9.2 – July 2018 meeting)

The Chair of the AWERB Hub had been e-mailed to see whether she could check if there was interest in attending other AWERB meetings as an observer. She had responded to say that she thought it was a good idea and would take forward upon her return from leave (in September). A reminder would be sent.

4.6 ARRIVE Guidelines (Item 4 – June 2018 meeting)

The new study request form was being worked on that would also help researchers follow the ARRIVE guidelines.

4.7 Virtual tour of BSU (Item 6.7 – June 2018 meeting)

The filming of both Camden and Hawkshead animal units was underway. Once completed a demo would be made available at a AWERB meeting for review. Having a virtual tour available would enable people to tour the units without being there in person and so avoid stressing the animals. A query was raised that although this was a step in the right direction, how beneficial was it really? There were some really good virtual tours though that should be looked at to make sure the College achieved the same high standard. It was also recognised that there was a fine balance in publicising the work being done in the units with that of the welfare of the animals. One option for the future was to invest in webcams which would enable users to watch what was happening and scan around the unit.

4.8 Training Records (Item 11 – June 2018 meeting)

A sample copy of the training folder and the concept behind it would be bought to a future AWERB meeting.

4.9 Refresher training (item 2.2 – April 2018 meeting)

The refresher training course was still being added to. Information in relation to the Home Office courses was being added.

5 ANIMAL RESEARCH NEXUS PROJECT

The attendees from the Animal Research Nexus Project were welcomed and introduced. They explained that this was a research project funded by the Wellcome Trust (2017-2022), which had bought together leading researchers on the social and historical dimensions of animal research. Five institutions were involved. Their work sought to understand the changing nature of these relations and obligations through new social and historical research on:

- The historical relations that forged the shared understandings across scientific practice, animal welfare and health benefits embodied in A(SP)A.
- The contemporary challenges emerging as scientific practices and social expectations change established patterns of laboratory animal use and supply, professional roles and responsibilities, and public and patient engagements.
- The forms of dialogue between stakeholders, scientists and publics that might contribute to remaking social contracts across the animal research nexus in the UK.

There were 6 components to the Animal Research Nexus Project:

- Collaboration and communication (dialogue)
- History and Cultures (relations)
- Species & Spaces (care)
- Markets & Materials (assurance)
- People & Professions (trust)
- Engagement & Involvement (credibility)

The aim of the Animal Research Nexus project was to improve communication and collaborations in relation to animal research: both outwardly facing to the public, internally and also with science communicators so that all were working together for a more transparent dialogue.

Work was being done to develop innovative and exciting pubic engagement on the animal research nexus. One element of this was a large scale immersive theatre experience which would enable people to explore ethical decisions made and ask questions. Work was being done with a theatre company to set this up. The aim was to create performance to engage, challenge and thrill their audiences. As part of this project, members from the theatre company were aiming to experience as many aspects of animal research as possible, particularly those where ethical decisions were discussed hence why they had asked to observe this AWERB meeting.

AWERB indicated that the College were very supportive of the aims of this project and would be happy to be involved and were also happy to receive advice on how to be more open on the research that it did. The RVC were taking steps to be more open, for example via the virtual tours of the animal units that were being set up; and also the recent media engagement to promote an international collaborative research project exploring the potential for gene editing to treat Duchenne Muscular Dystrophy (DMD) and the RVC's key role in that research

6 NVS UPDATE

There were no health or welfare concerns about the animals in either of the units to report. There was a discussion about the dog unit and how it was run. The Home Office Inspector was frequently kept

updated on the progress in the unit and the steps that were being put in place to continually improve the unit.

7 AMENDED PROJECT LICENCES GRANTED BY THE HOME OFFICE

AWERB noted that one project licence had been amended since the previous AWERB meeting.

8 MID TERM REVIEWS

There had been one mid term review due, however as no work had been done under the project licence there was no report to provide.

9 END OF PROJECT LICENCE REVIEW

One of end of project review had been received.

10 SCHEDULE 1 REGISTER REVIEW

This was being reviewed alongside the assessors review and an updated schedule 1 register would be bought to a future meeting.

11 ANY OTHER BUSINESS

11.1 AWERB Feedback

The attendees from the Animal Research Nexus Project asked AWERB members whether there were areas that they would like to cover as an AWERB but were unable to do so due to lack of time or for other reasons. The following comment was made:

- Being able to involve more of the technicians who would like to attend these meetings but were unable to do so due to work commitments in the Units. This would be addressed by getting technicians to attend on a rotating basis.

The Animal Research Nexus Proect were asked for their feedback on the AWERB meeting:

- Interesting to see the processes happening and the types of discussions that had been held. There was generally a gap in understanding how decisions were made – this helped with that.
- It was good to see that there was more than one person making the decisions and that there was a mixture of view points and people on the Committee.
- They liked the collaborative nature of the Committee and how discussions were held with scientists and how that was an ongoing process.
- 3Rs was a general embodiment in each decision rather than a separate element.
- The agenda had a lot of variety and the meetings were not just focused on reviewing project licences, which could be seen as the primary role of an AWERB. It had been interesting to see how diverse it was. It was also good to see that sharing of information was encouraged.

12 DATE OF NEXT MEETING

This was scheduled for 8th November at 2pm.

Secretary
5 October 2018