Educating the Next Generation of *In Vivo* Scientists: Meeting the Needs of Industry and Academia

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Summary

At present, complementary experimental techniques and preparations cannot fully replace the use of research animals in the development and regulatory approval of new medicines. Universities therefore have a responsibility to meet the needs of industry and academia by educating the next generation of in vivo scientists and by providing a select cohort of undergraduate students with the knowledge, expertise, and skills to be able to undertake integrative physiology and pharmacology investigations. This education must include hands-on experience of integrative techniques and preparations but also encompass a much broader education, including knowledge and understanding of animal welfare, ethics, and the 3Rs, as well as knowledge of complementary experimental techniques and an appreciation of the role of integrative studies in modern biomedical research.

Keywords: in vivo sciences, education, physiology, pharmacology

1 Introduction

Over the last twenty years, the development of powerful molecular biological techniques and technologies has led to a marked reduction in the use of animals in scientific and medical research in the United Kingdom (Home Office, 2011). However, studies at the molecular and cellular levels do not allow us to fully understand how individual organs function, how they interact with other body systems, or indeed, how the body as a whole works. Therefore, the use of research animals continues to be essential for scientific progress. However, the increasing adoption of reductionist approaches by the scientific community has resulted in a global shortage of individuals with the knowledge, skills, and expertise to be able to undertake whole animal or *in vivo* research. In the United Kingdom, surveys undertaken by the Association of the British Pharmaceutical Industry of their membership in 2005, and subsequently in 2008, highlighted the shortage of trained graduate, postgraduate, and post-doctoral *in vivo* physiologists and pharmacologists within the UK, to the extent that respondents were concerned about the future of these disciplines (ABPI, 2005, 2008).

2 Education in *in vivo* sciences versus complementary experimental techniques

Increases in student numbers, coupled with decreases in staff and financial resources, have resulted in marked reductions in practical teaching within UK Higher Education (British Pharmacological Society and Physiological Society, 2006). This is most marked within *in vivo* sciences. Despite the fact that *in vivo* studies are an essential component of the drug discovery process and a requirement for regulatory approval for new medicines, fewer than 160 out of the 8,000 undergraduate students in the UK who graduate every year in physiology, pharmacology, or related disciplines will receive any hands-on training in *in vivo* sciences during their studies (Leggett, 2005). Could this lack of hands-on training be replaced by an increased use of complementary techniques and preparations, videos, or computer simulations (including those simulating *in vivo* studies)? The use of these alternative teaching methods certainly has a role to play, for example, in providing knowledge, reinforcing concepts, and supporting lecture materials (British Pharmacological Society and Physiological Society, 2006). However, considerable skill, manual dexterity, and care are required for both isolated tissue and whole animal experimental studies – an appreciation of which can only be gained from hands-on practical experience. The use of computer simulations also reinforces student misapprehensions that scientific experiments always work. With limited experimental time within courses, practicals within both high school and university curricula are increasingly being designed so that they always produce reliable and reproducible data, leading students to believe this is always the case. This misapprehension causes problems when students are subsequently exposed to novel science in their final year research projects or future careers when things don't work or they get experimental data they don't expect. Scientists also are inspired by the excitement of actually doing the experiments themselves rather than watching others. Feedback from final-year students suggests that their teaching, particularly in practicals, influences their career decisions (British Pharmacological Society and Physiological Society, 2006). Participation in studies involving research animals is not for everybody. Without hands-on experience of integrative experimental techniques and preparations, students are not going to be able to make informed decisions as to whether they wish to develop a research career in this field. Limited exposure to research animals and *in vivo* preparations during their undergraduate studies will engender an appreciation of the responsibilities required to undertake such studies and will affirm, or otherwise, their personal aptitude for this type of research. With respect to responsibilities, we want students who are going to use research animals in their future careers to actively apply the 3Rs rather than just having knowledge of these principles. Requiring students to reflect on their application of the 3Rs before and after they undertake an *in vivo* physiological or pharmacological investigation is going to achieve this to a far greater extent than a didactic lecture or discussions after watching a video or computer simulation.

Future *in vivo* scientists also require far more than practical skills training; they need a much broader education in the discipline. Indeed, the use of research animals for training (except for the training of practicing surgeons in micro-vascular techniques) is not a permissible purpose under the UK Animal (Scientific Procedures) Act (H.M. Government, 1986). The ABPI and Bioscience Federation report "*In-vivo sciences in the UK: Sustaining the supply of skills in the 21st Century*" (APBI and Biosciences Federation, 2007) recommended that this education should include, for example, training in experimental and statistical design with respect to animal studies, animal welfare, ethics and the principles of the 3Rs, knowledge of animal models of disease, complementary experimental techniques and preparations, and an understanding of the role of *in vivo* studies in modern biomedical research. Provision of this education in *in vivo* sciences is expensive; it requires considerable staff,

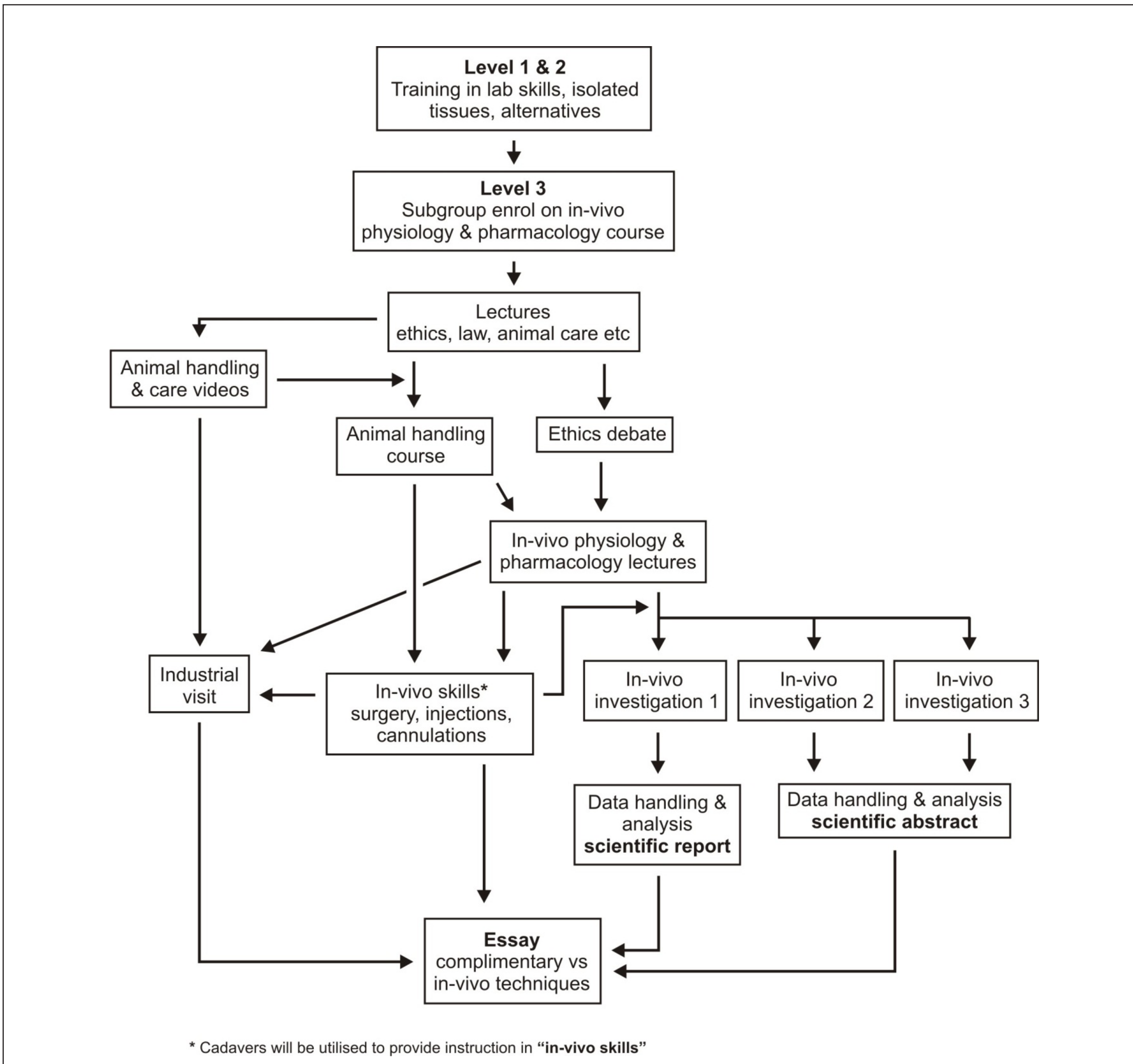

Fig. 1: A model for a final year undergraduate module which provides an education in integrative physiology and pharmacology

resources, dedicated facilities and, most importantly, the use of research animals (British Pharmacological Society and Physiological Society, 2006). It is essential, therefore, that this education is provided only for those undergraduate students who will directly use it in their future career, i.e., the select few that intend to go on to careers in scientific research rather than to entire cohorts of students. One model by which this education in *in vivo* sciences could be provided is outlined in Figure 1.

3 A model for undergraduate education in *in vivo* sciences

Within a three year undergraduate degree program, students would be provided with training in basic laboratory skills and complementary experimental preparations and techniques (including isolated tissues studies) during the first two years of their studies. In the third (final) year, students would apply to be considered for enrollment in a specialist module or course that provides an education in *in vivo* sciences, with registration restricted to those students who could demonstrate that they intend to use the knowledge and experience gained in their future careers, either in scientific research or in other areas of the drug development process.

The educational learning objectives for this integrative physiology and pharmacology course would be:

1. To provide students with experiential learning of integrative physiology and pharmacology;
2. To enable students to gain experience in studying physiological and pharmacological responses using appropriate animal models, techniques, and preparations;
3. To develop student understanding of the potential and the limitations of integrative experimental techniques and preparations in biomedical research;
4. To educate students in the alternatives to the use of animals and, where there is no alternative to their use, the application of the 3Rs in the design of these experiments;
5. To instill insight into best practice in terms of ethical awareness, experimental design, statistical analysis, practical details of anesthesia and surgical technique;
6. To develop key transferable scientific skills.

A combination of lectures, seminars, and experimental sessions would be used to achieve these objectives.

Students would be provided with lectures covering the law, animal welfare and husbandry, ethics and the principals of the 3Rs. They also would receive lectures on the use of *in vivo* techniques/models in specific areas of research, for example, psychopharmacology, cancer biology, cardiovascular studies. To promote knowledge and understanding of the arguments for and against the use of animals in scientific and medical research, students would participate in a debate on the ethics of animal experimentation, using role-play to argue from different perspectives. Experimentally, students would be provided with training in the handling, restraint, and identification of rats and mice. An education in surgical techniques, including cannulations, could be provided using rodent cadavers, removing the need to use live animals while still providing the same level of student experience. Students also would have the opportunity to observe and assist, where appropriate, in physiological and pharmacological investigations using freely moving animals, *ex vivo*, and terminally anesthetized experimental preparations. Where possible, this course would include a site visit to a pharmaceutical company, enabling students to observe a wider range of studies and species, but, more importantly, to gain a greater appreciation of the wide range of complementary experimental studies required to develop and obtain regulatory approval for new medicines. Assessments for the course would be designed to develop key scientific transferable skills such as reviews of the literature, scientific abstract and report writing, oral communication, and the public communication of science.

This short course would not result in fully trained *in vivo* scientists. Its principle aim would be to provide students with exposure to *in vivo* physiological and pharmacological studies and, thereby, a greater appreciation of the role of *in vivo* sciences in modern biomedical research. To further their appreciation and understanding, students would be required to integrate all they have learned into an assessed end-of-module essay in which they would discuss the role of *in vivo* versus complementary experimental techniques and preparations in a research area of their choice.

4 The next step: Accredited degrees in *in vivo* sciences

The UK is currently at the forefront of global research and development in the Life Sciences. UK employers are becoming increasingly concerned, however, that difficulties in recruiting sufficient numbers of “research-ready” graduates who possess the knowledge and skills they require is threatening this position (ABPI and Bioscience Federation 2007; ABPI, 2008). As a consequence, the UK Government tasked the Society of Biology to develop an accreditation program for undergraduate degrees in the biosciences (Office of Life Sciences, 2009). The aims of the accreditation program are not to accredit all courses but to recognize programs that will deliver the research and development leaders of the future, initially in areas where there is significant global demand, such as *in vivo* sciences (Society of Biology, 2010). The essential features of accredited programs are that they would equip students with a broad base of knowledge, understanding, and skills, as well as specific knowledge, understanding, and skills within the accredited discipline. The program should include a sizeable research element that allows the student the opportunity to develop and utilize skills specifically in the accredited discipline (Society of Biology, 2011). This requirement for a substantial research project means that accreditation would be restricted to students enrolled in a 4-year integrated Master’s program or those whose 3-year undergraduate program included an additional placement year in industry. Accreditation would not be afforded to all students in the cohort but only to those whose path within a program of study met the above criteria. In addition, by the end of their program of study, students must have met discipline-specific learning objectives, drawn up in consultation with relevant Learned Societies, industry representatives, funding bodies, and sector skills councils (Society of Biology, 2011).

For *in vivo* sciences, the learning objectives are:

- an in-depth comparative knowledge of the principal mammalian body systems, articulated meaningfully using appropriate anatomical, physiological, and pharmacological terminology;
- an appreciation of the role and limitations of "models" within all aspects of biomedical research through evaluation and appropriate application;
- the ability to employ independently and appropriately a range of *in vivo*, *in vitro*, and other experimental approaches in modern biomedical research while demonstrating knowledge and appreciation of and adherence to accepted procedural protocol, conduct, and performance.

The content of the individual accredited program could vary between institutions. However, examples of relevant opportunities and experiences that would enable students to fulfill the above learning outcomes to the required levels of depth and competency could include successful completion of the mandatory training courses required to obtain a personal license to undertake studies regulated by the UK Animal (Scientific Procedures) Act, advanced training in animal welfare, ethics and the 3Rs, opportunities to demonstrate competence in specific *in vivo* procedures, preparations, and techniques, and undertaking physiological or pharmacological investigations using either freely moving animals or anesthetized preparations. Students also would have to undertake a minimum six-month program of research that involved a substantial element of hands-on, self-directed *in vivo* research.

5 Concluding remarks

It is essential that a select cohort of undergraduate students in physiology, pharmacology, and related disciplines are provided with an education in *in vivo* sciences, including hands-on practical experience in order to ensure that the United Kingdom has sufficient *in vivo* scientists with the necessary knowledge, skills, and expertise to maintain its position as a world leader in biomedical research. This education could not be provided solely with the use of complementary experimental preparations and teaching methods. It should be restricted, however, to those students who can demonstrate that they will utilize it in their future careers, whether these are in scientific research or other disciplines within the drug discovery process. The proposed development of accredited degree programs in *in vivo* sciences will ensure that the UK Higher Education sector provides industry and academia with the research-ready graduates they require.

References

ABPI – Association of the British Pharmaceutical Industry (2005). Sustaining the skills pipeline in the pharmaceutical and biopharmaceutical industries. http://www.abpi.org.uk/our-work/mandi/Documents/2005-STEM-Ed-Skills-TF-Report.pdf

ABPI and Biosciences Federation (2007). In-vivo sciences in the UK: Sustaining the supply of skills in the 21st Century. http://www.abpi.org.uk/our-work/library/industry/Pages/in-vivo-report.aspx

ABPI (2008). Skills Needs for Biomedical Research. http://www.abpi.org.uk/our-work/library/industry/Documents/skills-biomedical-research.pdf

British Pharmacological Society and the Physiological Society (2006). Tackling the need to teach integrative pharmacology and physiology: problems and ways forward. *Trends. Pharmacol. Sci. 27*, 130-133.

H. M. Government (2006). Guidance on the Operation of the Animals (Scientific Procedures) Act 1986. http://tna.europarchive.org/20100413151426/; http://www.archive.official-documents.co.uk/document/hoc/321/321.htm

Home Office (2011). Statistics of Scientific Procedures on Living Animals, Great Britain 2010. http://www.homeoffice.gov.uk/publications/science-research-statistics/research-statistics/other-science-research/spanimals10/

Leggett, M. (2005). Teaching of in vivo research techniques in UK universities – wide-ranging and prompt action is needed. *Physiol. News 60*, 39-40.

Office of Life Sciences (2009). Life Sciences Blueprint. http://www.bis.gov.uk/assets/biscore/corporate/docs/l/life-sciences-blueprint.pdf

Society of Biology (2010). Degree Accreditation. http://www.societyofbiology.org/education/hei/accreditation

Society of Biology (2011). Accreditation Handbook. http://www.societyofbiology.org/documents/view/735

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