EUROPEAN SCIENCE FOUNDATION
SETTING SCIENCE AGENDAS FOR EUROPE

Exploratory Workshops Scheme

Standing Committee for the European Medical Research Councils (EMRC)

European Science Foundation Exploratory Workshop on Genetic Models of Disease Resistance in Livestock

Edinburgh, UK,
1-2 October 2007

Convenor: Bruce Whitelaw
Co-convenor: Helen Sang

Scientific Report

This workshop was held under the authority of the ESF Standing Committee for the European Medical Research Councils (EMRC).

Administrator: Valerie Allspach-Kiechel

Representative from EMRC in attendance: Martin Rollinghoff

This report contains:

1. Executive summary
2. Scientific content of workshop
3. Assessment of results, contribution to future direction of the field
4. Final programme
5. Statistical information on participants
6. Final list of participants

EXECUTIVE SUMMARY

Summary

1. **Workshop brought together experts in host-pathogen dialogue and GM technology animals.**
2. **European scientists are involved in cutting-edge GM technology development.**
3. **Europe has the potential, expertise and opportunity to lead in this field.**
4. **Three priority diseases that could be addressed by GM strategies were identified; these could provide focus for European effort on this topic.**
5. **Identified a need for improved co-ordination of research in this area.**
6. **Recommendation to form a Network.**

Background

- The expanding knowledge of the genomics of host-pathogen interactions of key livestock diseases, together with latest techniques on genetic modification, now allow us to establish a new platform for research into genetic models of disease resistance in farm animals.
- This research will have major impact on animal welfare, food safety, the economy of the sector and human health.

Participants

- Total Workshop budget = £8990.
- ESF contribution = £6990.
- The Workshop was co-sponsored (£2000) by Genesis-Faraday Partnership, a UK Government funded organisation working to improve the co-ordination of the use of genetic and genomic technologies by the livestock breeding and animal health industries. It promotes and co-ordinates basic research and assists with technology transfer.
- There were 17 participants from 8 countries.
- Participants expertise included research scientists, veterinarians, an ethicist and scientists from industry.

The objectives of the Workshop were:

1. Identify expertise that resides within Europe to enable an overview of the European position with regard to International activities.
2. Identify how to best utilise new GM technology to overcome limitations.
3. Identify highest priority disease projects to establish European science as leading the field.
4. Make the appropriate European community (through the invited participants) aware on the initiative to build a Scottish Network of Excellence "Development of Novel Technologies to Fight Viral Diseases in Farm Animals".
5. Provide input into the International Symposium on Animal Genetics for Animal Health to be held at OIE Headquarters 23rd-25th October, 2007.

All were achieved with the following conclusions:

1. Europe has the potential, expertise and opportunity to lead in this field.
2. Demonstration projects needed to show feasibility, applicability and to focus societal debate.
3. European scientists are involved in cutting-edge developments of GM technology.
4. No co-ordination between European labs (although participants indicated willingness to work together).
5. Priority diseases which could be addressed through GM approach identified; generally recognised that this technology has greater likelihood of successfully contributing to disease mitigation when targeted against viral infections.
6. Further debate required to identify 'top' three targets (see below).

Future plans:

1. Build new bilateral collaborative projects.
2. Actively engage in dialogue with potential European funding agencies to raise profile of this topic and the potential lead role Europe could play.
3. Actively pursue funding for a European Network in this topic.
4. The need for a Network was very strongly supported at the Workshop with several participants offered their assistance to progress this concept; core team of individuals formed. First priority of this team to identify the key disease targets (between 1 and 3) on which to basis for such a Network (below).
5. This team identified three priority targets: transmissible spongiform encephalopathy (BSE and scrapie), flu and PRRSV.

Additional comment

- There was discussion about the value of combining the effort in this topic (infectious disease of animals) with the activity in Europe to develop, evaluate and utilise non-rodent animal models of human disease.

SCIENTIFIC CONTENT OF WORKSHOP

The expanding knowledge of the genomics of host-pathogen interactions of key livestock diseases, together with latest techniques on genetic modification, now allow us to establish a new platform for research into genetic models of disease resistance in farm animals. This research will have major impact on animal welfare, food safety, the economy of the sector and human health.

This exploratory workshop took place in Edinburgh on the 1st and 2nd October 2007. There were 17 delegates.

The scientific themes of the workshop were:

- state-or-art in combating virus infection in animals
- new genetic technologies
- future priorities and potential collaborative projects

These were achieved through presentations on:

1. What was required and how (Ivan Morrison, Graham Plastow, Ken Boyd)
2. GM technologies:
    - nuclear transfer / cloning (Heiner Niemann)
    - viral vectors (Bruce Whitelaw, Chamsy Sarkis)
    - transfer of large genomic DAN transgenes (Llusi Montoliu)
3. Example projects:
    - mastitis in cattle (Bob Wall)
    - flu in birds (Helen Sang)
    - prp in cattle/sheep (Dario Brunetti, Bruce Whitelaw)
    - jaagsiekte in sheep (Massimo Palmarini)
    - transgenic rabbit possible projects (Zsuzsa Bosze)

ASSESSMENT OF RESULTS, FUTURE CONTRIBUTION TO FIELD

The objectives of the Workshop were:

1. Identify expertise that resides within Europe to enable an overview of the European position with regard to International activities.
2. Identify how to best utilise new GM technology to overcome limitations.
3. Identify highest priority disease projects to establish European science as leading the field.
4. Make the appropriate European community (through the invited participants) aware on the initiative to build a Scottish Network of Excellence "Development of Novel Technologies to Fight Viral Diseases in Farm Animals".
5. Provide input into the International Symposium on Animal Genetics for Animal Health to be held at OIE Headquarters 23rd-25th October, 2007.

1. Identify expertise that resides within Europe to enable an overview of the European position with regard to International activities. Having assessed the current status of the European research community in this scientific area through email interactions with colleagues it became apparent that only a limited number of projects were being performed at this time. There was however considerable interest and effort in developing the technology. One of the reviewers suggested the inclusion of experts in risk analysis; from my comment above we considered this inappropriate due to very early stage of the science (see future plans).

The convenors therefore decided to focus the invitations to groups actively involved in this area and those actively involved in developing the technologies. This posed a problem due to a concurrent Stem Cell meeting in Italy and various National meetings (especially in Germany relating to Xenotransplantation) and specific individuals having discussion meetings in Brussels. Nevertheless, a good coverage of European activity in this area was represented at the Workshop. Specifically we were able to stimulate a multidisciplinary debate by bringing together experts in molecular genetics, farm and companion animal disease, immunology, and virology (with emphasis on virus of livestock) with ethicist. In addition we were able to identify both the International and animal breeding perspectives through the invited participants.

To summaries the European position:

- The Workshop identified the research activity in Europe.
- Europe has world leading experts in the technologies to generate transgenic animals; these experts are willing to work together.
- There are a limited number of projects currently being performed in Europe; primarily funded through National funding agencies.
- Active European debate with regards to GM animals.
- There is no current networking activity on this topic.
- Recognised the need to evaluate biosafety and risk of technology/strategies.
- Recognised the need to have debate with 'public' in parallel to scientific progress.

International context:

- Only limited research within Americas but increasing

- Activity in Far East unknown.
- Commercial interest in seeing research performed; but caution with regards to actually getting involved in GM animal projects due to public opinion.

Conclusion 1: Europe has the potential, expertise and opportunity to lead in this field.

Conclusion 2: Demonstration projects needed to show feasibility, applicability and to focus societal debate.

2. Identify how to best utilise new GM technology to overcome limitations. There are now a number of GM technologies that could be applied to this topic. Each has benefits and limitations with different approaches to different diseases likely (see future plans). There is considerable effort within Europe to improve and refine GM methodology. In this regard, Europe is Internationally competitive.

There was some very exciting discussions about novel and challenging intervention strategies.

Conclusion 3: European scientists are involved in cutting-edge developments of GM technology.

Conclusion 4: No co-ordination between European labs (although participants indicated willingness to work together).

3. Identify highest priority disease projects to establish European science as leading the field. There was much discussion around this. The following criteria were proposed to assist prioritisation of diseases; known route (mutation) to genetically intervene (and current experimental projects), high impact disease (food safety, zoonotic, industry need), no current treatment/vaccination programme, scientific challenge, ethical considerations. The following diseases are recognised as high priority targets (not in priority order):
- BSE (in cattle) and scrapie (in sheep)
- PRRSV infection in pigs
- flu virus infection in poultry (and pigs)
- Jaagsiekte retroviral infection in sheep
- FMDV in cattle

Conclusion 5: Priority diseases which could be addressed through GM approach identified; generally recognised that this technology has greater likelihood of successfully contributing to disease mitigation when targeted against viral infections.

Conclusion 6: Further debate required to identify 'top' three targets (see future plans).

4. Make the appropriate European community (through the invited participants) aware on the initiative to build a Scottish Network of Excellence "Development of Novel Technologies to Fight Viral Diseases in Farm Animals". The Scottish Higher Education Funding Council has recently supported the establishment of this Network co-directed by Massimo Palmarini (workshop participant) and Bruce

Whitelaw (workshop convenor). This is an example of a National activity in this area and one that could contribute to a European wide Network.

5. Provide input into the International Symposium on Animal Genetics for Animal Health to be held at OIE Headquarters 23rd-25th October, 2007. One participant (Graham Plastow) and both convenors were involved in this Symposium.

Forward plans. There are three objectives. Each relates to the other.

Objective One: Build new bilateral collaborative projects.
- Discussions were initiated between the groups of Whitelaw and Galli (prepresented by Dario Brunetti at workshop).
- Discussions were initiated between the groups of Whitelaw and Wall.
- Discussions were initiated between the groups of Sang and Sarkis.

Objective Two: Actively engage in dialogue with potential European funding agencies to raise profile of this topic and the potential lead role Europe could play. Offer of assistance from Genesis-Faraday (co-sponsor of Workshop), for example, promote project on "Combating endemic viral disease in livestock" through EU FABRE Technology Platform.

Objective Three: Actively pursue funding for a European Network to:
- facilitate communication between scientists involved in host-pathogen interaction and GM technology.
- provide forum for multidisciplinary debate between stakeholder; scientists, ethicists, risk assessors, industry, society and others.
- provide focus on topic (driver for increased projects)

The need for a Network was very strongly supported at the Workshop. Several participants offered their assistance to progress this concept: Bruce Whitelaw, Helen Sang, Heiner Niemann, Imre Kasckovics, Cesare Galli (represented by Dario Brunetti at Workshop), Lluis Montoliu, Chamsy Sarkis. At the workshop this group agreed to discuss the priority disease list to identify the key targets which to basis for such a Network; subsequent discussions have identified the following three diseases: **transmissible spongiform encephalopathy (BSE and scrapie), flu and PRRSV**. This is based on current research activities, public perception, commercial concerns, and the lack of current intervention products. These topics will enable the range of current GM technologies across a number of animal species to be covered. Note: this priority list does not simply reflect disease-status in Europe but is a combination of what GM can address (with current technology and understanding of disease biology) and the criteria indicated above.

It was identified that ESF or COST could possibly support such an initiative.

Additional comment. There was considerable discussion about the value of combining the effort in this topic (infectious disease of animals) with the activity in Europe to develop, evaluate and utilise non-rodent animal models of human disease.

FINAL PROGRAMME

Monday 1 October 2007

12.00-14.00 Arrival and Lunch
14.00-14.20 Welcome by the convenors

14.20 - 15.30 Session One: What models are needed (chaired by Bruce Whitelaw)
What diseases are important - Ivan Morrison (Edinburgh, UK)
What does industry want - Graham Plastow (Edmonton, CA)
What does our conscience want - Kenneth Boyd (Edinburgh, UK)

15.30-16.00 Coffee

16.00-18.00 Session Two: GM technologies (chaired by Helen Sang)
Nuclear transfer - Heiner Niemann (Neustadt, DE)
Lentiviral transgenesis - Bruce Whitelaw (Edinburgh, UK)
Large transgenes - Lluis Montoliu (Madrid, ES)
New transgenic vectors - Chamsy Sarkis (Paris, FR)

Free time for discussion

Dinner and discussion

Tuesday 2 October 2007

9.00-11.00 Session Three: Example Projects (chaired by Bruce Whitelaw)
Mastitis and other US projects - Bob Wall (Beltsville, US)
Combating flu in birds - Helen Sang (Edinburgh, UK)
Prp-null cattle - Dario Brunetti (Cremona, IT)
Transgenic rabbit projects - Zsuzsa Bosze (Gödöllö, HU)
Investigating Jaagsiekte in sheep - Massimo Palmarini (Glasgow, UK)

11.00-11.30 Coffee

11.30-12.30 Session Four: Wash-up (chaired by Bruce Whitelaw and Helen Sang)
Presentation of the ESF by Martin Röllinghoff (Standing Committee for the EMRC)

12.30-14.0 Lunch and Departure

During the afternoon of the 2nd October there was an impromptu meeting of some of the participants to further discussion on disease priorities.

STATISTICAL INFORMATION ON PARTICANTS

I present details on the participants under the following headings:

- total numbers and geographical distribution
- role at workshop
- research discipline

Participation at the Workshop was by invitation only.

Number and geographical distibution

- There were 17 participants.
- The participants came from Europe (15) and North America (2).
- European distribution: UK (7), Germany (2), France (2), Hungary (2), Spain (1); Italy (1) - number of UK participants (included representative from Genesis-Faraday, co-sponsor of Workshop) agreed with Valerie Allspach-Kiechel in advance of workshop.
- One participant came from Canada.
- One participant came from the USA (not funded by ESF; attendance at workshop was financially supported by Genesis-Faraday Partnership).

Role at workshop

- 12 speakers
- 4 invited participants
- 1 ESF representative

Research discipline

- Research scientists (12) specialising in:
  - transgenesis (7)
  - molecular genetics (2)
  - infectious disease (1)
  - virology/vectorology (1)
  - immunologist (1)
- Veterinarians (2)
- Animal breeding industry (1)
- ESF representative (1)
- Ethicist (1)
- Across these participants expertise in a range of animal species was provided:
  - cattle, pigs, sheep, poultry, rabbits, companion animals (and mouse)

Age profile:	<35	3
	35-50	7
	>50	7

Addition information:

- 1 was a PhD student.
- 2 were female.

FINAL LIST OF PARTICIPANTS

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