# Research on Agricultural Animals Jeopardized at Land Grant Institutions: Key Obstacles and Solutions

**Abstract:** Despite the enormous economic value of U.S. animal agriculture (>$110 billion), only 0.034% of USDA's $106 billion ($36.5 *million* in 2004) annual budget is allocated to the National Research Initiative (NRI) for extramural competitive research grants involving agricultural animals (cattle, hogs, sheep, goats, poultry, horses, and aquatic species). The U.S. Department of Health and Human Services allocates 4.1% of its $548 billion ($22.4 *billion* in fiscal year 2004) to NIH for extramural competitive grants programs. However, despite the likelihood that high priority human health research areas could be enhanced by use of agricultural species as biomedical models, rodents are the predominant biomedical animal model. These limitations jeopardize the future competitiveness of U.S. animal agriculture, and the use of agricultural animals as novel comparative biomedical models to resolve high priority human health issues.

Because the USDA extramural competitive grants program is insufficient to fully support research directly related to production, health and well-being of farm animals, many talented animal scientists must seek biomedical related sources of funding to maintain their research programs. Consequently, unless the traditional research focus of animal science departments is expanded to include biomedicine, bright young scientists may not be attracted to animal agriculture, and research involving agricultural animals is likely to become a minor part of life sciences in colleges and universities throughout the U.S. As a result of these concerns, USDA, NICHD/NIGMS, Texas A&M University and Michigan State University organized a workshop that identified the following as key obstacles impeding use of agricultural animals as biomedical models: lack of broad advocacy, long-standing cultural barriers at land grant institutions, poor grantsmanship by animal scientists and "genus inequity" (rodents favored over agricultural animals) at NIH, and scarcity of key reagents and resources. Solution to these problems included: development of a vigorous proactive education program to explain how research on agricultural animals benefits both animal agriculture and human health; development of a new "mindset" within land grant institutions that fosters greater cooperation among basic and applied researchers in a variety of departments; development of intensive training opportunities and incentives for animal scientists to write NIH grants and justify animal models; greater interagency (NIH, USDA) cooperation to advocate use of agricultural animals as novel alternative comparative animal models in high priority areas of biomedical and agricultural research; revision of the NIH peer review system to remove inappropriate "genus inequity" problems; improved networking among scientists that use agricultural species as comparative animal models; and organization of the research priorities, strategic plans, and financial support necessary to develop the critical resources for research with agricultural animal species.

The immediate challenge is to form a task force willing to implement the changes necessary to increase use of agricultural species as comparative animal models for biomedical research.

**Introduction:** Abundant safe, high quality, nutritious and affordable meat, milk and eggs, which are important components of nearly every human being's diet, are vital to U.S. consumers, to agriculture, and thus to USDA's mission. Consequently, a strong innovative research and development program dedicated to U.S. animal agriculture is clearly necessary to ensure food safety and to improve the quality and affordability of meat and milk, especially in an increasingly competitive global marketplace. However, despite the enormous economic value of animal agriculture to the U.S. (>$110 billion, [1]), and the presence of many well-trained animal scientists at the 94 land grant institutions in the U.S. [2], only about 0.034% of USDA's $106 billion ($36.5 *million* in fiscal year 2004) annual budget is allocated to the National Research Initiative (NRI) for extramural competitive grants for basic and applied research that directly involves agriculturally important animals (cattle, hogs, sheep, goats, poultry, horses, and aquatic species). On the other hand, the U.S. Department of Health and Human Services, which is the principal federal agency that protects human health and provides health services, allocates 4.1% of its $548 billion ($22.4 *billion* in fiscal year 2004) to NIH for extramural competitive grants programs. However, despite the likelihood that numerous high priority human health research areas (*e.g.*, cancer, obesity, aging, cardiovascular disorders, infectious diseases, diabetes, fetal development and infertility) could be enhanced by the appropriate use of agricultural species as biomedical models, at present, rodents are the predominant comparative animal model used for biomedical studies. Taken together, these limitations jeopardize not only the future competitiveness of U.S. animal agriculture, but also the potential use of agricultural species as novel comparative biomedical animal models to resolve high priority human health issues. Consequently, a task force of policy makers, officials and administrators at land grant institutions and federal funding agencies, scientists, and the public must be formed to work cooperatively and vigorously towards a resolution of these complex problems.

In large part because the USDA extramural competitive grants program is woefully insufficient to fully support research directly related to production, health and well-being of farm animals, many talented animal scientists must seek biomedical related sources of funding to maintain their research programs. Consequently, unless the traditional research focus of animal science departments is expanded to include biomedicine, bright young scientists may not be attracted to animal agriculture, and research involving agricultural animals is likely to become a minor part of life sciences in colleges and universities throughout the U.S. As a result of these concerns, USDA, NICHD/NIGMS, Texas A&M University and Michigan State University organized a workshop (October 29-31, 2004, *Advantages of Agriculturally Important Domestic Species as Biomedical Models* [3]), with the following objectives:

- To provide a forum to exchange ideas among scientists that use agricultural animals as biomedical models with officials from NIH and USDA, and university administrators at land grant institutions.

- To emphasize the scientific importance of agricultural animals as biomedical models and acknowledge the numerous ways they are contributing to our current understanding of human and animal health and well-being, and animal agriculture.
- To identify high priority research areas that could be enhanced by use of agricultural animals as biomedical models (Table 1).
- To explore the potential need and justification for an interagency program that would be co-funded by one or more institutes within the NIH and by USDA-CSREES and perhaps others (industry, state governments) to support high priority research that could be advanced by use of agricultural animals as comparative biomedical models.

The workshop was attended by 114 invitees with broad experiences relevant to reliable assessment of the general "status" of research involving agricultural animals. These experiences included principal investigators of USDA- and NIH-funded research programs that use agricultural animals, members of the National Academy of Sciences, directors of university centers of excellence, career scientists with extensive service on USDA and NIH panels, editors of scientific journals, university administrators, USDA and NIH administrators, USDA science advisors, current and past presidents of national scientific societies, and invited graduate students and postdoctoral trainees. This group, though quite varied in its perspectives, was able to bring a mixture of balance, insight, and on-the-job experience to what is an issue of great concern.

During the workshop, 13 lectures were presented by internationally recognized scientists representing a diversity of research areas (reproduction and development, nutrition, health and disease, and genomics and advanced technologies). Also, a series of intensive discussions were held to address a variety of questions relevant to enhanced use of agricultural animals as biomedical models.

The highlight of the workshop was identification of a number of key obstacles impeding use of agricultural animals as biomedical models within four major interrelated areas (advocacy, land grant institutions, NIH and resources) and potential solutions to these obstacles.

## I. The Advocacy Obstacle:

A lack of advocacy is the prime impediment to the use of agricultural animals for biomedical research. Simply put, scientists unfamiliar with agricultural species as animal models, university administrators, officials at USDA and NIH, politicians, and the public at large do not appreciate the advantages of agricultural animals as comparative animal models for biomedical research. They are also unaware of the past impact such research has had on societal well being and human health and are generally scornful of the high quality of basic science being done in animal science departments (The "Moo U" factor!). This knowledge void creates prejudice and major institutional and funding barriers throughout academia.

**Solution:** A vigorous, broad, and proactive advocacy/education program, administered jointly by land grant institutions (*e.g.*, Academic Programs Committee on

Organization and Policy, ACOP, and National Association of State Universities and Land Grant Colleges, NASULGC [4]; and Experiment Station Committee on Organization and Policy, ESCOP [5]), federal funding agencies and appropriate animal industries, will be necessary to explain the potential impact and past contributions of research on agricultural animals and their value as comparative animal models for research that benefits animal agriculture and human health. The advocacy/education program could take many forms, including symposia at universities, funding agencies and scientific and public meetings, and development of an informative web site.

## II. Land Grant Barriers:

The long-standing "cultural" idiosyncrasy that biomedical research is "inappropriate" to the land grant mission is an unfortunate attitude permeating the culture of traditional agriculture and of many of its administrators and influential faculty members. This cultural barrier in part explains why agricultural colleges have historically been segregated from colleges of human and veterinary medicine and the basic life sciences disciplines. This science-segregation policy at land grant institutions diminishes communication, sharing of resources, and collaboration among scientists who could benefit from much closer association with their colleagues. At many institutions, the isolation of animal science programs, in particular, has contributed to lack of recruitment of top notch researchers into the area and a failure to tap into the funding available for biomedical research on agriculturally important animal species. There is often little incentive, and frequently disincentives for animal scientists to collaborate with biomedical scientists, engineers and others who could bring an interdisciplinary perspective and novel insights into traditional animal science thinking. The Land Grant Schools, hidebound by their traditional concepts of what sort of research should be supported, have also failed to provide mechanisms to encourage scientists to think "outside the box".

**Solutions:** Enhanced use of agricultural animal species for biomedical research depends especially on development of a new "mindset" within land grant institutions that fosters greater cooperation among basic and applied researchers within and among a variety of departments including medical and basic science faculty and industry. Administrators are aware that the "protected island fortress" of agriculture is becoming an anachronism and no longer viable as state and federal support declines. Indeed, traditional agricultural research cannot thrive in isolation. Consequently, administrators must not back away from defending needed changes in farm animal research in animal science departments, especially when dealing with their traditional stakeholders. It is highly recommended that leaders of land grant institutions seek guidance from two or three successful institutions with existing strong cooperation between Colleges of Agriculture and the rest of the campus (*e.g.*, University of Illinois, University of Missouri). Suggested ways to strengthen cooperation between animal science departments, medical schools, and basic science departments include the following:

- Creating a list of the high priority research areas at NIH that currently use or could benefit by use of agricultural animals as biomedical models (Table 1) and using

these high priority research areas as a "blueprint" for future faculty hires and incentive plans to foster interdisciplinary/multidisciplinary research.

- Hiring of new administrators with leadership skills and vision to: **i**) resolve philosophical differences between animal science departments, basic science departments and medical schools, and **ii**) enhance cross-departmental research programs.
- Hiring of faculty and chairs who are not simply trained in traditional animal sciences, but who also have experience or at least the appreciation of newer and emerging technologies and the broad scope of animal sciences for society as a whole. Such leaders should be prepared not only to serve traditional agricultural stakeholders, but also to interact with the broader life science community. Such leaders should be encouraged to continue to be active in research rather than becoming full time administrators.
- Hiring new faculty with joint appointments in medical schools and basic science departments and/or interfacing existing animal scientists with cutting-edge research programs in medical schools, veterinary schools and basic science departments.
- Creating incentives for collaborations between animal, basic and clinical research scientists by:

**i.** Providing leverage and seed funds for interdisciplinary research.

**ii.** Facilitating and promoting sharing of facilities and resources.

**iii.** Encouraging animal science faculty to collaborate with non-agriculture colleagues to submit NIH grants and to increase publications in high-impact biomedical and basic science journals.

**iv.** Creating centers of excellence committed to use of agricultural animal species as comparative animal models. One long-term approach to generate the funds necessary to stimulate interdisciplinary research is to reduce the duplication of research, extension and teaching efforts in agriculture at land grant institutions. The cost savings from formation of "regional clusters" of land grant universities to conduct extension, education and research, coupled with USDA formula funds, could be used to sponsor creative research by new or existing productive faculty interested in generating preliminary data important for both agriculture *and* biomedicine.

## III. Grantsmanship and "Genus Inequity":

Grantsmanship by animal and veterinary scientists is probably not strong when compared with biomedical and basic scientists because pressures to write NIH grants are less at many land grant institutions compared with their biomedical and basic science counterparts. Nevertheless, scientists with successful track records of NIH funding and with experience on NIH review panels indicate that "genus inequity" (rodents favored over agricultural animals as biomedical models) clearly exists in NIH review panels for a variety of reasons:

• Grant applications that use agricultural species as comparative animal models require extensive justification and additional preliminary data compared with applications using rodent models.

• Lack of appropriate expertise on review panels (*e.g*., some panels are composed primarily of members experienced with rodent or primate models or only have experience with transgenic mice or cell lines.).

• Limited knowledge of resources available to scientists that use agricultural animal species as models.

• The quality of publications describing research in agricultural animals, which is the foremost criteria used to assess the "track record" of principal investigators, may be perceived as inferior because the preponderance of livestock publications are in commodity-related rather than biomedical journals.

**Solutions:** Better tactics are necessary to overcome the obstacles impeding use of agricultural species as comparative animal models:

• Universities must create intensive training opportunities for animal scientists to write NIH grants and justify animal models (Table 2), and provide the "motivation" for participation.

• Proactive forms of advocacy should be implemented to enhance awareness of the broader scientific community, NIH officials and policy makers of the potential uses and benefits of agricultural animals as biomedical models. To accomplish this objective most effectively, greater interagency (NIH, USDA) dialog and cooperation must be established not only to advocate use of agricultural animal models in an effective manner, perhaps by sponsoring symposia or workshops with awardees from both agencies at biomedical meetings, but also to develop requests for applications (RFAs), training grants, leverage grants and seed grants for use of agricultural species as novel alternative comparative animal models in high priority areas of biomedical and agricultural research.

• Working with the NIH Center for Scientific Review, a key revision of the NIH peer review is necessary to address real and perceived "genus inequity" problems by explaining in application kits the major sources of concern for agricultural animals as biomedical models that should be addressed in applications, by ensuring that Scientific Review Administrators (SRAs) and reviewers have appropriate expertise and appreciation for agricultural animals as biomedical models, and by ensuring that the SRAs prohibit "inappropriate" criticisms of agricultural species as animal models during written and oral reviews of research applications.

• NIH could improve networking among scientists that use agricultural species as comparative animal models by advertising to land grant universities the successful NIH grants using agricultural animals as biomedical models. Better networking would lead to better utilization of expensive resources and provide additional opportunities for motivated animal scientists to generate preliminary data.

**IV. Research tools are limited:**

Resources to conduct creative research for some agricultural animals are limited compared with rodents. Challenges faced by animal scientists include: 1) lack of available species-specific tools and reagents, including antisera and antibodies; 2) small or poorly managed collections of cell lines, germplasm, and databases for computational biology and bioinformatics; 3) inadequate genetic resources such as defined inbred lines with characterized genetics; and 4) lack of required genetic tools, such as genomic sequences for pigs, sheep, turkeys, horses and aquatic species, inexpensive microarrays for a range of agricultural animal species, and clone sets and primer sets for major genes.

**Solutions:** To resolve these problems, universities, federal funding agencies, and industry must work cooperatively to develop strategic plans, set priorities for research, and generate the financial support necessary to fund development of critical resources for research with agricultural animal species.

## V. Action Plan and the Future:

The immediate key challenge is to form a task force willing to communicate, cooperate and work unselfishly to develop and implement an action plan to enhance use of agricultural animal species as biomedical models. The action plan will have short- (Table 3), intermediate- (Table 4), and long-term (Table 5) goals to begin to resolve obstacles and implement solutions to increase use of agricultural species as comparative animal models for biomedical research.

The spirit of this initiative can be summarized in part through recognition that agriculturally important animals have a rich history as models for the study of human medicine. This is especially true in the fields of biochemistry, enzymology, and endocrinology where many proteins were first isolated and purified from various agricultural animal species. Agriculturally important animals have been and are experimental models of choice in reproductive physiology where the basic techniques of artificial insemination, superovulation, oocyte culture, *in vitro* fertilization and embryo transfer were developed and where fundamental sciences are being extended to cloning and stem cell research.

Cattle, for example, have long been studied for complex traits influenced by multiple genes as well as environmental factors. These so called “quantitative traits” are now targeted by the human health research community. Cardiovascular health, obesity, and several cancers are examples of complex traits segregating in breeding populations of cattle. The understanding of what makes cattle breeds different with respect to reproduction, lactation, growth, bone structure, fat deposition, altitude and heat tolerance, and resistance to specific pathogens will be invaluable in elucidating related physiological processes important to human health.

Genomic variation is clearly a major factor in host resistance to pathogens in humans and animals. Identification of specific genome sequences that predispose

susceptibility/resistance to disease will be fundamental to advancing animal health within the livestock industry, to averting accidental or terrorist-initiated epidemics, and to developing models of human gene/pathogen interaction. Genomic variation also underlies traits such as growth, body composition, lactation, and reproductive health. The working draft of genome sequences of agriculturally important animals will, therefore, provide an invaluable resource for discovery of genes and their functions to benefit human health, animal health and production animal agriculture. The present long-term challenge is to chart a course for funding for both rodent and agriculturally important animal models that will ensure that we continue to provide citizens of the world with the basic need for a safe and abundant supply of food, excellent healthcare, and a high quality of life.

**Table 1. Research areas (not prioritized) that potentially could be advanced by use of agricultural animals as biomedical models.**

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| Epigenetics and environment: effect of photoperiod, global warming, seasonality, and elevation on modification of gene function |
| Reproduction: gametogenesis, gonadal function, infertility |
| Aging: skeletal diseases, especially chicken and pig models; bone metabolism and osteoarthritis, especially the horse model; reproduction, especially beef cattle and mares |
| Obesity: genetic, dietary, hormonal influences on pre- and post-natal adipose tissue development using pig model |
| Pregnancy: placental growth, angiogenesis, congenital and birth defects, developmental biology especially chickens, fetal programming especially sheep to study stress, malnutrition, effects of exposure of fetuses to androgens and environmental toxins on adults, molecular/cellular basis of parturition and premature birth |
| Diabetes Types I and II |
| Therapeutics: xenotransplantation, gene therapy, stem cells, "Farmaceuticals"; |
| Toxicology, environmental endocrine disrupters |
| Neurobiology: behavior, stress, learning, pheromonal communication, neuroendocrinology |
| Immunology: autoimmune disease, inflammation, innate and mucosal |
| Cardiovascular disorders such as diet-induced artherosclerosis and lethal cardia tachyarrhythmias (ventricular fibrillation) using minature or normal pigs |
| Nutrition: energetic balance including homeostatic mechanism, regulation of metabolism, use of neonatal piglet as pediatric model for studies of nutrition, metabolism and gastroenterology |
| Ophthalmology: retinal degeneration, retinitis pigmentosa, macular degeneration |
| Comparative physiology (*e.g*., Understanding of what makes cattle breeds different with respect to reproduction, lactation, growth, bone structure, fat deposition, altitude and heat tolerance, and resistance to specific pathogens will be invaluable in elucidating related physiological processes important to human health.) |
| Radiation biology |
| Biomechanics |
| Renal biology |
| Diseases: Transmissible Spongiform Encephalopathies (TSE); Respiratory Syncytial Virus (RSV); Crohn's Disease; sexually transmitted diseases (STD); enteric including Transmissible Gastroenteritis (TGE); viral, *E. coli* 01578; cancer including prostate, breast, ovary (chicken), hematopoiesis, leukemia; cattle as a model for salmonellosis, tuberculosis and cryptosporidiosis; pathogen transmission of emerging diseases that infect animals and humans such as use of cattle to study tick-borne infections |
| Disorders: liver, epilepsy, and sleep such as narcolepsy |
| Microbial ecology |

**Table 2. Attributes of successful NIH grants.**

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| ♣ Simple questions with appropriate background were posed |
| ♣ Substantial and compelling preliminary data were included |
| ♣ Current gaps in knowledge were addressed |
| ♣ Unique comparative value of the chosen model was explained (*cannot recapitulate observations in rodents*) |
| ♣ How the model led an area of research and was used to answer the questions posed were explained carefully |
| ♣ A broad range of disciplines and expertise was employed to resolve problems |
| ♣ Potential bias of reviewers was addressed |
| ♣ Senior investigators had a significant track record of success including publications in high quality journals |
| ♣ Applications were critiqued by experienced investigators *prior* to submission and the advice of the panel manager, SRAs, and reviewers was heeded |

**Table 3. Short-term goals.**

- Engage "top" university administrators at land grant institutions to provide incentives for faculty to compete for extramural grants at agencies other than USDA and to assist motivated scientists in preparation of such applications for review.
- Advertise attributes of successful grant applications to NIH to motivated faculty (see Table 2).
- Meet and seek advice from Director of Center for Scientific Review on NIH obstacles.
- Identify advocates at NIH, USDA and other agencies to assist scientists in the implementation of strategies to enhance use of agricultural animals in biomedical research.
- Hold workshops at NIH to inform SRAs and appropriate administrators of advantages of agricultural animals as biomedical models.
- Form committees to engage organizers of scientific meetings to promote/showcase agricultural animals, primate and rodent models addressing high priority human health problems (*e.g*., To promote agricultural species as important comparative animal models, a central fund from all land grant institutions could be created and used to partially sponsor the aforementioned special animal models' symposia at national meetings.).

**Table 4. Intermediate-term goals.**

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| • Set up "brainstorming" sessions between USDA and NIH to improve interagency cooperation. |
| • Improve awareness of scientists using rodents as models of the importance of agricultural animal species as models for biomedical research by publicizing models to other research groups (*e.g.*, hold joint meetings with scientists using agricultural animal and rodent models). |
| • Organize follow-up meetings involving scientific administrative staff at the NIH National Center for Research Resources and various other institutions at NIH, other federal funding agencies, and USDA. |
| • Seek joint NIH-USDA support for symposia to identify novel uses of agricultural animals in biomedical research. |
| • Establish NIH-USDA databases for central sharing of resources. |
| • Institutions must strongly encourage faculty to apply for more NIH grants. |
| • Scientists need to publicize/promote better animal models to colleagues in agriculture and biomedicine. |
| • Develop advocates in agriculture and biomedical communities: include and inform commodity groups, animal industry, and pharmaceutical and biotechnology industries. |
| • Joint NIH-USDA training grant program to integrate biomedical and animal sciences. |
| • Organize meeting with USDA, NCRR and NHGRI to develop the strategic plans and research priorities necessary to develop key reagents and "tools" to advance research with agricultural animals as biomedical models. |

**Table 5. Long-term goals.**

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| • Organize inter-agency program for new alternative models to rodents for high priority areas of biomedical research. |
| • Ensure the "agricultural perspective" is maintained at land grant institutions. Either USDA officials must be engaged/convinced to increase dramatically the USDA budget allocation for competitive grants in animal research and/or political support must be garnered to create a new funding agency (*e.g.*, National Institute of Agriculture and Food Science [6]). |
| • Develop alternative high margin markets for animal products to re-invigorate industry support for animal research. |
| • Develop interagency support for training, sabbaticals and career development for scientists to use agriculturally important animal species as models for high priority problems in agriculture and biomedicine. |

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