

1st INTERNATIONAL CONGRESS ON THE FUTURE OF ANIMAL RESEARCH; SUMMARY REPORT

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INTRODUCTION

The 1st International Congress on the Future of Animal Research (1st ICFAR) was convened at the Instituto Militar de Engenharia (IME) in Rio de Janeiro during October 21-24, 2003. The objective was to bring together laboratory animal scientists and veterinarians from around the world to discuss current trends in animal research, to develop a collective vision of future opportunities, to foster the international harmonization of standards in the care and use of laboratory animals, and to establish international collaborative opportunities for established scientists as well as students and postdoctoral fellows. One hundred and fifty-seven registrants from ten countries participated in the meeting, which featured invited talks and contributed talks and posters, as well as lively discussion sessions. The participants explored future directions in research with laboratory animals and alternatives, and in the humane care and use of laboratory animals. The scientific sessions included Human Disease Models, Gene Mapping and Cloning, Genetics and Epigenetics, Transgenics and Knockouts, Alternatives, Animal Welfare, and Education.

The rich diversity of topics and of the backgrounds and expertises of the participants elicited many contrasts in the content of the presentations, in the perspectives presented, and in the roundtable discussions that followed each session.

OPENING ADDRESS

The theme of contrasts was established during the Opening Address, which was entitled **Famous Animal Experiments: A Historical Perspective**. Dr. William Stone presented a fascinating account of some highlights in the history of animal research, beginning in the early 1600s with Dr. William Harvey's description for the first time of the circulation of blood in animals. One of the contrasts that the Opening Address made obvious throughout the meeting was the naïveté of early researchers and the experiments they conducted by comparison with modern science. For example, cutting off the tails of 20 generations of rats to determine if the inheritance of tail length would be affected seems to have been unnecessary even in the 1880s, since the tails of lambs had been docked for centuries without leading to the inheritance of taillessness. The elegant experiments of recent years have enabled the growth of knowledge and the sophistication of experimental inquiry at an exponential rate. The lectures and posters presented at this meeting were testimony to the elegance of modern science. However, because of the exponentially increasing rate of progress, we should expect our own perspectives and experimental strategies to be considered naïve in the not so distant future.

Another contrast that was evident from the Opening Address and throughout the meeting was the contrast in the animal species used historically and currently to advance our understanding of biological characteristics and the mechanisms by which they are controlled. Although the concept of the mouse as “king” of the species used in animal research surfaced at the meeting on several occasions, it was apparent that the collage of animal species used historically and currently is essential for modeling the human condition in its entirety. Thus, the famous experiments cited by Dr. Stone involved the use of mice, rats, guinea pigs, dogs, cattle, sheep, chickens, monkeys, and opossums. Many other species have played and continue to play critical roles in animal research, but the time allotted for the lecture allowed only a sampling of representative species.

Another theme of the Opening Address was the great extent to which research with animals has changed the course of human history, as well as the lives of all individuals who have access to modern medical care. Whereas the concept of research results from the bench providing treatments at the bedside has great popularity, Dr. Stone aptly modified the phrase “from bench to bedside” to “from bench to animals to bedside.”

HUMAN DISEASE MODELS

That concept appropriately led into the first session, Human Disease Models. Dr. Gerhard Hunsmann from the German Primate Centre presented an overview of **Biomedical Research in the EU Employing Nonhuman Primates**. Of the less than 10,000 nonhuman primates used in experiments annually in the EU, more than 50% are used in toxicology and other safety related tests, and the remainder are used in research development, quality control, and biological studies of a fundamental nature. Most breeding is done in the United Kingdom, Germany, and the Netherlands; however two-thirds of the 3,750 new primates acquired each year are imported, primarily from China. Dr. Hunsmann emphasized that this level of dependence on imported monkeys is dangerous, particularly since the U.S. and Japan import manyfold that number of monkeys. Furthermore, in addition to the potential threats of shortages of animals available for import and of airlines ceasing to carry monkeys, the quality of the imported animals is a serious problem. It was concluded during the discussion that followed this presentation that efforts to establish new breeding colonies in the EU, the U.S., and Japan, and to expand existing breeding colonies, will be essential to protect against severe setbacks to progress in biomedical research and testing.

The next presentation, ***Trypanosoma cruzi* Infection in Rhesus Monkeys**, provided an example of the impediment to research caused by the worldwide shortage of captive rhesus macaques. Dr. Maria Glória Bonecini de Almeida of the Oswaldo Cruz Foundation in Rio de Janeiro presented fascinating observations of progression of Chagas’ disease in Indian-origin rhesus monkeys that were experimentally infected with *Trypanosoma cruzi* years ago. The characteristics of disease progression were remarkably similar to humans, of which an estimated 16 million Latin Americans are infected with *T. cruzi*. The pathogenesis of Chagas’ disease is quite different in rodents, emphasizing the need for a collage of animals to model the human condition. However, despite the detailed documentation of Indian-origin rhesus as a model that has all of the characteristics of human Chagas’ disease, the worldwide shortage of Indian-origin rhesus available for biomedical research precludes the expansion of this work with that model.

Therefore, plans have been made to establish the baboon, which is readily available, as a model for experimentally induced Chagas' disease. However, the change from one model species to another for a disease that takes many years to progress through its natural history will be a costly endeavor. The need to augment captive breeding of Indian-origin rhesus is emphasized by this example, as is the need to augment production of other primate species to ensure an adequate supply to meet the new demands of investigators who switch from rhesus to other species.

The following presentation, on **The Mouse as a Model Organism - Inducing New Mutations**, was one of several contributed papers presented by young scientists and students. Sylvia Maria Gomes Massironi from the University of São Paulo, Brazil, presented her group's strategy for inducing new mutations in mice using ethyl nitrosourea (ENU) in order to bridge the gulf between available mouse mutant resources and the full range of phenotypes that are essential to fully exploit the mouse as a model organism. To date, thirteen new mutations have been discovered in their program; these mutations affect skin, behavior, balance, and the muscular system, and one causes anemia. Genome wide scans are being conducted in order to localize the mutant genes. Some of the mutant genes can be expected to increase the breadth of mouse mutant resource, as loci not previously recognized as contributing to the respective phenotypes; and others can be expected to increase the depth of the resource, as new mutations at known mutant loci.

GENE MAPPING AND CLONING

The discussion of the previous paper led naturally into the session on gene mapping and cloning. The first presentation, **Mapping High Blood Pressure Genes in the Spontaneous Hypertensive Rat (SAHR)**, was made by José Krieger of the University of São Paulo Heart Institute. He presented an elegant gene mapping strategy that involved a combination of a 13,000 clone rat cDNA microarray, bioinformatics tools and databases, and comparative genomics tools and databases to identify candidate genes that regulate blood pressure. How far we have come technologically since the famous animal experiments in history! But, as Dr. Krieger, pointed out, the big challenge today is not to identify positional candidate genes, but to validate that a candidate gene is truly the one responsible for the phenotype.

Ana Lucia Brunialti Godard from the Federal University of Minas Gerais then presented the second of the contributed papers, **Genetic Mapping of the Mouse Mutation *Careca* (*ca*) Induced by ENU**. This presentation was a sequel to the earlier presentation on ENU mutagenesis, and provided details on one of the thirteen new mutations discovered by their group. This autosomal recessive mutation causes thin hair around the eyes, limbs, and belly. The responsible locus was mapped to distal end of mouse chromosome 7, in a region homologous to human 10q25-26, 11p15.5, and 11q13.3.

The final paper in this session, **Bovine Somatic Cell Cloning in Brazil**, was presented by Walt Yamazaki of the State University of São Paulo. While animal cloning has had a high profile in the scientific literature and the popular press since the cloning of Dolly the sheep in 1997, Dr. Yamazaki pointed out the often overlooked problems with cloning: problems that occur in the embryos (e.g., morphology, chromosome anomalies, and cellular number), in the fetuses, and neonatally (e.g., mortality, oversized offspring, obesity, other phenotypic

abnormalities). Just as we recognize the shortcomings of technology in historical experiments with animals, so also will the problems with cloning be considered as historical curiosities; the research of today will solve these problems and technology will deliver on its great promise for genetic improvement of livestock species, preservation of endangered species, creation of novel animal models in sufficient numbers of individuals for experimental manipulations, and even therapeutic cloning for treating human diseases.

GENETICS AND EPIGENETICS

This session was included in the program to emphasize the contrast between the genetic determination of an individual's phenotypic characteristics and epigenetic determination. Jean-Louis Guénet of the Pasteur Institute gave a fascinating overview of **Investigating the Function of Genes by Genome Manipulation**. He began his lecture with some critical facts, including among others the following: the mammalian genome written in 12-point font would reach from Paris to Recife, 99% of mouse genes have a homologue in the human genome, and 96% of mouse orthologs lie within a conserved syntenic interval in the human genome. However, despite all that we know about the mammalian genome, we do not know the function of 80% of human genes. The mouse will play a critical role in determining the functions of those genes both through the "top down approach" and the "bottom up approach". The top down approach begins with a specific gene and involves investigating that gene by techniques such as introducing genes by transgenic methodologies, replacing genes by homologous recombination, and inducing mutations by knockout technologies. The bottom up approach begins with a genetically controlled phenotypic variable and involves identifying the responsible gene(s) by detecting quantitative trait loci (QTLs) and identifying them by such methods as QTL mapping by genome scans and positional cloning. Although positional cloning is extremely tedious, it is nevertheless critical for identifying new genes, and advances in technology will make it a more efficient and even more widely utilized technology in the future.

Dr. Guénet's presentation on genetics was followed by two equally elegant presentations on epigenetics, by Maria de Fátima L. Santos and Miguel Constância of the Babraham Institute, Cambridge, U.K. Epigenetics is the study of mitotically and meiotically inherited changes in gene function that can not be explained by changes in DNA sequence. Epigenetic modifications are typically caused by changes in DNA methylation or in the protein constituents of chromatin. Dr. Santos, in her lecture entitled **DNA and Histone H3 Lysine 9 Hypermethylation in Bovine Preimplantation Embryos Following Somatic Nuclear Transfer**, presented compelling evidence of genome-wide hypermethylation patterns in most cloned bovine preimplantation embryos, and particularly in the trophectoderm, which gives rise to the placenta. These methylation abnormalities may be a major barrier to improving the efficiency of somatic nucleus transfer; a first step toward improving the efficiency might be to assess methylation patterns of embryos prior to implantation in order to select those that appear to be most nearly normal.

Dr. Constância presented a contributed talk detailing the results of investigations on **Regulation of Supply and Demand for Maternal Nutrients in Mammals by Imprinted Genes**. His model system is based on the fact that epigenetic modifications that occur during gametogenesis and cause paternal genes to be expressed in the embryo enhance fetal growth, whereas expression of maternal genes suppresses fetal growth. The demand for nutrients is

controlled by growth of the fetus, whereas supply is controlled by the placenta. Dr. Constância and his colleagues have created a mouse model for intrauterine growth restriction by knocking out placental specific *Igf2* (insulin-like growth factor 2); surprisingly, fetal growth restriction was apparent only in late gestation even though the nutrient supply to the fetus was reduced much earlier. The knock-out strategy clearly has great potential for understanding the balance between paternally and maternally expressed genes in the placenta, as well as in the fetus, and the relationships between fetal and placental genes in controlling fetal growth.

TRANSGENICS AND KNOCKOUTS

The application of the knock-out strategy to assessing supply and demand of maternal nutrients to the fetus led naturally to two sessions on Transgenics and Knockouts.

Chella David from the Mayo Clinical and Medical School spoke about **HLA Transgenic Mice as Models for Human Diseases**. He has developed a series of transgenic mice stocks in which human HLA class II molecules are the only molecules involved in antigen presentation to the mouse CD4 T cells. These mice are ideal humanized models to study autoimmune diseases. To date, it has been shown that HLA-DQ8 transgenic mice are highly susceptible to collagen induced arthritis, HLA-DR4 transgenic mice are mildly susceptible to the same disease, HLA-DQ8/DR3 double transgenics can be induced to exhibit a progressive severe disease similar to multiple sclerosis, and HLA-DQ8/B7-1 double transgenics are susceptible to spontaneous diabetes. Humanized mouse models such as these will have a major impact on the future of animal research.

Lygia Pereira from the University of São Paulo presented an impressive overview of her laboratory's progress in establishing the methodology of generating knockout mice by gene targeting in embryonic stem (ES) cells. Her lecture was entitled **Generation of Mouse Models for Human Genetic Diseases: Establishment of Research Tools in Brazil**. Four new lines of ES cells have been established in her laboratory; and two lines of *Fbn-1* (fibrillin-1) knockout mice, models for Marfan syndrome, have been developed and are under investigation. Plans for the future include establishing ES cell lines from agriculturally important species for biotechnological applications and, after Brazilian legislation is finalized, the establishment of human ES cell lines for use in cell-transplant based therapy.

Dr. Pereira's presentation was followed by contributed papers by Enrique Santos and Christian Merkel, both of whom are members of her laboratory. They elaborated on the technical details pertinent to the creation of the *Fbn-1* knockout mice and on the characterization of these mice as models for Marfan syndrome. The titles of their respective presentations were **Development of Animal Model for Marfan Syndrome through Genetic Manipulations of Mouse Genome** and **Analysis of a Knockout Mouse for Fibrillin 1 and Its Implications to Marfan Syndrome**.

Heloisa Baptista from the Federal University of São Paulo spoke about **Transgenic Animals: Principles, Techniques, and Applications**. Her presentation was a comprehensive overview of all major technologies used to generate transgenic models, including, gene overexpression, gene modification, gene inactivation, and conditional transgeneses.

The final paper in this session, **Developmental Defects in *Msx 1* Null Mice**, was presented by Eliana Abdelhay of the Federal University of Rio de Janeiro. *Msx 1* is a homeobox-containing gene which exhibits a complex spatial-temporal expression pattern during mammalian embryogenesis. This gene is believed to be particularly important for craniofacial development because *Msx 1* homozygous knockout mice exhibit severe craniofacial abnormalities. Double knockouts of *Msx 1* and *Msx 2*, a related homeobox-containing gene, develop no bones in the head and are not viable.

ALTERNATIVES

The session on Alternatives began with a lecture by William Stokes of the National Institute of Environmental Health Sciences, NIH on ***In Vitro* and *In Vivo* Alternatives in Safety Testing**. He pointed out the magnitude of the need for improved and more efficient methods for toxicity testing. There are 80,000 chemicals in commerce and 2,000 new chemicals introduced each year; for each one we need to know if it is a hazard in a single exposure or in repeated exposures. Alternative methods are needed to improve public health and safety, to improve efficacy, to meet legal and statutory responsibilities, and to address animal welfare concerns. Dr. Stokes proposed that future work will lead to more refinement in the use of alternatives (earlier, humane endpoints with less pain and distress); reduced use of animals (through deriving more information for one animal, using genetically engineered animal models that are more relevant, developing better *in silico/in vitro* predictive capability, and reducing group sizes by better controlling genetic and environmental factors); and replacement (partial replacement in the near term, in part, by the use of tiered testing strategies).

Octavio Presgrave from the Oswaldo Cruz Foundation, Rio de Janeiro, presented a lecture on **Alternative Methods in Toxicology**. His results demonstrated that the use of HET-CAM (Chorion-Allantoic Membrane), NRU (Neutral Red Uptake), and RBC (Red Blood Cell Assay) as alternatives provide results with good correlations to results of the Draize test and can be used reliably in place of it. Experiments are in progress to determine if cytokine release in a Whole Blood Assay can reliably replace the rabbit pyrogen test, and to establish protocols for re-using rabbits on multiple occasions for testing biological products. Dr. Presgrave predicted that re-use of rabbits could reduce the number required by 66%. He concluded his lecture by emphasizing that it is not possible to replace animals in all toxicology testing, and that the goals are to replace them when it is possible to do so without compromising the integrity of the conclusions and to refine methods to reduce pain and distress.

G.M. Oliveira presented a new strategy in his contributed talk entitled **Evaluation of *Trypanosoma cruzi*, Infection Course Employing Non-invasive Parameters in Mice**. Current practice is to kill mice serially at various time points after experimental infection with *T. cruzi* to monitor disease progression at necropsy. Dr. Oliveira's strategy is to use biochemical, hematological, electrocardiographic, and ergonomic tests to monitor disease progression in individual animals. This approach not only reduces the number of experimentally infected animals required for an experiment, but provides longitudinal data. The availability of longitudinal data is especially valuable for interpreting the results in research on *T. cruzi* infection because individual response is variable even in inbred mice.

ANIMAL WELFARE

John Miller of the Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC) International opened the first of two Animal Welfare sessions with a presentation entitled **Animal Welfare and Science: Growing Together**. He stressed the benefits of high quality animal care and use to science, to animals, and to scientists. A major benefit to science is minimization of variables, which leads to increased reproducibility, statistical significance, and comparability among studies of experimental results. The benefits to animals include minimization of numbers required for statistically significant results and reduction in pain and distress. The benefits to scientists include increased competitiveness for funding, greater willingness of colleagues to collaborate, and higher likelihood of acceptance of manuscripts for publication. Dr. Miller outlined the elements of a high quality animal care and use program, identified those that are most important for a successful outcome, and explained how setting and meeting high standards need not be prohibitively expensive.

H.R.N. Marona from the State Paulista University in the state of São Paulo, presented a contributed talk entitled **A New Protocol to Refine Intestinal Motility Test in Mice**. Intestinal motility in mice is typically assessed at necropsy as the distance that a charcoal plug travels in the intestine during a set time period. Dr. Marona's protocol involves fasting the animals for only 3 hours, rather than the 12-24 hours in the traditional test, administering a charcoal suspension rather than a charcoal plug, and observing the mice at 5 minute intervals for the presence of charcoal in the stool. Thus, intestinal motility is measured as the time it takes for a charcoal suspension to traverse the entire length of the gut, rather than the distance a charcoal plug travels in the gut during a fixed time period. This protocol not only reduces the animals' distress, but also enables them to be used on multiple occasions. Furthermore, since a single animal can serve as its own control and in several alternative treatment regimens, the data are likely to be more robust than when a different animal is used to obtain each data point.

ANIMAL WELFARE

Gilles Demers, President of the International Council on Laboratory Animal Science (ICLAS) and Assessment Director of the Canadian Council on Animal Care spoke on **Implementing Endpoints in Animal Experimentation, A New Reality**. He emphasized the mandate to choose the earliest endpoint compatible with scientific objectives, the potential need to conduct a pilot study to identify the earliest valid endpoint, and the need to evaluate the selected endpoint as an experiment progresses. He also emphasized the importance of teamwork involving investigators, clinical veterinarians, and animal technicians and caretakers in ensuring proper selecting, monitoring, recording, and applying the chosen endpoint.

Miguel Gonçalves presented a contributed talk on **Environmental Enrichment for Behavioral Studies in a Selected Group of Rhesus Macaques** which are maintained at his institution, the Oswaldo Cruz Foundation, Rio de Janeiro. The experimental design involved the construction of three creative enrichment devices from PVC pipe. The three devices had different levels of complexity. Seventy-seven activities were recorded during one month and grouped into four categories: locomotion, inactivity, ingestion, and social. Behaviors varied in

relation to age and social dominance; however, all of the monkeys spent more time utilizing the less challenging of the three enrichment devices.

Gianpaolo Milite from Tecniplast Gazzada s.r.l. in Buguggiate, Italy, presented a contributed talk entitled **Individually Ventilated Cages and Open Cages With or Without Environmental Enrichment: A Comparative Study on Body Weight, Major Organ Weight and Blood Parameters in HSD:ICR (CD-1) Mice**. Mean combined weight of adrenal glands was lower in mice that had access to a Mouse House (where they could “hide” from observers, although observers could see the mice through the red colored plastic walls and roof), suggesting that stress levels might be lower in the presence of this enrichment device. In addition, HDL cholesterol levels were higher in mice housed in individually ventilated cages with the Mouse House by comparison with mice housed in open cages.

EDUCATION

The final session, on Education, consisted of two presentations.

The first lecture, a contributed talk entitled **Computer-based Learning Resources as an Alternative to the Use of Animals in a Physiology Course for Biology Undergraduate Students**, was given by Paulo Montenegro of the Rural Federal University of Pernambuco, Brazil. Dr. Montenegro evaluated student responses to three different simulation programs designed to teach specific principles of physiology. In general, the students preferred the computer simulation programs to experimentation with living animals for the purpose of learning these physiological principles. The advantages of computer simulations are that the students can repeat the experiment as many times as they want, they can change one variable at a time and observe the results, and they can learn at their own pace and can take the diskette home for study there. In addition, the cost is minimal and no animals are subjected to pain and distress. Disadvantages were that some students did not have sufficient computer skills and that the programs exist only in English, creating a language problem for some students. These problems were alleviated in part by having the students work in groups that contained at least one student proficient with computers and at least one student proficient in English.

The final presentation, **ILAR Programs and Activities**, was presented by William Stokes, who is a member of the Council of ILAR (Institute for Laboratory Animal Research). ILAR is a program unit in the U.S. National Academies and functions as an advisor to the U.S. federal government, the biomedical research community, science educators, and the public. It has created and published many authoritative reports on subjects of importance to the care and use community. Many of those reports are accessible on the ILAR web site (dels.nas.edu/ilar). It is responsible for the preparation of the *Guide for the Care and Use of Laboratory Animals* and for its translation into many languages. The Portuguese translation was completed and printed just prior to the 1st ICFAR, and copies were distributed to the Portuguese-speaking participants.

AWARD CEREMONIES

In addition to the scientific sessions, the Congress featured two award ceremonies. At one of them, Dr. Jean-Louis Guénet from the Pasteur Institute was presented the ICLAS 2003 Mühlbock Award, in recognition of his distinguished career as a mammalian and mouse geneticist, and his great influence on developing nations to advance laboratory animal science. The award was presented by Dr. Gilles Demers, President of ICLAS.

At the other award ceremony, Tecniplast Gazzada s.r.l., a manufacturer of animal cages and accessories, presented several awards to outstanding young Brazilian scientists. First prize was awarded to Reneta Spalutto Fontes for her work entitled “Environmental Influences on Responses to Behavioral Tests and Well-being of Rats Maintained in Two Different Ventilation Systems.” The prize will cover her expenses to travel to an Italian laboratory and to work there for 2 months. Previously, Tecniplast Gazzada s.r.l. had awarded a similar prize to a young Italian investigator to work for an equal period of time in Brazil.

These award ceremonies strengthened the spirit of international collaborations in laboratory animal science, which was a focal point of the Congress. The organizers are grateful to ICLAS and to Tecniplast Gazzada s.r.l. for including these events in the program of the meeting.

SUMMATION AND CONCLUDING REMARKS

The Congress was organized to be unusually broad in order to foster communications among people who might not normally communicate and to develop a collage of diverse perspectives about the future of animal research.

The final session of the Congress was a panel discussion led by Sylvia Ortiz, Gilles Demers, Gerhard Hunsmann and John VandeBerg. They concurred that the overriding themes that emerged during the Congress were 1) that improving the quality of human life will continue to be heavily dependent on the use of animals in research, 2) that the rate of progress in animal research will be dependent on appropriate care of laboratory animals and their judicious use to achieve experimental objectives, 3) that new technologies will lead to better assays for testing chemicals for safety while reducing the number of animals used in testing, 4) that the use of animals, particularly rodents and primates, will increase as new opportunities arise for solving major worldwide health problems, 5) that the importance of education in the appropriate care and use of laboratory animals will continue to grow in emphasis.

The diversity of participants and perspectives at the meeting led to a number of contrasts that are pertinent to the future of animal research, including the following:

- the naïveté of animal experimentation in its first few centuries and its sophistication today
- the diverse types of animals that have contributed so much to advancement of science and human and animal health

- how much we know as a consequence of animal research (e.g., the number of genes that exist in many species, the genome sequences, how to manipulate genes) and how much we do not know (e.g., the functions of 80% of the genes present in the mammalian genome, how to prevent or cure the majority of human diseases)
- the success of cloning mammals versus the difficulties in implementing cloning on a routine basis to advance genetic research, to save species from extinction, to improve livestock, and to treat human diseases
- the importance of traditional genetics in determining phenotypic characteristics of animals (including human beings) and the importance of epigenetics
- the decreasing use of animals in testing as a consequence of brilliant new alternatives versus the increasing use of animals (particularly transgenics and knockouts, as well as nonhuman primates) in research as a consequence of new tools and strategies for understanding biological mechanisms and disease processes.

A contrast that was conspicuous in its absence was in the quality of the presentations. In addition to the 16 invited presentations, the program included 10 contributed presentations which were selected on the basis of quality of submitted abstracts and relevance to the session topics (the Congress also included an outstanding poster session). The contributed papers presented by graduate students, postdoctoral students, and junior faculty were every bit as elegant and thought-provoking as the invited lectures by established scientists; this observation is a tribute to the young investigators as well as to their teachers. Likewise, presentations from investigators from developed countries and from developing countries were equally outstanding. These observations attest to the future of animal research being in good hands and having a strong international foundation.

CONCLUSIONS

The speakers were asked to conclude their presentations with a statement about the future of animal research in their own fields of interest, or more broadly. Several themes emerged from these statements and from the roundtable discussions at the end of each session. They are summarized as follows:

1. The concept “from-bench-to-bedside” is being replaced by “from-bench-to-animals-to-bedside”. This trend is likely to continue.
2. Nonhuman primates (NHPs) for biomedical research are in short supply, and there is risk of losing the supply of tens of thousands of NHPs imported to the U.S., the EU, and Japan each year from China and elsewhere. It is imperative that captive breeding programs be expanded in countries that use NHPs in biomedical research to ensure that future needs can be met.
3. The mouse is king and will continue to be king. Mice will continue to be the predominant animal model for research that has genetic underpinnings.
4. There will be increased use of laboratory rodents, genetically engineered animals, varieties of strains (e.g., congenics), rate of interchange among laboratories, competence of technicians, and cost of animal research.
5. Progress in animal research (e.g., cloning) will accelerate as molecular mechanisms responsible for basic biological phenomena are defined.

6. The need for alternatives in testing will increase as the number of new chemicals in commerce increases dramatically, for the purposes of increasing efficiency and the accuracy of results, meeting legal and statutory responsibilities, and addressing animal welfare concerns. New alternatives will be developed using molecular biomarkers designed for high throughput strategies, improved *in vitro* cell/tissue models, genetically engineered cells systems and animals, noninvasive imaging and labeling techniques, and *in silico* approaches designed to help triage new chemicals.
7. The emphasis is on animal well-being will continue to grow; good animal care and good science are inextricably linked.
8. Increased capabilities in nanotechnology, computing technology, and imaging technology will enhance opportunities for less invasive and non-invasive experimental methods.
9. International collaborations and exchanges in research with animals will continue to increase; harmonization of standards for animal care and use will have increasing importance for facilitating international interactions.
10. The number of animals used in testing is likely to decrease as efficient and accurate alternatives are developed; however, the use of animals in research, primarily rodents and primates, will increase as more *in vivo* research is needed to understand complex mechanisms of phenomena discovered through molecular and genomics research.

The 2nd ICFAR

When the 1st ICFAR began, it was not known when and where the 2nd ICFAR would take place. As the meeting progressed, the enthusiasm of the participants grew, together with the excitement of participating in this highly interactive meeting which was the first in what may well be a long series of congresses. By the end of the meeting, it was decided to hold the 2nd ICFAR in conjunction with the 5th South American Veterinary Conference in Rio de Janeiro during August 18-21, 2005. Individuals who want to be included on the mailing list should contact Dr. John VandeBerg (e-mail: jlvsfbr.org).

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