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Debate

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ARTs in action in non-human primates: Introduction to workshop proceedings

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The workshop upon which these proceedings are based was designed with three objectives in mind: 1) to review the current state of reproductive research employing the assisted reproductive technologies (ARTs) in non-human primates (NHPs), including both basic concepts and specific applications; 2) to enhance interactions and collaborative efforts within and between National Primate Research Centers (NPRC) and academic institutions concerning these technologies and reproductive research; and 3) to identify and discuss new developments in reproductive physiology, gamete/embryo biology and efforts to exploit the ARTs in nonhuman primate species. Our underlying premise is the understanding that NHPs have, and should continue to play a significant role in biomedical research by offering a biological substratum remarkably similar to that of the human species, that is, they represent a clinically relevant model. Of course, the impact that research with NHPs will have on the overall understanding of the pathophysiology and treatment of human diseases is dependent upon animal availability and here it is assumed that meeting the NHP needs of the biomedical research community will require the use of the ARTs.

Unlike in many fields where knowledge flows from NHP research to clinical application in humans, the development of the ARTs in NHPs historically postdates human application. The ARTs have been perfected for the treatment of human infertility and as practiced clinically, have seen rapid advances in many areas including ovarian follicular stimulation, treatment of male infertility by intracytoplasmic sperm injection (ICSI) with ejaculated, epididymal or testicular sperm (both fresh and frozen), culture medium development for the production of blastocysts, low temperature storage of sperm and embryos and non-surgical embryo transfer at the blastocyst stage. The experience in macaques, while nowhere nearly as extensive, has been associated with several landmark accomplishments and the methods for establishing pregnancies were reviewed in this workshop.

The ARTs in NHPs carry the potential to impact diverse areas in biomedical research and several examples were considered. The availability of NHP embryos has supported the isolation of embryonic stem cells raising the possibility of cell-based therapy for the treatment of human degenerative diseases. Many of these applications will undoubtedly be previewed in the NHP and several presentations at this workshop addressed translational research efforts in NHPs in this newly emerging field of regenerative medicine.

With an estimated 33 million individuals in the world infected with the AIDS virus, the need for an effective vaccine is recognized as one of the highest priorities of the biomedical research community, yet the supply of Indian-origin, Mamu-A*01 positive, rhesus macaques for vaccine development studies is grossly inadequate. The ARTs can significantly impact this shortage based on the ability to propagate a founder animal of defined MHC genotype. An even greater need in the vaccine development or tissue transplantation fields where immune system function is under study, is access to genetically-identical animals. Progress in somatic cell cloning and monozygotic twinning was summarized in this workshop.

Although fertility control is an issue of global and national public health concern, little progress has been made toward the development of new birth control methods. NHPs of Old World origin are the ideal species in which to pursue development of novel contraceptive methods because of the similarity of their menstrual cycles and reproductive organs to those of women. Recent advances in cell biology were summarized that have led to the elucidation of novel mechanisms that can be targeted to specific sites in the reproductive tract for contraceptive development.

Neurogenetic diseases cause tens of thousands of deaths in the United States each year, inflict immeasurable pain and suffering, and consume a substantial portion of scarce healthcare resources. A mouse counterpart for many of these human diseases does not exist necessitating the creation and use of new animal models that in some cases can only be served by NHPs. The ARTs can be used to create these disease models employing a combination of gene targeting and somatic cell nuclear transfer. Thus, gene targeting would first be conducted in cell lines that subsequently serve as the source of nuclei for cloning. Embryos created by nuclear transfer from these targeted nuclei and then transferred into surrogate mothers could provide a reliable source of affected, genetically-modified infants for the study of human neurogenetic diseases. Progress in gene targeting and somatic cell cloning, the prerequisite technologies to create genetically-modified monkeys, are summarized in the workshop proceedings.

In summary, we believe that a NHP model is essential in efforts to study human health with direct implications to biomedical investigations of infertility and contraception, infectious diseases and vaccine development, drug and alcohol addiction, neurological disorders and regenerative medicine using gene-, stem cell and tissue-based therapies. Despite significant advances in the past decade, the ARTs in NHPs, while potentially very useful have yet to be realized on a scale adequate to impact the needs described above. We hope that the proceedings of this workshop will contribute in a significant way to the intelligent and expanded use of the valuable NHP animal model in biomedical research.