

LANDMARK AREA OF EXCELLENCE: REPRODUCTIVE BIOLOGY

Introduction and Significance

The study of Reproductive Biology addresses basic aspects of reproduction as well as factors affecting animal and human clinical reproductive health, by examining physiological, cellular, molecular and genetic mechanisms regulating reproductive function. Reproductive biologists within the College of Veterinary Medicine and Biomedical Sciences (CVMBS) investigate gametogenesis, gamete preservation, fertilization, early embryonic development, ovarian and uterine biology, and fetal growth and placental development, and also address the effects of the environment -- such as behavior, circadian rhythms, nutrition, and toxins -- on reproduction.

Reproductive disorders affect society in diverse ways, from reducing the efficiency of food production to impacting survival of endangered species. A major limitation to improved reproductive efficiency in mammals species is embryonic mortality, which is estimated to be 25% to 60%, depending on the species. In the United States, high rates of unexplained infertility and peri-implantation embryonic loss occur in both humans and domestic animals. The 1995 National Survey of Family Growth indicated that 15% of women of reproductive age have infertility-associated health-care visits, and the Centers for Disease Control reported 16% of couples in the U.S. experience infertility. Many pregnancy losses in both humans and domestic animals are attributed to asynchrony in signaling between the conceptus (fetus and placenta) and uterus or to endometrial dysfunction, resulting in defective pregnancy recognition, implantation, and/or placentation. In addition, intrauterine growth restriction, a major human health problem in the United States and worldwide, causes significant perinatal complications and may contribute to adult-onset diseases due to involvement of multiple genetic and environmental factors.

From a male perspective, population-based retrospective studies suggest a global decline in semen quality of men and wildlife, influenced by geographical location. The incidence of testicular cancer and congenital reproductive tract abnormalities such as cryptorchidism and hypospadias has increased in men in several study populations. Man-made endocrine-disrupting chemicals, ranging from plastics to pesticides, are thought to play a causal role in these disturbances. Some of these toxins may disrupt sensitive genes in the developing fetal gonad; others affect the post-pubertal male.

Rationale

Research in reproduction in the CVMBS is both applied -- related to assuring an ongoing and plentiful food supply, efficient production of livestock for specific industries, and production of animals for biomedical research -- and translational, in its exploration of the physiology of normal fertilization and pregnancy and of mechanisms underlying male and female infertility. Basic research is transferred from the laboratory to the classroom and clinics (human and veterinary), to the field (animal agriculture), and to the community (education and information). *In vitro* fertilization, stem cell biology, animal cloning, and other assisted reproductive technologies have been developed to address infertility and disease in both animals and humans, and to help preserve valuable genetics in domestic animals, wildlife and endangered species.

Mammalian reproductive biology has been an area of emphasis at Texas A&M University (TAMU) since 1956, with the establishment of the Physiology of Reproduction degree program. Current research in reproductive biology at TAMU is both intercollegiate and interdisciplinary. The College of Veterinary Medicine and Biomedical Sciences is a major contributor in this area, being one of the two main participants (with the College of Agriculture and Life Sciences, COALS) in the Interdisciplinary Faculty of Reproductive Biology (IFRB; <http://repro.tamu.edu>). Twenty-one faculty members holding full or joint appointments in the CVMBS perform research in three main areas of reproductive biology: uterine biology and pregnancy, gamete biology and biotechnology, and equine reproductive biology. Texas A&M is regarded as a world leader in all of these fields.

Work in the area of **uterine biology and pregnancy** is strongly intercollegial, with faculty in the CVMBS and in COALS collaborating to conduct basic research in uterine and placental biology using an integrated approach involving physiology and genomics. The aim of this research is to understand the hormonal, cellular, and molecular mechanisms regulating uterine development and function in the non-pregnant female, as well as the interactions between the uterus and conceptus (embryo/fetus and associated membranes) during pregnancy. The goal of this program is the development of management and clinical therapies to diagnose, prevent and treat infertility and fetal growth retardation in humans and domestic animals.

The mammalian **gamete biology and biotechnology** program at the CVMBS has pioneered work in embryo transfer, in vitro fertilization and nuclear transfer in the domestic species. Because of the strong ties between basic and clinical science faculty in this area, the CVMBS has successfully cloned more species of animals than any other institution in the world, including the first cloned cat and white-tailed deer, and the first cloned horse in North America. The research focus of the gamete biology and biotechnology program involves the application of assisted reproductive technologies and animal biotechnology in livestock and domestic species. Current research activities range from basic studies on mechanisms of oocyte activation at the time of fertilization, assessment of embryonic health through preimplantation genetic diagnosis, and characterizing the epigenetic control of early normal and abnormal embryonic gene expression, to the production of genetically engineered livestock with improved production traits or modifications that make them useful as models for biomedical research. The goal of this research program is to develop reproductive biotechnologies for translational and biomedical use, and to decrease the incidence of embryonic and fetal defects in both humans and domestic species.

As befits a Texas institution, the **equine reproductive biology** program at Texas A&M University is regarded as one of the most successful in the world. This program has a strong history of research that addresses basic equine reproductive physiology while also having direct clinical application. With nine CVMBS faculty participating in this area, including five Diplomates of the American College of Theriogenologists, Texas A&M University has pioneered research in causes and treatment of stallion subfertility/infertility; in assisted reproduction techniques such as intracytoplasmic sperm injection, oocyte transfer, in vitro fertilization, gamete preservation, and low dose insemination; and in nuclear transfer (cloning) in the horse. The goal of the equine reproductive biology research program is to increase reproductive efficiency in horses with valuable genetics, and to explore the comparative reproductive physiology of this species.

Interdisciplinary impact

In addition to the strong collaborative interactions among the CVMBS, COALS and Texas AgriLife Research and Extension faculty, reproductive research in the CVMBS has synergy with other TAMU programs as they relate to embryonic, fetal and maternal health. Of particular note are strong interactions with Toxicology, Genetics, Nutrition, Neuroscience and Biotechnology, with the Texas A&M Health Science Center, and also with interdisciplinary initiatives in women's health with the Colleges of Education and Liberal Arts through the TAMU Women's Studies Program. Emerging areas of interaction include those with Engineering and Chemistry.

Assessment / Expectations

Reproductive Biology represents a Landmark Area of Excellence in the College of Veterinary Medicine & Biomedical Science. Strong multidisciplinary and intercollegiate collaborations exist through the Interdisciplinary Faculty of Reproductive Biology, and these should continue to strengthen in the future, as exploration of physiology proceeds to deeper molecular and genomic levels. The CVMBS supports recognition of Reproductive Biology as a Landmark Area of Excellence at Texas A&M University.

Additional faculty and facilities are critical to maintaining TAMU's reputation as an international leader in reproductive biology research. Enhanced faculty retention programs and continued investment in new faculty and new facilities will strengthen our competitiveness for NIH and USDA center and Training grants. The programmatic goal of the IFRB, supported by faculty of the CVMBS, is to obtain an NIH Program Project grant to sustain high levels of activity in integrated, multi-project research, and to further foster collaboration among investigators in reproductive biology at TAMU. To provide the resources required to further these goals, as a Landmark Area of Excellence at Texas A&M University the IFRB will recruit two to three senior faculty members with active NIH-funded programs in molecular, epigenomic or translational reproductive biology. These faculty members will integrate with and strengthen current research in all areas of focus in the IFRB, and provide the depth necessary for TAMU to acquire a federally-funded Program Project Grant in the area of Reproductive Biology.

Indices of Excellence

Over the last 5 years, research performed by CVMBS reproductive biology faculty has resulted in over 300 original publications in top peer-reviewed journals, including the Proceedings of the National Academy of Sciences, Biology of Reproduction, Endocrinology, Reproduction, the American Journal of Physiology, Journal of Biological Chemistry, FASEB Journal, Cancer Research, Journal of Nutrition, and Pediatric Research. Reproductive biology faculty in the CVMBS have participated as Principal or Co-Investigator in 16 grants from the National Institutes of Health in the last 5 years, including two Center grants, totaling over \$20 million in funding. Additional funding since 2003 includes:

- USDA: 15 grants totaling over \$4 million
- Other external granting agencies, including the American Quarter Horse Foundation, the Texas Heart Institute, the Juvenile Diabetes Research Foundation, and the Grayson-Jockey Club Foundation: over \$1.8 million

- Funding from private foundations, individuals and corporations: over \$1.3 million
- Intramural funding, including the Link Equine Research Endowment: \$1.8 million

Reproductive faculty in the CVMBS are highly respected in their fields, serving as editors or editorial board members on journals such as *Biology of Reproduction*, *Tissues, Cells, and Organs*, *Journal of Applied Toxicology*, *Domestic Animal Endocrinology*, *Theriogenology* and *Animal Reproduction*, on grant review committees and study sections for the NSF, NIH, USDA, National Cancer Institute, Veterans Health Administration, and March of Dimes, and as officers in the governance of their professional and scientific associations. Faculty at the CVMBS serve as advisors on public policy on reproduction and biotechnology at the State and National levels. Leadership in international scientific and professional societies, invited presentations at international meetings, and international collaborations with colleagues around the world demonstrate the global impact of this program. CVMBS reproductive biology faculty include Regents, University, and Texas AgriLIFE Research Faculty Fellows, and three endowed chairs. Awards garnered by the faculty include honorary doctorates, the Pioneer Award from the International Embryo Transfer Society, honorary diplomate status in the American College of Theriogenologists, three faculty awarded Theriogenologist of the Year from the American College of Theriogenologists – more than any other institution -- the Society for Research and Fertility Distinguished Research Award, Vice Chancellor's Award in Excellence for Team Research, and the Society for the Study of Reproduction Carl Hartman and New Investigator Awards, among many others.

PARTICIPANTS

Name	CVMBBS Department	Major Areas of Interest
Arosh, Joe	VIBS	Uterine Biology and Pregnancy
Bazer, Fuller	VIBS/VTPP	Uterine Biology and Pregnancy
Blanchard, Terry	VLCS	Equine Reproductive Biology
Brinsko, Steve	VLCS	Equine Reproductive Biology
Burghardt, Bob	VIBS	Uterine Biology and Pregnancy
Cudd, Tim	VTPP	Uterine Biology and Pregnancy
Forrest, David	VIBS	Equine Reproductive Biology
Hinrichs, Katrin	VTPP	Reproductive Biotechnology Equine Reproductive Biology
Ing, Nancy	VIBS	Equine Reproductive Biology
Jaeger, Laurie	VIBS	Uterine Biology and Pregnancy
Johnson, Greg	VIBS	Uterine Biology and Pregnancy
Johnson, Larry	VIBS	Equine Reproductive Biology
Kraemer, Duane	VTPP	Reproductive Biotechnology
Long, Chuck	VTPP	Reproductive Biotechnology
Love, Charles	VLCS	Equine Reproductive Biology
Romano, Juan	VLCS	Reproductive Biotechnology
Spencer, Tom	VIBS	Uterine Biology and Pregnancy
Varner, Dickson	VLCS	Equine Reproductive Biology
Welsh, Tom	VIBS	Equine Reproductive Biology
Westhusin, Mark	VTPP	Reproductive Biotechnology
Wu, Guoyao	VIBS	Uterine Biology and Pregnancy