



Reproduction and Perinatology Update

A publication of the D.H. Barron Reproductive and Perinatal Biology Research Program and the Center for Perinatal Outcomes Research

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Distinguished Scientists to Present Barron and Warnick Lectures

Dr. **Ronald R. Magness** will visit UF to present the Fall Barron Lecture on October 18. Magness is Professor of Obstetrics and Gynecology and Director of the Perinatal Research Vascular Center at the University of South Florida. Prior to taking his current position in 2016, Magness was on the faculty at Wisconsin (from 1994) and University of Texas Southwestern Medical Center (1982-1994).



Ronald Magness

His group has pioneered work on vascular biology changes during pregnancy with a particular emphasis on endothelial NO and angiogenesis via ATP, placental growth factors (VEGF/FGF-2), and shear stress. The lab has also made major contributions in studying

uterine, systemic and placental vascular signaling and vasodilatory function as related to placental derived steroid (estrogens and progesterone) and angiogenic growth factor regulation of endothelial and vascular smooth muscle function.

The Fall Warnick Lecture will be given on November 8 by Dr. **Pablo Ross**, associate professor of reproductive physiology in the Department of Animal Sciences, University of California Davis. Dr. Ross was born and raised in Argentina, where he received a Degree in Veterinary Medicine from La Plata National University in 1999 and an MS in Animal Science from Mar del Plata National University/INTA Balcarce in 2002. He obtained a PhD in Animal Science from Michigan State University (2007) and held a Research Assistant Professor position at that institution, until he joined the faculty at Davis in 2010.

Dr Ross' studies are aimed at understanding the mechanisms of epigenetic remodeling and transcriptional reprogramming that occur during preimplantation embryo development. His laboratory makes extensive



Pablo Ross

use of next generation sequencing approaches to determine transcriptome and epigenetic profiles in livestock embryos. Work at the Ross laboratory also relates to developing embryo and pluripotent stem cell technologies for use in agriculture and biomedicine.

The Donald Henry Barron and Alvin C. Warnick Lectures were created to recognize the achievements of these two early reproductive biologists at Florida. Donald Barron was a leader in the formation of the Reproductive and Perinatal Biology Group.

**Contribute IDC to
Support Our
Program**

Our reproductive biology effort is supported by the Center for Perinatal Outcomes Research. This is a source of funds that are generated by indirect costs from us - up to 7.5% of IDC that otherwise goes to the Deans Office can be designated to the Center. These funds are used to invite speakers to campus, organize retreats and are used as a source of seed grants. Please consider designating some of your IDC to the Center

**Identify Our
Program on Your
Next Paper**

Please consider including the D.H. Barron Reproductive and Perinatal Biology Research Program as one of your affiliations

Research Highlight - Physiology of the Late Gestation Fetus

Charles E. Wood, Department of Physiology & Functional Genomics

The research performed in the Wood laboratory is focused on the physiology of the late-gestation fetus and the mechanisms that ready the fetus for birth and transition to extrauterine life. The Wood laboratory has contributed to our understanding of the responses to stress (hypoxia and hypotension) in the fetus in utero and on the mechanisms controlling the timing of birth. The laboratory has published research results which have played a leading role in elucidating the function of the fetal arterial baroreceptors and chemoreceptors in the control of fetal cardiovascular and endocrine function. Other research performed in the laboratory has identified the cardiovascular neural receptors which are involved in the integrated cardiovascular and endocrine response to alterations in blood gases and blood pressure in the fetus. Complementary to this work has been discovery of the influence of the fetal endocrine systems, especially the hypothalamus-pituitary-adrenal axis and the adrenal-placental steroid axis, on the physiological mechanisms supporting survival and growth of the fetus.

Recent discoveries in the laboratory have focused on the intersection between stress, inflammation, and normal birth. The laboratory has made seminal contributions to our understanding of the role that prostaglandins play in fetal development. Recently, collaborative work between the Wood laboratory and the Triplett laboratory in the College of Agricultural and Life Sciences has discovered that fetal brain inflammation after fetal and maternal stress is caused by movement of live bacteria from the mother to the fetus. This is a scientific breakthrough that changes our understanding of the fetal consequences of stress. This new discovery has the potential to change treatment to prevent hypoxic-ischemic encephalopathy in the newborn infant.

Together, these studies interrelate to advance our knowledge of normal and abnormal fetal development, with the ultimate goal of improving outcomes for babies.



Members of the Wood and Keller-Wood laboratories. (l-r) Rachel Moran, Andrew Antolic, Serene Joseph, Maureen Keller-Wood, Charlie Wood, Maria Belen Rabaglino, Eileen Cheng, and Miguel Zarate

Faculty, Student, Postdoc and Alumni News

Since the last newsletter, the following students were awarded doctoral degrees:

Verónica M. Negrón-Pérez (Hansen lab) – currently a postdoc at Virginia Tech

Luiz Siqueira (Hansen lab) – currently a research scientist at Embrapa, Juiz de Fora, MG, Brazil

Paula Tribulo (Hansen lab) – currently a postdoc at University of Florida

Leticia Sinedino (Santos Lab) – currently a postdoc at Colorado State University

Miguel Zarate (Wood lab) – currently a postdoc at University of Colorado



Sinedino at graduation with major professor José Santos

Gulnur Jumatayeva (Hansen lab) completed a MS and is currently a Leading Researcher at the Kazakh Scientific Research Institute of Cattle Breeding and

Forage Production, Almaty, Kazakhstan.



Jumatayeva at her defense with John Bromfield and Pete Hansen

Mackensie Dickson (Bromfield lab) and **Ali Husnain** (Santos lab) have begun doctoral programs in the Animal Molecular and Cellular Biology Graduate Program.

Elizabeth Gordon (Biology) and **Beau Doerr** (Biotechnology) have begun MS programs in the Charles Wood laboratory.

Eileen Chang, a former graduate student of Charles Wood, has completed a postdoc at Oregon Health Sciences University and is moving to University of Colorado to take a new postdoctoral position.

Gregory M. Christman, Professor of Ob/Gyn, was recently appointed to the Scientific Research Committee of the Fibroid Special Interest Group of the American Society of Reproductive Medicine and to the Abbvie Pharmaceuticals Advisory Board on Medical Treatment of

Uterine Leiomyomas.

Geoff Dahl, professor and chair of Animal Sciences was the recipient of the H. Allen Tucker Lactation and Endocrinology Award of the American Society of Animal Science at its annual meeting in Baltimore in July. At the same meeting, **Peter Hansen** was honored as a Fellow of the American Society of Animal Science.



Geoffrey Dahl



Pete Hansen

Alice Rhoton-Vlasak, professor of Ob/Gyn, was the recipient of the Excellence in Teaching Award given by the Association of Professors of Gynecology & Obstetrics and the Golden Apple Outstanding Teaching Award.

Paige Swenson, a resident in Ob/Gyn doing an REI fellowship, won the resident prize paper at the Florida OB/GYN meeting for a paper on *FOXO3* expression in the human ovary.

Naohiro Terada was appointed this August as Director of the Experimental Pathology Division, Department of Pathology, Immunology and Laboratory Medicine.



Naohiro Terada



Luiz Siqueira on the Jumbotron

Memoriam – Alvin C. Warnick (1920-2017)

The reproductive biology group at Florida lost one of its most-devoted members in May when Alvin Warnick, professor emeritus of Animal Sciences and the first reproductive biologist at the University of Florida, died at the age of 97.

With his fraternal twin, Calvin, Alvin Warnick was born November 15, 1920 on a farm Hinckley, Utah. He attended Utah State University and graduated in June 1942 with a degree in Animal Husbandry. He joined the Army Air Corps in Salt Lake City. He was one of the first radar technicians in the military receiving training in both the U.S. and England before being assigned to the 100th Bomb Group in the 8th Air Force where he supported combat missions from 1943 to 1945. While training at Truax Field in Madison, Warnick met with Professor Lester Casida of the Dept. of Genetics at the University of Wisconsin. Casida offered him a fellowship to be taken up upon peacetime. After the war, Warnick returned to Wisconsin to study with Casida where he earned a MS in 1947 and a PhD in 1950. He also met and married his life-long love, Barbara Webster from Oshkosh, WI.

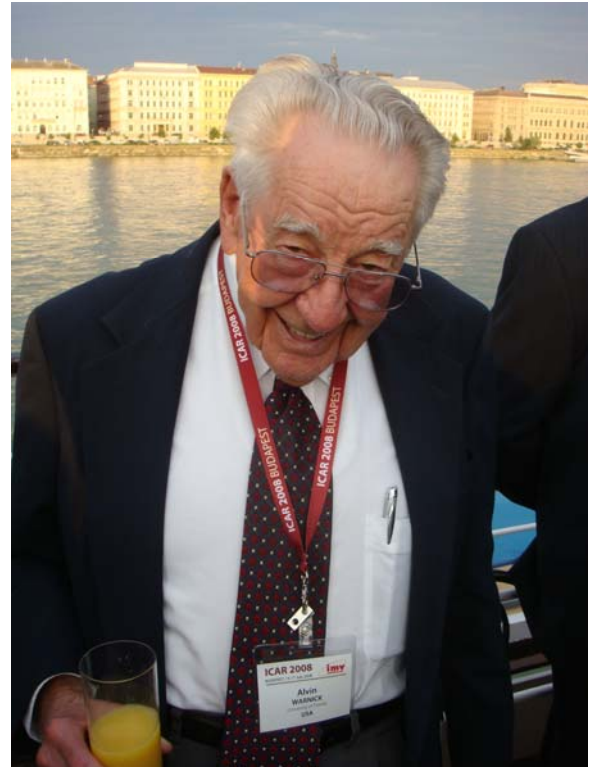
After graduation, Warnick served on the faculty at Oregon State University for three years and then took a position at the University of Florida in 1953. During this 37 year career at Florida, he authored or co-authored four books and published over 350 research papers, either as sole or joint author. He also did sabbatical research in Argentina for the Food and Agriculture Organization of the United Nations in 1962-63, and further research in Brazil in 1977 and in Ethiopia in 1986. Dr. Warnick supervised 70 MS and PhD students. He also served for 20 years as Assistant Chairman of the Animal Science Department at the University of Florida.

Warnick brought modern reproductive management to the Florida beef cattle industry. He was the first person to palpate cows for reproductive diagnoses in the state of Florida. He evaluated effects of crossbreeding, level of nutrition, and many other factors for their effects on reproduction and led efforts to incorporate artificial insemination and embryo transfer into cattle management schemes. He is probably best well known for his work characterizing reproductive function of *Bos indicus* cattle.

After retirement in 1990, Warnick continued as an active contributor and participant at beef cattle workshops throughout Florida (he was palpating cows into his 90s), taught reproductive physiology at the UF College of Veterinary Medicine and participated in international conferences in Canada, Brazil, Australia, Sweden and Hungary.

Warnick was elected a Fellow in the American Society of Animal Science (1984), was honored by Utah State University in 2004 and was inducted into the Florida Agricultural Hall of Fame in 2015. The Warnick Lecture Series sponsored by the Dept. of Animal Sciences was instituted to recognize his accomplishments.

He will be missed.



Schedule Fall Seminar Series

Reproductive & Perinatal Biology Seminar, Wednesday 4:00-5:00 PM
D.H. Barron Conference Room Medical Sciences Building M-304

- September 6: *Improving the detection of risk factors for stillbirth: The Fetal Longitudinal Assessment of Growth (FLAG) study*
Teresa MacDonald, MBBS (Hons), BMedSci, FRANZCOG
 Obstetrician and Gynaecologist, PhD Candidate, Mercy Perinatal, Mercy Hospital for Women and Translational Obstetrics Group, Department of Obstetrics and Gynaecology, University of Melbourne, Australia
- September 20: *Hemodynamically Significant PDAs: Are Tissues Oxygen Saturations the Missing Piece to the Puzzle?*
Lauren Ruoss, MD
 Assistant Professor, Department of Pediatrics, University of Florida College of Medicine
- September 27: *Utilizing inflammatory markers for prediction and prevention of prematurity*
Mehmet Genc, MD, PhD
 Professor, Division of Maternal-Fetal Medicine, Department of Obstetrics & Gynecology University of Florida College of Medicine
- October 4: *Intersex fish? Uncovering the molecular networks that initiate testis transformation following endocrine disruption*
Chris Martyniuk, PhD
 Associate Professor, Center for Environmental and Human Toxicology & Department of Physiological Sciences, University of Florida College of Veterinary Medicine
- October 11: *Power, Sex, Obesity: Tales of Mitochondrial ATP Transporters*
Naohiro Terada, MD, PhD
 Professor, Department of Pathology, Immunology, & Laboratory Medicine, UF College of Medicine
- October 18: **Barron Lecture: Mechanisms Controlling Endothelial Adaptations Modulating of Uteroplacental Blood Flows during Gestation May Underlie Developmental Origins of Health and Disease (DoHAD)**
Ronald Magness, PhD
 Director, Perinatal Vascular Research & Professor, Department of Obstetrics & Gynecology University of South Florida College of Medicine
- October 25: *Bovine Growth Hormone: Friend or Foe?*
Ricardo Chebel, DVM
 Associate Professor, Dept. of Large Animal Clinical Sciences & Dept. of Animal Sciences University of Florida College of Veterinary Medicine
- November 1: *Cell-based therapies in pre-immune embryos to prevent inherited diseases of childhood: hypothesis driven studies*
Joaquin Santolaya-Forgas, MD, PhD
 Clinical Professor, Department of Obstetrics & Gynecology, University of Florida College of Medicine
- November 8: **Warnick Lecture: Transcriptional and epigenetic control of bovine preimplantation development**
Pablo J. Ross, PhD
 Associate Professor, Department of Animal Science, University of California Davis
- November 15: *Preimplantation development of bovine embryos and strategies to reduce pregnancy loss in dairy cattle*
Rafael Bisinotto, DVM, PhD
 Assistant Professor, Department of Large Animal Clinical Sciences, University of Florida College of Veterinary Medicine
- November 29: *Novel Mechanisms for Microbial Trafficking in the Late-Gestation Fetus: Challenging the Sterile Womb Hypothesis*
Michelle Rodriguez
 Graduate Research Assistant, Department of Microbiology & Cell Science, University of Florida Institute of Food and Agricultural Sciences
- December 6: *(Title TBA)*
Kirk Conrad, MD
 Professor, Depts. of Physiology & Functional Genomics and Ob/Gyn, UF College of Medicine

Recent Contracts and Grants

Abbvie. A phase 3 study to evaluate the safety and efficacy of elagolix in combination with estradiol/norethindrone acetate in subjects with moderate to severe endometriosis-associated pain. Protocol MI4-702. G. Christman (site PI). 2017. \$320,000.

NIH. Role of estrogen receptor 1 in uterine epithelial response to estrogen. P. Cooke (PI). R21 HD088006. 2017-2019, \$250,000.

NIH. Research supplement to promote diversity in health-related research. P. Cooke (PI). 2017, \$10,465.

USDA/NIFA. The role of dickkopf-1 to enhance embryonic competence for establishment of pregnancy in cattle. PJ Hansen and G. Dahl (PIs). Grant No. 2017-67015-264522017-2020. \$480,000.

Selected Publications

Ahmed BMS, Younas U, Asar TO, Dikmen S, Hansen PJ, Dahl GE. Cows exposed to heat stress during fetal life exhibit improved thermal tolerance. *J Anim Sci.* 2017;95:3497-3503.

Cho J, Zhang Y, Park SY, Joseph AM, Han C, Park HJ, Kalavalapalli S, Chun SK, Morgan D, Kim JS, Someya S, Mathews CE, Lee YJ, Wohlgemuth SE, Sunny NE, Lee HY, Choi CS, Shiratsuchi T, Oh SP, Terada N. Mitochondrial ATP transporter depletion protects mice against liver steatosis and insulin resistance. *Nat Commun.* 2017;8:14477.

Cooke PS, Nanjappa MK, Ko CJ, Prins GS, Hess RA. Estrogens in male physiology. *Physiol Rev.* 2017;97: 995–1043.

Hamazaki T, El Rouby N, Fredette NC, Santostefano KE, Terada N. Concise review: induced pluripotent stem cell research in the era of precision medicine. *Stem Cells.* 2017;35:545-550.

Negrón-Pérez VM, Vargas-Franco D, Hansen PJ. Role of chemokine (C-C motif) ligand 24 in spatial arrangement of the inner cell mass of the bovine embryo. *Biol Reprod.* 2017;96:948-959.

Ogunleye O, Campo B, Herrera D, Post Uiterweer ED, Conrad KP. Relaxin confers cytotrophoblast protection from hypoxia-reoxygenation injury through the phosphatidylinositol 3-kinase-Akt/protein kinase B cell survival pathway. *Am J Physiol Regul Integr Comp Physiol.* 2017;312:R559-R568.

Petersen JW, Liu J, Chi YY, Lingis M, Williams RS, Rhoton-Vlasak A, Segal MS, Conrad KP. Comparison of multiple non-invasive methods of measuring cardiac output during pregnancy reveals marked heterogeneity in the magnitude of cardiac output change between women. *Physiol Rep* 2017;5:e13223.

Rhoton-Vlasak A, Roussos-Ross K, Cua GM, Odera EL, Irani TA, Vasilopoulos T. Obesity and reproduction: a study to determine how effectively medical education enhances awareness of the reproductive risks related to obesity. *JBRA Assisted Reproduction.*

Sinedino LD, Honda PM, Souza LR, Lock AL, Boland MP, Staples CR, Thatcher WW, Santos JE. Effects of supplementation with docosahexaenoic acid on reproduction of dairy cows. *Reproduction.* 2017;153:707-723.

Siqueira LGB, Dikmen S, Ortega MS, Hansen PJ. Postnatal phenotype of dairy cows is altered by in vitro embryo production using reverse X-sorted semen. *J Dairy Sci.* 2017;100:5899-5908.

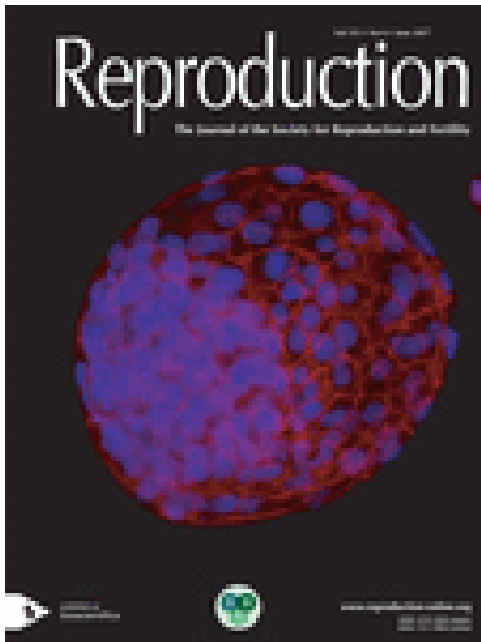
Styer AK, Jin S, Zhang H, Polotsky AJ, Christianson MS, Vitek M, Engmann L, Hansen K, Wild RA, Legro RS, Coutifaris C, Alvero R, Robinson RP, Casson P, Christman GM, Eisenberg E, Diamond MP, Christy A, Santoro N for the NICHD Reproductive Medicine Network. Association of uterine fibroids and pregnancy outcomes after ovarian stimulation-intrauterine insemination for unexplained infertility. *Fertil Steril.* 2017; 107:756-62.

Vieira-Neto A, Lima IRP, Lopes F Jr, Lopera C, Zimpel R, Sinedino LDP, Jeong KC, Galvão K, Thatcher WW, Nelson CD, Santos JEP. Use of calcitriol to maintain postpartum blood calcium and improve immune function in dairy cows. *J Dairy Sci* 2017; 100:5805-5832.

UF Research Featured on Two Journal Covers

Two papers describing University of Florida research on the preimplantation bovine embryo have made the covers *Reproduction* and *Journal of Assisted Reproduction and Genetics*.

The June 2017 issue of *Reproduction* featured an image showing localization of β -catenin in a bovine embryo that was taken from a paper by **Paula Tribulo** and co-authors (Tribulo P, Moss JI, Ozawa M, Jiang Z, Tian XC, Hansen PJ. WNT regulation of embryonic development likely involves pathways independent of nuclear CTNNB1. *Reproduction*. 2017;153:405-419). The paper described the nature of WNT signaling in the preimplantation bovine embryo. Among the key findings was the absence of nuclear β -catenin even when WNT signaling was stimulated. The paper suggested that WNT signaling in the preimplantation embryo occurs independent of actions of nuclear β -catenin.



Cover of the June 2017 issue of *Reproduction*

In the same month, the *Journal of Assisted Reproduction and Genetics* featured another image from the same laboratory on its cover. The paper by **Veronica Negrón-Pérez** and **PJ Hansen** examined whether the bovine blastocyst shows any preference for the site of hatching from the zona pellucida (Negrón-Pérez VM, Hansen PJ. The bovine embryo hatches from the zona pellucida through either the embryonic or abembryonic pole. *J Assist Reprod Genet*. 2017;34:725-731). Hatching was

found to occur with nearly equal probability from the embryonic or abembryonic pole of the blastocyst. The cover image shows the inner cell mass of a bovine blastocyst being extruded from an opening in the zona pellucida. It is believed to be the first image showing this phenomenon.



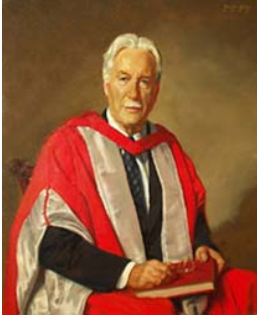
Cover of the June 2017 issue of the *Journal of Assisted Reproduction and Genetics*

Work in Progress Meetings

Organized by **Kirk Conrad** of the Dept. of Physiology & Functional Genomics, the Work in Progress Conference is a forum for presentation of new ideas and new data. Here one can solicit feedback from one's peers, educate trainees, and find common ground for new NIH R01 and P01 applications. We meet at the New Deal Café at 3443 West University from 4 to 6 PM approximately one Friday each month. Beverages and hors d'oeuvres are provided! It is preferred that presentations should be really informal and spontaneous, with NEW IDEAS and data to back them up. PowerPoint slides should be used sparingly and the white board liberally.

The schedule for the fall semester is as follows:

September 22	Charlie Wood
October 20	Diana Montoya-Williams
November 3	Maureen Keller-Wood
December 8	Hayley Kamin



DH Barron Reproductive & Perinatal Biology Research Program

University of Florida

Repro & Perinatal Update is issued each August and January

Send items of interest to P.J. Hansen at Hansen@animal.ufl.edu

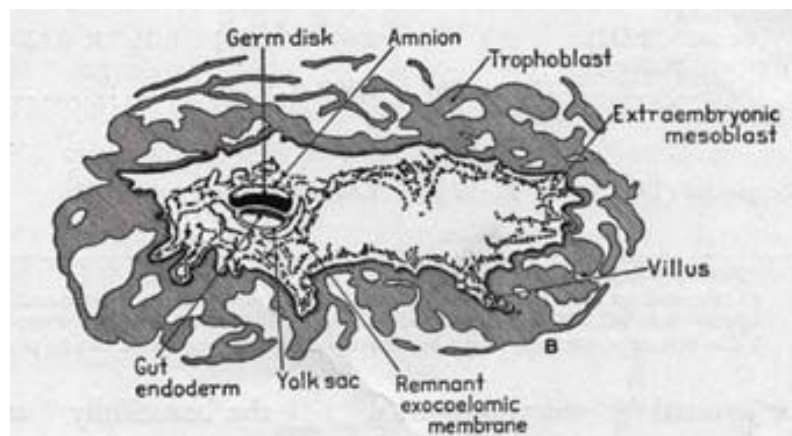
We're on the Web!
www.perinatal.ufl.edu

About the D.H. Barron Reproductive and Perinatal Biology Research Program

History: The Repro program was founded in 1969 by Donald Henry Barron, Fuller Bazer and others. Seminars have been held continuously since that time. Donald Henry Barron (1905-1993) came to UF as the J. Wayne Reitz Professor of Reproductive Biology after a career at Cambridge and Yale. His research in fetal physiology led to his being referred to as the Father of Scientific Obstetrics and the Father of Fetal-Placental Physiology. Known to his colleagues and students as "Dr. B.", his portrait is on the masthead. In 1969, Fuller Bazer, currently the O.D. Butler Chair in Animal Science at Texas A&M University, was an assistant professor in the Dept. of Animal Sciences. Since then, he has become one of the pioneers in understanding the nature of communication between the embryo and mother. Among the many recognitions he has received was the Wolf Prize in Agriculture in 2003.

Mission: To foster collaborative, multidisciplinary, and integrative approaches to basic and translational research that (i) improves the health of pregnant women and their babies, (ii) enhances the reproductive success of agriculturally important animals and wildlife, and (iii) prepares the next generation of scientists in these research disciplines.

Scope: Basic, translational and clinical research aimed at understanding (i) the biology of reproduction in humans and animals from fertilization to delivery and early postnatal development, and (ii) genetic, epigenetic or environmental influences that cause abnormal pregnancy outcomes, including those influences that predispose the mother and offspring to adult diseases.



The Yale Embryo

This human embryo at about day 14 of gestation was collected in July 1932 from the uterus of a woman who died as a result of arsenic ingestion. The collector was Elizabeth M. Ramsey, a young pathology intern on her third day on the job. The embryo was received by the scientific community with much excitement because it represented one of the earliest stages of development observed and was a very well-preserved specimen. It was donated to the Carnegie Institute Department of Embryology (Carnegie Number 6734), which was one of the world's leading organizations devoted to characterizing embryonic development. Ramsey herself would go on to have an important career at Carnegie as an embryologist and placental biologist. In 1971, she recollected that "on that day in July, the career of the young interne was firmly set in embryology and placentology".