SENIOR TRAINER
BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
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NAME: **Golos, Thaddeus G.**

eRA COMMONS USER NAME (credential, e.g., agency login): **golost**

POSITION TITLE: **Professor and Chair**

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Marquette University, Milwaukee, Wisconsin	B.S.	05/1978	Biology
University of Illinois at Urbana-Champaign	M.S.	05/1982	Physiology and Biophysics
University of Illinois at Urbana-Champaign	Ph.D.	10/1984	Physiology and Biophysics
University of Pennsylvania	Postdoctoral	09/1987	Obstetrics and Gynecology

NOTE: The Biographical Sketch may not exceed five pages. Follow the formats and instructions below.

A. Personal Statement

The Golos lab has pioneered the use of the nonhuman primate model in reproductive immunology and the placental expression and regulation of nonclassical MHC class I molecules. Study of the maternal-fetal immune dialogue includes nonpolymorphic MHC class I molecules expression on placental cells and their interactions with the maternal immune system, particularly endometrial natural killer cells and macrophages in promoting pregnancy success, including effects on placental and endometrial differentiation and vascularization. Recent studies have developed models with immune-mediated pregnancy loss and placental insufficiency in the rhesus. I have an ongoing funded R01 on nonhuman primate *in vivo Listeria* infection, and previous published work with anti-placental passive immunization and reproductive tract immune cells which provide animal model expertise. My lab is collaborating on additional NIH-funded studies of *Porphyromonas gingivalis* infection in rats and monkeys. We are funded in a new U01 application with colleagues in Ob-Gyn and Medical Physics to apply magnetic resonance imaging methodologies to primate models of inflammation and adverse pregnancy outcomes. This technology and experience will be invaluable in monitoring fetal well-being in new studies of Zika-infected pregnancies in the rhesus model, with a multi-faceted investigational team at UW. My position as a senior scientist at the Wisconsin National Primate Research Center, and faculty appointments in the Department of Comparative Biosciences in the School of Veterinary Medicine and Obstetrics and Gynecology in the School of Medicine and Public Health, facilitate cross-disciplinary research and specifically provide insight for translational approaches for human adverse pregnancy outcomes based on basic research with nonhuman primate resources. A second major area draws on previous experience in primate *in vitro* fertilization to establish new approaches and resources for the application of nonhuman primates to translational medicine application with embryonic genomic editing and stem cell biology.

I have broad experience in training graduate and postgraduate scholars. My laboratory has been at the Wisconsin National Primate Research Center since 1987. I have trained 9 postdoctoral fellows, 11 Ph.D. students, and 3 M.S. students, as well as numerous undergraduate researchers and veterinary student summer research fellows. My trainees have won Young investigator awards from national scientific associations, and independent fellowships, such as the HHMI/Burroughs-Wellcome Scholar Award. Current positions held by previous trainees include faculty appointments at Johns Hopkins University (Biochemistry), UW-Madison (Pathology and Laboratory Medicine), Tufts University School of Medicine (Oral Biology), and

UT-Health Science Center, San Antonio (Obstetrics and Gynecology), as well as competitive positions in the biotechnology industry (Covance Laboratories, Exact Sciences, Epicentre Technologies).

B. Positions and Honors

List in chronological order previous positions, concluding with the present position. List any honors. Include present membership on any Federal Government public advisory committee.

Positions:

1978-1984	Teaching/Research Assistant, University of Illinois, Urbana, Illinois.
1984-1987	Postdoctoral Fellow, University of Pennsylvania, Philadelphia, Pennsylvania.
1987-1994	Assistant Scientist, WI Regional Primate Research Center, Univ. of WI, Madison, WI.
1995-1999	Assistant Professor, Dept. of Obstetrics and Gynecology, University of WI Medical School, Associate Scientist, WI Regional Primate Research Center, Univ. of WI, Madison, WI.
1997-2003	Head, Reproduction Research Services, WRPRC.
1999-2003	Associate Professor (with tenure), Dept. of Ob/Gyn, University of WI Medical School
2003-present	Professor, Dept. of Ob/Gyn, University of WI School of Medicine and Public Health
2007-present	Professor, Dept. of Comparative Biosciences, Univ. of WI School of Veterinary Medicine
2015-present	Chair, Dept. of Comparative Biosciences, Univ. of WI School of Veterinary Medicine

Honors:

- NIH Predoctoral Fellowships, Reproductive Biology (1980-81), Cellular and Molecular Biology (1982-84), Univ. of Illinois
- USPHS Individual Postdoctoral NRSA, Univ. of Pennsylvania, 1985-87
- NICHD Lecturer, Perinatal Research Society, 2004
- Executive Committee, American Society for Reproductive Immunology, 2012-2016
- NIH Lecturer Award, Meeting of the International Federation of Placenta Associations, 2012
- Raymond O. Berry Lecturer in Reproductive Immunology, Texas A&M University, 2013
- Invited speaker, NICHD/NIAID Workshop on Maternal-Fetal Immune Interface, 2014
- Zoetis Award for Veterinary Research Excellence, UW-Madison SVM, 2015

Editorial Boards:

- Journal of Molecular Endocrinology, 1996-2000;
- Placenta, 2003-2009;
- American Journal of Reproductive Immunology, 2008-present.

NIH Study Section service:

Chartered study section member:

- Biochemical Endocrinology Study Section (1997-2001);

ad hoc study section member:

- Biochemical Endocrinology (1994)
- Human Embryology and Development (1997, 1999, 2001)
- RFA on Immune Tolerance (2001)
- Reproductive Biology (2002)
- Pregnancy and Neonatology (1999, 2000, 2010, 2015, 2017)
- Reviewer/site visitor, U54 Cooperative Centers in Reproduction (1999, 2007, 2011)
- Chair, NICHD P01 review panel (2004)
- R20 Stem Cell Center review panel, NIGMS (2005)
- Special Emphasis Review Panels, NICHD (2001, 2005, 2007, 2008, 2013)
- R24/P01 reviews, NCRR (2008, 2010, 2011)
- Therapeutic Approaches to Genetic Diseases (2015)
- NICHD Rapid Response Review- Rapid Assessment of Zika Virus (ZIKV) Complications (R21) (2016)

C. Contribution to Science

Defining MHC Class I expression in the macaque placenta. The observation that the fetal allograft survives within a maternal environment that would seem poised to respond to the paternal antigens represents a conundrum of mammalian pregnancy. In the early 90s it became clearer that maternal interactions with the placenta and fetus were exceedingly complex, and included a unique local immune environment. While most mammals have distinctly different placentation from humans, the hemochorial placentation of nonhuman primates is very similar to the human, however understanding whether this model can serve to provide insight into maternal-fetal immune interactions required a fundamental definition of the cellular and molecular aspects of nonhuman primate placental and decidual immune function. Initially in collaboration with the David Watkins lab, we have made seminal contributions to the field, defining placental MHC expression in macaques. Salient among these discoveries was the identification of a putative HLA-G homolog designated Mamu-AG, and the demonstration that anti-placental Mamu-AG treatment results in altered placental vascularization, growth, development, and maturation of the decidua. We have been essentially the only lab worldwide conducting these studies with the macaque model.

Boyson, J.E., K. Iwanaga, T.G. Golos, and D.I. Watkins. 1997. Identification of a novel MHC Class I gene, *Mamu-AG,* expressed in the placenta of a primate with an inactivated G locus. *J. Immunol.* 159: 3311-3321.

Slukvin, I.I., J.E. Boyson, D.I. Watkins and T.G. Golos. 1998. The rhesus monkey analogue of human lymphocyte antigen-G is expressed primarily in the villous syncytiotrophoblast. *Biol Reprod.* 58:728-738.

Slukvin, I.I., D.P. Lunn, D.I. Watkins, and T.G. Golos. 2000. Placental expression of the nonclassical MHC class I molecule Mamu-AG at implantation in the rhesus monkey *PNAS* 97: 9104-9109.

Bondarenko, G., M. Durning, D. Burleigh, E. Breburda, R. Grendell, and T.G. Golos. 2007. Deficient placental growth, vascularization, and delayed endometrial responses to implantation in rhesus monkeys passively immunized in early pregnancy against a placental nonclassical MHC class I molecule, Mamu-AG. *J. Immunol*: 179: 8042-8050.

Defining the decidual immune cells in the macaque decidua. In 1989 Judith Bulmer and colleagues clarified that the large granular lymphocytes which were uniquely identified in the pregnant decidua were natural killer (NK) cells. However, major differences between mammals regarding the mode of implantation and decidualization strained the ability to understand the impact of the maternal-fetal immune interface on pregnancy success. My lab pioneered the use of the nonhuman primate model in the reproductive immunology of pregnancy, extending our studies of MHC molecules to their interactions with the maternal immune system, particularly endometrial natural killer cells and macrophages in promoting pregnancy success. Our placental passive immunization studies demonstrated that the placental MHC effects endometrial differentiation and vascularization.

Bondarenko G.I., Burleigh D.W., Durning M., Breburda E.E., Grendell R.L., and T.G. Golos. 2007. Passive Immunization against the MHC Class I Molecule Mamu-AG Disrupts Rhesus Placental Development and Endometrial Responses. *J. Immunol.* 179:8042-8050.

S.V. Dambaeva, M. Durning, A.E. Rozner, and T.G. Golos. 2012 Immunophenotype and Cytokine Profiles of Rhesus Monkey $CD56^{bright}$ and $CD56^{dim}$ Decidual Natural Killer (NK) Cells. Biol. Reprod. 86: 1-10. PMCID: PMC3313663

Reyes L., Wolfe K.B., Golos T.G. **In press**. Hofbauer cells – placental macrophages of fetal origin. In: *Macrophages – Origin, Functions and Biointervention*. Malgorzata Kloc (eds), Springer, Part of Springer Science+Business Media, New York, Philadelphia.

Establishment of NHP embryo transgenesis and experimental embryology. While the macaque provides an important model for studying the physiology and pathophysiology of pregnancy in the intact animal, the role of specific genes, molecules and processes in embryonic development, implantation and placentation remains exceedingly difficult to address. We worked to use assisted reproductive technologies to develop the first robustly demonstrated ***expression*** of a transgene from nonhuman primate embryonic gene transfer. These

methods underpinned primate transgenesis and more recently, genomic editing for creation of improved primate models of human diseases.

Wolfgang, M.J., S.G. Eisele, M.A. Browne, M.L. Schotzko, M.A. Garthwaite, M. Durning A. Ramezani, R.G. Hawley, J.A. Thomson and T.G. Golos. 2001. Rhesus monkey placental transgene expression after lentiviral gene transfer into preimplantation embryos. *PNAS* 98:10728-10732.

Wolfgang, M.J., S.G. Eisele, L. Knowles, M.A. Browne, M.L. Schotzko and T.G. Golos. 2001. Pregnancy and live birth from nonsurgical transfer of *in vivo* and *in vitro* produced blastocysts in the rhesus monkey. *J. Med. Primatol.* 30:148-155.

Marshall, V.S., M.A. Browne, L. Knowles, T.G. Golos and J.A. Thomson. 2003. Ovarian Stimulation of Marmoset Monkeys (Callithrix jacchus) using Recombinant Human Follicle Stimulating Hormone*. J. Med. Primatol.* 32:57-66.

Establishment of nonhuman primate models of infectious disease and adverse pregnancy outcomes. The work in the Golos lab on placental MHC class I molecules and the immune cell environment of the decidua have logically led to a significant involvement and commitment to the development of infectious disease models of adverse pregnancy outcomes. The two most advanced areas include pregnancy loss caused by ingestion of *Listeria monocytogenes,* which the lab has recently shown colonizes the decidua, and causes 100% pregnancy loss in first trimester monkeys within 2 weeks of infection, and the Zika virus, which is cleared from nonpregnant monkeys within 10-12 days, but viremia persists for up to 70 days in pregnant macaques.

Hélène Marquis, Douglas A. Drevets, Michael S. Bronze, Sophia Kathariou, Thaddeus G. Golos, J. Igor Iruretagoyena. 2015. Pathogenesis of *Listeria monocytogenes* in humans. In: *Emerging and Re-emerging Human Infections.* John Wiley & Sons/Wiley Blackwell Press.

Dudley DM, Aliota MT, Mohr E, Weiler AM, Lehrer-Brey G Weisgrau KL Mohns MS Breitbach ME, Rasheed MN, Newman CM, Gellerup DD, Moncla LH, Post J, Schultz-Darken N, Schotkzo ML, Hayes JM, Eudailey JA, Moody MA, Permar SR, O'Connor SL, Rakasz EG, Simmons HA, Capuano III S, Golos TG, Osorio JE, Friedrich TC, O'Connor DH. 2016. A rhesus macaque model of Asian lineage Zika virus infection. Nat Comm: 7:12204 / DOI: 10.1038/ncomms12204.

Wolfe KB, Wiepz GJ, Schotzko ML, Bondarenko GI, Durning M, Faith NG, Simmons HA, Mejia A, Suresh M, Czuprynski CJ, Kathariou S, Golos TG. 2017. Acute fetal demise in early nonhuman primate pregnancy infection with *Listeria monocytogenes.* mBio 8: e01938-16.

Nguyen SN, *et al.* **(**39 authors; T.G. Golos, senior/corresponding author). 2017. Highly efficient maternal-fetal transmission of Zika virus in pregnant rhesus macaques. PLOS Pathogens: **in press.**

- Full list of published work in My Bibliography, maintained by the US National Library of Medicine. http://www.ncbi.nlm.nih.gov/sites/myncbi/thaddeus.golos.1/bibliography/41146380/public/?sort=date&direction=descending

D. Research Support

List both selected ongoing and completed research projects for the past three years (Federal or non-Federally-supported). *Begin with the projects that are most relevant to the research proposed in the application.* Briefly indicate the overall goals of the projects and responsibilities of the key person identified on the Biographical Sketch. Do not include number of person months or direct costs.

ONGOING:
R21 HD091163-01 (P.I.: T. Golos) 09/21/16-08/31/18
NIH
Nonhuman Primate Model to Assess Embryonic Zika Virus Infection

The goal of this grant is to assess the tropism and impact of Zika virus with *in vitro* fertilized rhesus monkey embryos and assess risk for human infertility patients.

R01EY026045-01 (PI: J. Stout, subcontract PI: T. Golos) 05/01/16-03/31/21
NIH
Non-human Primate Models of Ocular Disease
The goal of this grant is to expand screen macaque populations for gene mutations associated with human eye diseases and propogate selected lines with a nonhuman primate breeding program. Dr. Golos will direct the rhesus monkey breeding program.

R24 OD021322-01A1 (PIs: I. Slukvin, T. Golos) 05/01/16-01/31/20
NIH/ORIP
CCR5-mutant monkey model to facilitate the development of novel stem cell-based therapies for AIDS
This grant will use CRISPR genomic editing to produce cynomolgus macaques carrying a Δ 32 mutation in CCR5 shown to be protective against HIV infection. Animals will be used as bone marrow donors for piloting BMT therapy for curing SIV infection.

U01 HD087216-01 (PIs: D. Shah, O. Wieben, co-investigator: T. Golos) 10/01/15-09/30/19
NIH
Advanced MRI for Uteroplacental Flow, Perfusion, Oxygenation & Inflammation
The goal of this grant is to develop new imaging approaches to assess placental structure and function, in real time, for the purpose of providing predictive value to MRI for adverse pregnancy outcomes.

R24 OD019803-01 (PIs: T. Golos, M. Emborg) 05/01/15-04/30/19
NIH/ORIP
Transgenic Marmosets for Translational Stem Cell Research.
The goals of this grant are to derive iPSC from the common marmoset, develop transgenic animals expressing an allele of LRRK2 associated with human Parkinson's disease, and determine the feasibility of genomic editing of marmoset embryos with the CRISPR/Cas9 system.

R01 AI107157-01A1 (P.I.: T. Golos) 08/01/14-07/31/18
NIH
The Maternal-Fetal Interface in Listeria-Induced Pregnancy Loss
The goal of this grant is to define the mechanisms by which infection with *Listeria monocytogenes* causes pregnancy loss in a rhesus monkey model by studying decidual and placental infection and inflammation.

P51 OD011106-53 (P.I: M. Mailick) 05/01/2017-04/30/2022
NIH
Wisconsin National Primate Research Center
The Primate Center base grant provides modest salary support for Dr. Golos' role directing an embryology core in the Scientific Protocol Implementation Unit.

COMPLETED:
R21 AI100156-01A1 (T. Golos, P.I.) 08/12/13-06/30/15
NIH
Primate Placental Immunogenetics
This grant aims to define rhesus placental MHC polymorphism, the diversity of putative receptors in endometrial NK cells, and identify receptors for the rhesus placenta-specific MHC I molecule.

P51OD01106-53S2 (PI: M. Mailick; Supplement PIs: T. Golos, M. Emborg)
NIH/ORIP 07/08/14-04/30/16
Supplement title: CRISPR/Cas9 Genomic Editing for a Nonhuman Primate Model of Parkinson's Disease.
The long-term goal of this work is to provide investigators with genetically modified common marmosets as platforms for translational research in the treatment of diseases where nonprimate species are less suitable models.