BIOGRAPHICAL SKETCH

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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 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. He has an ongoing funded R01 on nonhuman primate *in vivo Listeria* infection. These studies have extended to adapting cutting-edge MRI methodologies to detect inflammation associated with adverse pregnancy outcomes, in an animal model project within a newly-funded U01 in the Dept of Ob/Gyn.

A second major area has been the use of embryonic stem cells and IVF-derived primate embryos to model implantation and placental morphogenesis, with 2-dimensional and 3-dimensional modeling. Past studies also merged the two areas with development of approaches for placental transgene expression to manipulate placental function. We have an ongoing funded R24 NIH grant to derive iPS cells from the common marmoset, and to use transgenesis and CRISPR-mediated genomic editing to establish new approaches and resources for the application of nonhuman primates to translational medicine.

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
- Invited Speaker, Illinois Reproductive Sciences Symposium, 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)
- 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)

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. Recently our study of pregnancy has expanded to the use of experimental infection to understand the reproductive tract responses to pathogens during pregnancy.

Slukvin, I.I., D.I. Watkins and T.G. Golos. 2001. Phenotypic and functional characterization of rhesus monkey decidual lymphocytes: rhesus decidual large granular lymphocytes express CD56 and have cytolytic activity. *J. Reprod. Immunol*. 50:57-79.

Breburda, E.E, S.V. Dambaeva, I.I. Slukvin and T.G. Golos. 2006 Selective distribution and pregnancy-specific expression of DC-SIGN at the maternal-fetal interface in the rhesus macaque: DC-SIGN is a putative marker of the recognition of pregnancy. Placenta 27(1): 11-21.

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

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

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.

Wolfgang M.J., V.S. Marshall, S.G. Eisele, M.L. Schotzko, J.A. Thomson, and T.G. Golos. 2002. Efficient method for expressing transgenes in nonhuman primate embryos using a stable episomal vector. *Mol. Reprod. Dev.* 62:69-73.

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 ESC methodologies for *in vitro* trophoblast differentiation. The formation of the trophectoderm/trophoblast lineage from the human embryo is the first differentiation event, yet it is not amenable to direct study in human development. We developed a novel approach to the study of trophoblast differentiation during placentation and placental development with the use of embryonic stem cells and primate embryos to model implantation and placental morphogenesis. We developed novel 2-dimensional and 3-dimensional modeling, including Matrigel culture paradigms, to demonstrate robust trophoblast differentiation from human ES cells.

Gerami-Naini, B, O. Dovzhenko, M. Durning, F. Wegner, M., Thomson, J., and Golos, T.G. 2004. Trophoblast differentiation in embryoid bodies derived from human embryonic stem cells. *Endocrinology* 145:1517-1524.

Douglas, G.C., C.A. VandeVoort, P. Kumar, T.C. Chang, and T.G. Golos, 2009. Trophoblast stem cells: Models for Investigating Trophectoderm Differentiation and Placental Development. *Endocrine Reviews.* 30:228-40.

Golos TG, Giakoumopoulos M, Gerami, BG. 2013. Trophoblast differentiation from human embryonic stem cells. *Placenta* 34, Supplement A, Trophoblast Research 27: S56-S61.

- 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:

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.

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.

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.

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.

P51 OD011106-53 (P.I: M. Mailick) 05/01/2013-04/30/2017
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:
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.

P01-HD38843 (Ronald Magness, Ph.D., PI; Core B, Project IV: T. Golos, PI) 05/01/07-04/30/13
NIH
Regulation of Endothelial Cells and Embryonic Stem Cells in Pregnancy
This was a program project grant to investigate uterine and placental endothelial cell regulation *in vitro* and trophoblast differentiation of human embryonic stem cells**.**

R01 HD37120-06A2 (P.I: T. Golos) 08/31/09-06/30/13
NIH
Uterine NK Cells in Primate Pregnancy
This project examined implantation and pregnancy success in rhesus monkeys immunodepleted of peripheral blood NK cells.

R01 HD021876 (P.I: T. Golos) 04/01/06 – 03/31/12
NIH
Primate ES Cell Model for Embryo Implantation
The goal of this grant was to study trophoblast differentiation from rhesus monkey embryonic stem cells only.

R21 AI076734-01A1 (P.I: T. Golos) 07/01/08-05/31/12
NIH
Primate Endometrial Responses to Placental MHC Class I Molecules
The goal of this grant was to produce soluble Mamu-AG for *in vitro* and *in vivo* studies.