

## Transgenic Swine Program

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*Executive Summary:* The pre-weaning period constitutes a critical phase in pork production as this period represents the time of greatest animal morbidity and mortality. The 1991 U.S.D.A National Swine Survey on Morbidity/Mortality and Health Management of Swine in the U.S. estimated that overall pre-weaning mortality was 15%, that nearly all cases of morbidity and mortality occurred in piglets  $\leq 7$  days of age and that 58% of the cases of morbidity were reportedly due to scours and 30% of the mortality was attributed to scours or starvation. These statistics indicate that improving growth performance in the early neonatal period could have important economic significance for U.S. Agriculture. Two current management practices, namely larger litters and earlier weaning, have imposed a further need to optimize sow milk production. Despite the clear benefit to be gained by improving lactation performance, little progress has been made in this area through conventional technologies. The overall goal of the C-FAR Sentinel program was three-fold. Firstly, to provide the infrastructure support required to maintain existing lines of transgenic swine and to support the research outcomes necessary to obtain regulatory approval of these animals for human consumption by the FDA. Secondly, to support the development of accurate and precise analytical methods necessary to characterize the lines. Thirdly, to provide funds needed to develop new lines of transgenic swine with improved productivity and health. Our novel approach will be to focus on transgenes directed towards the mammary gland and intestinal mucosa. The advantages to this approach are that both milk production and intestinal nutrient delivery have both been identified as constraints on optimal piglet growth. Thus, we can use the mammary gland and gastrointestinal tract to drive piglet production. Secondly, as neither mammary tissue or intestinal mucosa are normally consumed by humans, this approach will reduce a number of potential regulatory hurdles associated with safety approval of the resulting lines of transgenic animals for human consumption by the Food and Drug Administration (FDA). The C-FAR Sentinel funding has provided a wealth of new scientific information regarding the mechanisms of lactation and intestinal function. Beyond the obvious benefit to our knowledge base it has also provided funds that have been leveraged to provide an additional \$2.4 million dollars for discovery research. The results from this funding have been disseminated in a variety of media and venues including 22 invited oral presentation, 22 abstracts at scientific conferences, 6 conference and popular press articles, 3 patent disclosures with one issued and one about to be issued patents, and 15 refereed journal articles with 2 more articles pending. The economic impact to the producers of this work has been conservatively estimated at between \$45million and \$450 million dollars per year additional revenue and/or production cost savings. The investment by C-FAR in this project has been instrumental showing the potential uses of biotechnology in swine production.

### *Primary Objectives and Goals:*

A major focus of swine production management is to maximize reproductive potential via selection for high genetic merit pigs. However, in order to gain utmost benefit from larger litter sizes, there is a clear need to improve swine milk production and composition, as low milk production influences all subsequent aspects of swine management. Despite the clear benefit to be gained by improving lactation performance, little progress has been made in this area through conventional technologies. Therefore, the long-range goal of our research is to optimize swine lactation performance and piglet growth and development through the application of transgenic technology.

Genetic engineering of plants and animals has been practiced for hundreds of years through the selection of high producing seed crops and livestock. However, recent advances in biotechnology are providing unique opportunities to further our ability to efficiently produce cost-effective, high quality food for human consumption. Transgenic technology, or the introduction of specific genes from one species into the germplasm of another, allows for the rapid and efficient introduction of value added characteristics into livestock, including swine. In production species, transgenic approaches currently focus on introducing genes, which 1) improve productivity traits; 2) enhance animal health; or 3) lead to the production of biomedically useful protein products. In the latter case, the mammary gland is most often targeted as a bioreactor for protein production and secretion into milk. Additionally, transgenic livestock can be used as models to address questions pertinent to human health and disease.

Our approach to developing transgenic swine has been to promote the mammary-specific overexpression of milk proteins with the goal of improving porcine milk composition and yield. Studies have shown that these two factors account for 44% of the pre-weaning growth of the piglets. Pre-weaning growth impacts subsequent animal performance and piglets below 6.5 to 7 pounds at weaning may be culled from the herd, rather than weaned, due to their diminished growth capacity during the grower and finishing stages. Thus, modification of milk yield and composition through transgenic technology provides an important tool for addressing the problem of low milk production and its detrimental impact on all subsequent phases of swine production.

We have concentrated on the mammary-specific over-expression of two multifunctional milk proteins: alpha-lactalbumin ( $\alpha$ -LAC) and IGF-I. Alpha-LAC provides a source of dietary amino acids for the piglet and, as a component of the lactose synthase complex within mammary epithelial cells, plays a critical role in regulating lactose synthesis. Our data demonstrate that the lactose concentration in colostrum and early milk of  $\alpha$ -LAC transgenic sows is significantly greater than their non-transgenic full-sib controls (Bleck et al. 1998). Lactose is the primary regulator of milk volume therefore over-expression of ( $\alpha$ -LAC within the mammary gland provides a means to increase sow milk production. Milk volume of  $\alpha$ -LAC transgenic sows is 20-50% higher in early lactation and growth of piglets suckling transgenic sows is significantly greater from d 9 to 21 postpartum than that of piglets suckling non-transgenic sows (Bleck et al. 1998; Noble et al. 2000). This finding marks the first experimental evidence that transgenic approaches can be used to enhance livestock production. Currently, the University of Illinois leads the nation in the production of transgenic swine with the goal of improving productivity traits and enhancing animal health.

### **Goals:**

The overall goal of obtaining support from the C-FAR Sentinel program was three-fold. Firstly, to provide the infrastructure support required to maintain existing lines of transgenic swine and to support the research outcomes necessary to obtain regulatory approval of these animals for human consumption by the FDA. Secondly, to support the

development of accurate and precise analytical methods necessary to characterize the lines. Thirdly, to provide funds needed to develop new lines of transgenic swine with improved productivity and health. Our novel approach was to focus on transgenes directed towards the mammary gland and intestinal mucosa. The advantages to this approach are that both milk production and intestinal nutrient delivery have both been identified as constraints on optimal piglet growth. Thus, we can use the mammary gland and gastrointestinal tract to drive piglet production. Secondly, as neither mammary tissue or intestinal mucosa are normally consumed by humans, this approach will reduce a number of potential regulatory hurdles associated with safety approval of the resulting lines of transgenic animals for human consumption by the Food and Drug Administration (FDA).

### ***Specific Objectives:***

*Objective 1.* To support research necessary to translate the existing lines of transgenic swine into commercially-viable, federally-approved, food sources for human consumption.

*Objective 2.* Development of accurate and precise analytical techniques for measurement of milk production and safety testing.

### ***Outcomes and Impacts:***

This focus of this research was to use biotechnology to develop new and improved animal systems, which will increase animal productivity and was most relevant to C-FAR Research Focus #3. In addition, aspect of the Transgenic Animal Program were also relevant to Research Focus #1 in that we developed technologies to expand markets for Illinois agricultural products. The Transgenic Swine Program also promoted the aspect of multi-disciplinary methods to implement increased productivity.

Outcomes: As a result of C-FAR support, the University of Illinois was the first in the county to obtain FDA approval for the introduction of transgenic animals into the food supply, although not into the human food supply as yet. We have also been able to garner ~ \$2.5M dollars in extramural grant support from the United States Department of Agriculture, the National Institutes of Health and private industry.

The production of  $\alpha$ -lactalbumin in and IGF transgenic swine supported the improvement of piglet growth and health in swine production systems. These observations have profound effects on milk and meat production. Our results demonstrated that mammary over-expression of milk proteins can impact milk production, milk composition and piglet growth. For example, piglets suckling  $\alpha$ -LA transgenic swine are ~ 10% heavier at weaning, on average of ~5 kilograms per litter. An economic assessment using 2003 production figures from USDA reveals that the increased production efficiency of an additional \$5.00 (\$.50/lb) per litter x 9 million litters/year in the U.S. equals approximately \$45 million additional income for pork producers. Further, the increased weaning weight has the potential to decrease the time that the pigs are on feed by 3-5 days. The potential additional savings on production costs from this is \$3-5/head X 90 million head marketed = \$270 - 450 million/year. These figures are very conservative since the additional savings from reduced labor, facilities, and manure produced are not taken into consideration in these calculations. In summary this technology could increase the profits for producers, while decreasing the environmental impact of the production of pork.

## **Outreach:**

### *Extension Teaching and Outreach:*

- “Production of Transgenic Swine,” Advanced Swine Production Technology Course, Department of Animal Sciences, University of Illinois, July 20, 2001. (Matthew Wheeler)
- “Production of Transgenic Swine,” Council for Food and Agricultural Research (CFAR) Campus Visit and Workshop, University of Illinois, Urbana, IL, November 13, 2001. (Matthew Wheeler)
- “Transgenic Animals”, NCSA-sponsored National Teacher Workshop, University of Illinois, July 10, 2002. (Matthew Wheeler)
- “Transgenic Pigs in Modern Swine Production”, Senators from France, January 31, 2003. (Matthew Wheeler)

### *Invited Presentations:*

- “You be the Scientists: Transferring Genes to Improve Sow Health,” National Association of State Universities and Land-Grant Colleges, Rayburn Congressional Office Building, Washington, D.C., March 7, 2000. (Matthew Wheeler)
- “Application of Cloning, Transgenic and Embryo Transfer Technologies to the Pork Industry,” American Association of Swine Practitioners Meeting, Indianapolis, IN, March 11, 2000.
- “Pig Embryo Manipulation Technologies,” International Conference of the 50th Anniversary of the First Pig Embryo Transfer, Ukrainian Academy of Agrarian Science, Kiev, Ukraine, May 17, 2000. (Matthew Wheeler)
- “Transgenic over-expression of bovine  $\alpha$ -lactalbumin and human IGF-I in porcine mammary gland: effects on lactation and piglet growth and development,” Centro de Biotecnologia, Universidade Federal do Rio Grande do Sul, Porto Alegre, RS, Brazil, August 29, 2000. (Matthew Wheeler)
- “Transgenic Alteration of Sow Milk: Production and Characterization of Bovine  $\alpha$ -Lactalbumin and Human IGF-I Transgenic Swine,” Faculdade de Veterinaria e Zootecnia, Universidade do Sao Paulo, Sao Paulo, SP, Brazil, August 31, 2000. (Matthew Wheeler)
- “Production of Alpha-Lactalbumin Transgenic Swine,” Faculdade de Veterinaria, Universidade Estadual Paulista, UNESP, Aracutuba, SP, Brazil, September 1, 2000. (Matthew Wheeler)
- “Production of Alpha-Lactalbumin Transgenic Swine,” Louisiana State University, Baton Rouge, LA, September 27, 2000. (Matthew Wheeler)
- “Transgenic Alteration of Sow Milk,” Korean Society of Animal Reproduction. October 20, 2000. (Matthew Wheeler)
- “Transgenic over-expression of bovine alpha-lactalbumin and human IGF-I in porcine milk: effects on milk composition and neonatal outcome” Presented as part of a symposium entitled “Biologically Active Peptides and Proteins in Milk,” 2001 ADSA-ASAS Joint Meeting, Baltimore, MD. (Sharon Donovan)
- “Transgenic Alteration of Sow Milk to Improve Piglet Growth and Health,” 6<sup>th</sup> International Conference on Pig Reproduction, University of Missouri-Columbia, June 6, 2001. (Matthew Wheeler)
- “Animal Biotechnology and the Law,” Illinois Judiciary Academy, University of Illinois School of Law, June 7, 2001. (Matthew Wheeler)
- “Transgenic Alteration of Sow Milk: Effects on Lactation, Piglet Growth and Development,” University of Arkansas-Fayetteville, March 15, 2002. (Matthew

- Wheeler)
- “Transgenic Livestock: Promise Fulfilled,” Lactation Symposium, ADSA-ASAS Joint Meeting, Quebec City, Canada, July 20, 2002. (Matthew Wheeler)
- “Lactation Performance and Piglet Development in Bovine  $\alpha$ -Lactalbumin and Human IGF-I Transgenic Swine,” Transgenic Animal Research Conference IV, Granlibakken Conference Center, Tahoe City, CA, August 10-14, 2003. (Matthew Wheeler)
- “Transgenesis in mammals: Status and perspectives”, Sociedade Brasileira de Transferencia Embrioes (SBTE) Annual Meeting, Berberibe, CE, Brazil, August 28-31, 2003. (Matthew Wheeler)
- “Over-expression of IGF-I on piglet intestinal growth,” Presented as part of a symposium entitled “Impact of Intestinal Development and Health on Growth,” 2003 ADSA-ASAS Joint Meeting, Phoenix, AZ. (Sharon Donovan)
- “Developments in in vitro technologies for swine embryo production”, International Embryo Transfer Society, January 2004. (Matthew Wheeler)
- “Animal Traceability: Transgenic Animals and Clones”, 1<sup>st</sup> Cross Campus Initiatives Food Safety Traceability Conference, October 27-28, 2004. (Matthew Wheeler)
- “Impact of Biotechnology on Animal Production, Sixth International Symposium on Animal Reproduction, Cordoba, Argentina, June 24-26, 2005. (Matthew Wheeler)
- “Use of Transgenic Swine to Study Growth and Development”, Sociedade Brasileira de Transferencia Embrioes (SBTE) Annual Meeting, Angra Dos Reis-RJ, Brazil, August 25-28, 2005. (Matthew Wheeler)
- “Insulin-like growth factors and intestinal development of artificially reared pigs and piglets suckling IGF-I transgenic sows,” International Symposium on Swine in Biomedical Research”, Chicago, IL, January 2005. (Sharon Donovan)
- “Effect of milk components on intestinal gene expression in the piglet model,” 2006 Meeting of the International Society for Research in Human Milk and Lactation. Niagara-on-the Lake, Ontario, Canada, September 19, 2006. (Sharon Donovan)

### *Publications:*

#### *Book Chapters:*

- Wheeler, M.B., Davidson, T.R., Malusky, S.A., Ferguson, C.E., Lima, A.S., Mello, M. B. 2006. PRODUCTION OF TRANSGENIC LIVESTOCK: Technology and Applications. In: Biotécnicas Aplicadas à Reprodução Animal, eds. P.B. Goncalves & J. Figuriado, (new edition in press).

#### *Refereed Journal Articles:*

- Miller, K.D., G.T. Bleck, T. Wang, R. Feltes, L.B. Schook, F.K. McKeith, M.B. Wheeler and M. Ellis. 2000. Association of the porcine  $\alpha$ -lactalbumin gene to growth, carcass, meat quality and reproductive traits. *J. Appl. Anim. Res.* 17:109-124.
- Donovan, S.M., M.H. Monaco, G.T. Bleck, J.B. Cook, M.S. Noble, W.L. Hurley and M.B. Wheeler. 2001. Transgenic over-expression of bovine  $\alpha$ -lactalbumin and human insulin-like growth factor-I in porcine mammary gland. *J. Dairy Sci.* 84 (E. Suppl.): E216-E222. ([http://www.adsa.org/jds/papers/2001/jds\\_es216.pdf](http://www.adsa.org/jds/papers/2001/jds_es216.pdf))
- Wheeler, M.B. and E.M. Walters. 2001. Transgenic technology and applications in swine. *Theriogenology* 56:1345-1370.
- Boston, W.S., G.T. Bleck, M.B. Wheeler and D.J. Miller. 2001. The effects of increased expression of  $\alpha$ -lactalbumin in transgenic mice on milk yield and pup growth. *J. Dairy Sci.* 84:620-622.

- Wheeler, M.B., G.T. Bleck and S.M. Donovan. 2002. Transgenic alteration of sow milk to improve piglet growth and health. *Reproduction* 58:313-324.
- Wheeler, M.B. 2000. Transgenic alteration of sow milk. *Korean J. Anim. Reprod.* 24:321-333.
- Noble, M.S., G.T. Bleck, S. Rodriguez-Zas, J.B. Cook, W.L. Hurley and M.B. Wheeler. 2002. Lactational performance of first parity transgenic gilts expressing bovine  $\alpha$ -lactalbumin in their milk. *J. Anim. Sci.* 80:1090-1096.
- Wheeler, M.B. and S.A. Malusky. 2003. Transgenesis in mammals: status and perspectives. *Acta Scientiae Veterinariae* 31:119-136.
- Wheeler, M.B., E.M. Walters and S.G. Clark. 2003. Transgenic animals in biomedicine and agriculture: outlook for the future. *Anim. Reprod. Sci.* 79:265-289. The 3<sup>rd</sup> most downloaded article in the journal from January – June 2004.
- Donovan, S.M., J.L. Hartke, M.H. Monaco and M.B. Wheeler. 2004. Over-expression of IGF-I: Effects on piglet intestinal growth. *J. Dairy. Sci.* 87:(E. Suppl.): E47-E54
- Wheeler, M.B. 2003. Transgenic livestock: Promise fulfilled. *J. Anim. Sci.* 81(Suppl.3)32-37.
- Hartke, J.L., M.H. Monaco, M.B. Wheeler and S.M. Donovan. 2005. Effect of a short-term fast on intestinal disaccharidase activity and villus morphology in piglets suckling insulin-like growth factor-I (IGF-I) transgenic sows. *J. Animal Sci.* 83:2404-2413.
- Monaco, M.H., D.E. Gronlund, G.T. Bleck, W.L. Hurley, M.B. Wheeler and Donovan, S.M. 2005. Mammary specific transgenic over-expression of insulin-like growth factor-I (IGF-I) increases pig milk IGF-I and IGF binding proteins, with no effect on milk composition or yield. *Transgen. Res.* 14:761-773
- Malusky, S.A. and M.B. Wheeler. 2005. Impact of biotechnology on animal production. *VI Simposio Internacional de Reproduccion Animal* 6:23-51.
- Marshall, K.M., W.L. Hurley, R.D., Shanks and M.B. Wheeler. 2006. Effects of suckling intensity on milk yield and piglet growth from lactation-enhanced gilts. *J. Anim. Sci.* 84:2346-2351.

*Conference Papers and Popular Press Articles:*

- Noble, M.S., M.B. Wheeler and W.L. Hurley. 2000. Alpha-lactalbumin: a limiting factor in milk production. Illinois Dairy Report: Managing the New Millennium, Illinois Agricultural Experiment Station p.42-43.
- Knox, R. and M.B. Wheeler. 2000. Genic Modification. Illinois Agrinews, 7/21/2000, pg/D7.
- Wheeler, M.B. 2000. Transgenic alteration of sow milk. Proceedings of the Korean Society of Animal Reproduction Annual Meeting, pg. 1-12, Seoul, Korea, October 20, 2000.
- Noble, M.S., M.B. Wheeler and W.L. Hurley, W.L. 2001. Association of Total Milk Solids Intake and Litter Growth: Data from  $\alpha$ -Lactalbumin Transgenic Sows. Illinois Swine Report: Illinois Agricultural Experiment Station pgs. 131-133.
- Wheeler, M.B., S.M. Donovan and W.L. Hurley. 2000. Transgenic Swine Program. C-FAR Connection Fall 2000, p.5.
- Etherton, T.D., D.E. Bauman, C.M. Beattie, R.D. Bremel, G.L. Cromwell, V. Kapur, G. Varner, M.B. Wheeler and M. Wiedmann. 2003. Biotechnology in animal agriculture: An overview. Council for Agricultural Science and Technology Issue Paper, 12 pgs.

*Abstracts:*

- Noble, M.S., M.B. Wheeler, J.B. McCook and W.L. Hurley. 2000. Milk production and piglet growth in first parity gilts transgenic for bovine  $\alpha$ -lactalbumin. *Theriogenology* 53:519.
- Monaco, M.H., G.T. Bleck, J.B. Cook, M.B. Wheeler and S.M. Donovan. 2000. Overexpression of insulin-like growth factor-I in milk of transgenic swine using the bovine  $\alpha$ -Lactalbumin Promoter and Regulatory Regions. *FASEB J.* 2000;14:A507.

- Donovan, S.M., M.H. Monaco, G.T. Bleck, J.B. Cook, M. Noble, M., W.L. Hurley and M.B. Wheeler. (2000) Transgenic over-expression of bovine  $\alpha$ -lactalbumin and human IGF-I in porcine mammary gland: effects on lactation and piglet growth and development. *J. Dairy Sci.* 83(Suppl. 1):9.
- Noble, M.S., G.T. Bleck, J.B. Cook, M.B. Wheeler and W.L. Hurley. 2000. Milk composition in early lactation is affected by expression of a bovine  $\alpha$ -lactalbumin transgene in sows. *J. Anim. Sci.* 78 (Suppl. 1):708.
- Wheeler, M.B. 1999. Transgenic alteration of sow milk: production and characterization of bovine  $\alpha$ -lactalbumin and human IGF-I transgenic swine. *Transgen. Res.* 8:474-475.
- Wheeler, M.B. 1999. Transgenic Alteration of Sow Milk: Production and Characterization Bovine  $\alpha$ -Lactalbumin and Human IGF-I Transgenic Swine. 2<sup>nd</sup> International Transgenic Animal Conference, Granlibakken Conference Center, Tahoe City, CA, August 15-18, 1999, pgs.28-29.
- Monaco, M.H., G.T. Bleck, J.B. Cook, M.B. Wheeler and S.M. Donovan, S.M. Mammary-specific overexpression of IGF-I in transgenic swine increases milk IGF-I and IGF binding protein-2 and -5. 10th International Conference of the International Society for Research on Human Milk and Lactation. Tucson, Arizona, September 2000.
- Monaco, M.H., J.B. Cook, K. Tappenden, M.B. Wheeler and S.M. Donovan. 2001. Intestinal lactase activity is increased in piglets suckling IGF-I transgenic sows. *FASEB J.* 15:A644.
- Monaco, M.H., J.B. Cook, S.M. Donovan, and M.B. Wheeler. 2002. Development of swine transgenic for bovine  $\alpha$ -lactalbumin and human insulin-like growth factor-I: data on milk composition, milk production and piglet growth. *Theriogenology* 57:784.
- Rudloff S., C. Herkel, G. Poblentz, M.B. Wheeler, M.H. Monaco, S.M. Donovan and C. Kunz. 2002 Total oligosaccharide and sialyl-lactose content are elevated in the colostrum of  $\alpha$ -lactalbumin transgenic pigs. *FASEB J.* 2002;16:A265.
- Wheeler, M.B. 2002. Transgenic livestock: Promise fulfilled. *J. Anim. Sci.* 80(Suppl. 1):6.
- Donovan, S.M., J.L. Hartke, M.H. Monaco, and M.B. Wheeler. 2003. Over-expression of IGF-I: Effects on piglet intestinal growth. *J. Dairy Sci.* 86 (Suppl. 1): 134.
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- Hartke, J.L., M.H. Monaco, M.B. Wheeler and Donovan, S.M.. 2003. Effect of a short-term fast on intestinal disaccharidase activity and villus morphology in piglets suckling insulin-like growth factor-I (IGF-I) transgenic sows. *J. Dairy Sci.* 86 (Suppl. 1): 134.
- Hartke, J.L., M.H. Monaco, M.B. Wheeler and S.M. Donovan. 2003. Intestinal growth and development in piglets suckling insulin like growth factor-I (IGF-I) transgenic sows. *J. Dairy Sci.* 86 (Suppl. 1): 311.
- Gronlund, D.E., W.L. Hurley, M.H. Monaco, M.B. Wheeler and S.M. Donovan. 2003. Over-expression of insulin-like growth factor-I in lactating porcine mammary tissue has a differential effect on amino acid transport systems. *J. Dairy Sci.* 86 (Suppl. 1): 190.
- Marshall, K.M., R.D. Shanks and M.B. Wheeler. (2003) Increased nursing intensity stimulated greater lactational response in sows expressing a bovine alpha-lactalbumin transgene. *Biol. Reprod.* 68 (Suppl. 1) 202.
- Marshall, K.M., R.D. Shanks, R.D., W.L. Hurley, S.M. Donovan and M.B. Wheeler. (2004) Effect of increased suckling stimulation on piglet weight gain and daily milk yield of sows transgenic for bovine  $\alpha$ -lactalbumin. *Reprod. Fertil. Devel.* 16:291, abstr. 342.
- Monaco, M., M. Wheeler and S. Donovan. (2005) Transgenic over-expression of IGF-

- Imodulates the synthesis and secretion of pig milk IGFBP-2 and -5 in the early and post-lactation periods. *J. Dairy Sci.* 88 (Suppl. 1): 282.
- Hartke, J., M. Monaco, R. McCusker, M. Wheeler and S. Donovan. (2005) Small intestinal IGF-binding protein (IGFBP)-2 and -5 and IGF receptors in piglets suckling IGF-I transgenic sows. *J. Dairy Sci.* 88 (Suppl. 1): 282.
- Hartke J.L., J.M. Drnevich, M.B. Wheeler and S.M. Donovan. 2006. Transgenic Overexpression of Insulin-Like Growth Factor-I (IGF-I) in Milk Influences Intestinal Development and Gene Expression in Piglets. 13th Int. Conference Int. Soc. Research Human Milk and Lactation, Niagara-on-the-Lake, Ontario, Canada, September 22-26, 2006.
- Marshall, K.M., W.L. Hurley, R.D. Shanks and M.B. Wheeler. 2007. Effects of suckling intensity on milk yield and piglet growth from lactation-enhanced gilts. *Reprod. Fertil. Devel.* (accepted).

*Patents and Disclosures:*

- Wheeler, M.B., Donovan, S.M., Bleck, G.T., Monaco-Seigel, M. "Production of Transgenic Pigs Containing the Gene Encoding Human Insulin-Like Growth Factor I (IGF-I) Under Control of the Bovine  $\alpha$ -Lactalbumin Promoter and Regulatory Regions, a disclosure, RTMO, UIUC, July 2000.
- Wheeler, M.B., Donovan, S.M., Bleck, G.T., Monaco-Siegel, M. "Animals Expressing Exogenous IGF-I in Their Milk", U.S. Patent Application # T00086, May, 2000. November 6, 2000.
- Wheeler, M.B., Donovan, S.M., Bleck, G.T., Monaco-Seigel, M. "Animals Expressing Exogenous IGF-I in Their Milk", PCT Application Number WO 02/14473 A2, February 21, 2002.
- Wheeler, M.B., Donovan, S.M., Bleck, G.T., Monaco-Seigel, M. "Animals Expressing Exogenous IGF-I in Their Milk." U.S. Patent 6,677,500, issued January 13, 2004.

*Grants Funded: (Total of \$2,400,409 funded and pending funds):*

- Production of Nuclear Transfer Transgenic Pigs, \$1,203,098, Infigen, Inc. DeForest, WI, January 1, 2000-December 31, 2001, funded. (Wheeler MB [PI])
- Impact of IGF-I Overexpression in Pig Mammary on Lactation and Piglet Intestine. \$328,918, USDA NRICGP AG-00-35206; 10/00-9/03 (funded). (Donovan SM [PI], Hurley WL, Wheeler MB [Co-PI])
- Risk Assessment of  $\alpha$ -Lactalbumin Transgenic Pigs \$371,952, USDA CSREES (funded) 9/1/05-8/30/08. (Wheeler MB [PI])
- Enhancing Internationalization of Teaching, Research, and Extension Programs Through a Student-Centered Learning Abroad Program, (Co-P.I., 5% effort), \$100,545, USDA (funded). (Hurley, WL, [PI], Wheeler MB [Co-PI])
- Neonatal Dietary Lipids and Genetics: Effects on Brain Development and Learning Behavior, \$395,896, NIH NIMH (PA-06-181), 1/1/07-21/31/08 (pending). (Wheeler MB [Co-PI]).