



O.P.P.

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Genetic association of *Ovar-DRB1* with ovine progressive pneumonia virus (OPPV): A Next Phase in Genotyping Sheep?

(Article prepared for the OPP Concerned Sheep Breeders Society at the Board's request)

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Ovine progressive pneumonia virus (OPPV) is a lentivirus, which is horizontally transmitted predominantly through direct contact of infected adult animals with naive animals and affects the lungs, mammary gland, joints, and in rare cases, the brain of infected sheep. One in five are infected with OPPV within the United States, and this increases to one in two sheep in open range-land sheep. It is estimated that OPPV costs 2.7 million dollars annually to the U.S. Sheep Industry, and the presence of OPPV in ewes has been recently shown in Canada to significantly lower weaning weights and increase lamb mortality. The vast majority (70-80%) of OPPV infected sheep do not manifest outward clinical signs in the forms of respiratory distress, mastitis, arthritis, wasting, and ataxia. The disease is typically insidious and inconspicuous whereby producers often times do not know they have the infection in their flock unless they test serum from the whole flock for the presence of anti-OPPV antibodies.

OPPV diagnosis is confirmed by detecting anti-OPPV antibodies in the serum of sheep 1 year of age and older using a competitive enzyme linked immunosorbent assay (cELISA) or agar gel immunodiffusion assay (AGID). In addition, diagnosis can now be confirmed by quantifying OPP virus levels in the peripheral blood leukocytes of sheep using a new, validated OPPV real-time quantitative PCR (qPCR) assay. These diagnostic tests are highly sensitive and specific, but because of the insidious nature of OPPV, in order to keep an OPPV free flock, annual diagnostic testing for at least 3 years and testing of new flock members prior to placing them into the flock is strongly recommended. Because of this, diagnostic testing can be quite expensive. In a flock of 500, cELISA tests can approach \$2-2.5K per year and OPPV qPCR can approach 10-times the cost of cELISA per year. Some other test is needed to help lower OPPV seroprevalence while keeping the cost low for producers.

The obvious and best example of a test that helps to lower disease incidence is genotyping at codon 171 in the prion gene (PRNP) for scrapie. Removing animals with homozygous PRNP genotypes encoding for Q at codon 171 (QQ171) has greatly aided the sheep industry in reducing scrapie incidence. Although initial costs for genotyping are high whereby a flock of 500 would cost ~\$5.5K, this price substantially lowers after the first year when only rams and new ewes are tested.

... Genotyping, continued on page 5

MSU Names OPP-Savvy Producer/Researcher/Educator

Dr. Richard Ehrhardt

New Small Ruminant Specialist — January 2009

Press Release from Michigan State University

EAST LANSING, Mich. -- Richard Ehrhardt will be joining the faculty in the departments of Animal Science and Large Animal Clinical Sciences at Michigan State University (MSU) as an Extension specialist focusing on small ruminant management, effective Jan. 1, 2009.

He will be responsible for providing leadership to maintain the competitiveness of Michigan's sheep and goat industries. This will include conducting research and working with faculty members across the MSU College of Agriculture and Natural Resources to address issues related to small ruminant production, management and health. As part of the MSU Extension system, he will work with the county-based educator network to disseminate research-based information across the state.

"OPPV is a disease caused by the maedi visna virus that greatly reduces ewe productivity and eventually becomes a terminal illness."

Dr. Richard Ehrhardt
<http://ehrhardtfarm.com>

... Ehrhardt, continued on page 6

Why SFCP? My Perspective

By: Mark Lelli, DVM
Muleflock@aol.com

Editor's note: This article first appeared in the Bluefaced Leicester Breeders Association newsletter and is used here with permission.

Changes in USDA rules that regulate importation of ovine semen from countries other than AU and NZ, allow producers to import and use imported semen in any flock that's listed in the scrapie national database (i.e. the "mandatory" program). These rules also require that records of any sale of F1 progeny including buyer information be kept for 5 years and made available to an APHIS representative on request. Rules pertaining to scrapie surveillance of the exporting country and the donor animals remain unchanged. For the most part these countries use OIE¹ guidelines for their animal health regulations and often meet or exceed our importation requirements. In June of 2007, USDA APHIS revamped the standards for flocks enrolled in its voluntary scrapie surveillance program, (SFCP). These rule changes put additional burdens on enrolled producers. Most notably, all animals over 14 months of age found dead must be reported. For complete monitored flocks the producer may or may not be required to arrange for fallen stock to be processed and evaluated for scrapie as designated in appendix 1 of the SFCP standards. For export monitored flocks, all fallen stock over 14 months of age or that has lambled in the flock must be processed in such a manner in addition to other more stringent requirements. So what is the point of all this?

For some time now USDA has prohibited the importation of live animals and embryos of certain species, mostly because there has been no effective mechanism in place to contain and monitor these animals and their progeny for specific diseases. This responsibility is not just from a need to maintain the health of the national flock/herd and food supply, but also to address the concerns of the constituency to which the USDA answers; the American consumer. For sheep, the revamped SFCP rules will help move the surveillance of scrapie in enrolled US flocks to a level equal to that of the international community. I see this as the mechanism needed to begin a process that could open the door for exportation of live animals and other sources of germplasm, (embryos), to Canada and other countries and possibly also facilitate importation. Although new import requirements have not been proposed yet, the current inclination is to move closer to the OIE guidelines². SFCP export certification does just that. In the end, I suspect flocks wishing to import such will be required to be export certified. So how hard is that?

Becoming SFCP export certified shouldn't be that difficult for most small purebred flocks as long as;

- 1) Those flocks are maintained in such a manner that they do not experience high adult losses from endemic infectious diseases or poor management.
- 2) It is economically feasible to codon test all animals in the flock and live animal test* all animals in the flock that are considered 'genetically susceptible animals' as defined in the SFCP program standards.

The new program standards will result in higher producer costs in most circumstances. However, it also increases the overall value of those flocks that are able to comply with the requirements leading to certification in the complete monitored or export monitored categories.

Since the inception of the SFCP, importation of semen from countries not considered scrapie free resulted in considerably improvement in the genetic base of many purebred flocks in the US. Unfortunately, there are many breeds in the EU that have the genetic diversity we need but do not have. These purebred genetics will become essential as we move from a grain based lamb production model to a balance of forage and grain finish in our market lambs. The bottom line is that as sheep producers we could move forward with this transition at a faster rate if we were allowed to import embryos or live animals of breeds that could assist us in those endeavors. To that extent, USDA/APHIS should assist us as if we are to participate in program that matches that of the countries we wish to import from.

1) The World Organization for Animal Health (OIE)

2) OIE Terrestrial Animal Health Code (2007) CHAPTER 1.4.1.
http://www.oie.int/eng/normes/mcode/en_chapitre_1.4.1.htm

* USDA APHIS now accepts the rectal biopsy test anywhere in the scrapie program where the use of an antemortem test for scrapie is authorized.

Update: OPP A RISK FACTOR IN THE TRANSMISSION OF SCRAPIE?

Readers will recall Dr. Mark Lelli's 2006 article about ongoing research in Switzerland led by Professor Adriano Aguzzi at the Institute of Neuropathology, University Hospital of Zurich. Aguzzi and his team were investigating the possibility of concurrent disease (scrapie plus maedi visna/OPP) increasing risk for TSE transmission. The following papers, including one just brought to our attention by Mark earlier this month, build on Aguzzi's work. Only abstracts and summaries printed here. Note URLs to read complete text online.

Evidence of scrapie transmission via milk **BMC Veterinary Research 2008, 4:14**

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Publication date 8 April 2008

Article URL <http://www.biomedcentral.com/1746-6148/4/14>

Abstract

Background

The risk of scrapie infection increases with increased duration and proximity of contact between sheep at lambing. Scrapie infectivity has not been detected in milk but cellular prion protein, the precursor of disease-associated prion protein PrP^{Sc}, has been found in milk from ruminants. To determine whether milk is able to transmit scrapie, 18 lambs with a prion protein genotype associated with high susceptibility to scrapie (VRQ/VRQ) were fed milk from twelve scrapie-affected ewes of the same genotype, and 15 VRQ/VRQ sheep reared on scrapie-free dams served as controls.

... *Scrapie transmission, continued next page*

Results

Three lambs fed milk from scrapie-affected ewes were culled due to intercurrent diseases at 43, 44 and 105 days of age respectively, and PrPd was detected in the distal ileum of the first two lambs, whilst PrPd was not found in lymphoreticular tissues in the third lamb. A control lamb, housed in a separate pen and culled at 38 days of age, was also negative for PrPd in a range of tissues. Samples of recto-anal mucosa associated lymphoid tissue collected from the remaining 15 live lambs at seven months of age (between five to seven months after mixing) were positive for PrPd in the scrapie milk recipients, whereas PrPd was not detected in the remaining 14 controls at that time. A subsequent sample collected from control lambs revealed PrPd accumulation in two of five lambs eight months after mixing with scrapie milk recipients suggestive of an early stage of infection via lateral transmission. By contrast, the control sheep housed in the same building but not mixed with the scrapie milk recipients were still negative for PrPd.

Conclusions

The presence of PrPd in distal ileum and rectal mucosa indicates transmission of scrapie from ewe to lamb via milk (or colostrum) although it is not yet clear if such cases would go on to develop clinical disease. The high level of infection in scrapie-milk recipients revealed by rectal mucosal testing at approximately seven months of age may be enhanced or supplemented by intra-recipient infection as these lambs were mixed together after feeding with milk from scrapie-affected ewes and we also observed lateral transmission from these animals to lambs weaned from scrapie-free ewes.

Prions in Milk from Ewes Incubating Natural Scrapie

Caroline Lacroux¹, Stéphanie Simon², Sylvie L. Benestad³, Séverine Maillet², Jacinthe Mathey¹, Séverine Lugan¹, Fabien Corbière¹, Hervé Cassard¹, Pierrette Costes¹, Dominique Bergonier¹, Jean-Louis Weisbecker⁴, Torffin Moldal³, Hugh Simmons⁵, Frederic Lantier⁶, Cécile Feraudet-Tarisse^{1,2}, Nathalie Morel², François Schelcher¹, Jacques Grassi², Olivier Andréoletti¹, (o.andreoletti@envt.fr)

1 UMR INRA ENVT 1225, Interactions Hôte Agent Pathogène, Ecole Nationale Vétérinaire de Toulouse, Toulouse, France; **2** CEA, Service de Pharmacologie et d'Immunoanalyse, IBItec-S, DSV, CEA/Saclay, Gif sur Yvette, France; **3** National Veterinary Institute, Sentrum, Oslo, Norway; **4** INRA Domaine de Langlade, Pompertuzat, France; **5** VLA Weybridge, New Haw, Addlestone, Surrey, United Kingdom; **6** INRA IASP, Centre INRA de Tours, Nouzilly, France

Publication date 12 December 2008

Article URL <http://www.plospathogens.org/article/info%3Adoi%2F10.1371%2Fjournal.ppat.1000238>

Abstract

Since prion infectivity had never been reported in milk, dairy products originating from transmissible spongiform encephalopathy (TSE)-affected ruminant flocks currently enter unrestricted into the animal and human food chain. However, a recently published study brought the first evidence of the presence of prions in mammary secretions from scrapie-affected ewes. Here we

report the detection of consistent levels of infectivity in colostrum and milk from sheep incubating natural scrapie, several months prior to clinical onset. Additionally, abnormal PrP was detected, by immunohistochemistry and PET blot, in lacteal ducts and mammary acini. This PrP^{Sc} accumulation was detected only in ewes harbouring mammary ectopic lymphoid follicles that developed consequent to Maedi lentivirus infection. However, bioassay revealed that prion infectivity was present in milk and colostrum, not only from ewes with such lymphoproliferative chronic mastitis, but also from those displaying lesion-free mammary glands. In milk and colostrum, infectivity could be recovered in the cellular, cream, and casein-whey fractions. In our samples, using a Tg 338 mouse model, the highest per ml infectious titre measured was found to be equivalent to that contained in 6 µg of a posterior brain stem from a terminally scrapie-affected ewe. These findings indicate that both colostrum and milk from small ruminants incubating TSE could contribute to the animal TSE transmission process, either directly or through the presence of milk-derived material in animal feed-stuffs. It also raises some concern with regard to the risk to humans of TSE exposure associated with milk products from ovine and other TSE-susceptible dairy species.

Author Summary

A decade ago, a new variant form of Creutzfeldt-Jakob disease was identified. The emergence of this prion disease in humans was the consequence of the zoonotic transmission of bovine spongiform encephalopathy through dietary exposure. Since then, the control of human exposure to prions has become a priority, and a policy based on the exclusion of known infectious materials from the food chain has been implemented. Because all investigations carried out failed to reveal evidence of infectivity in milk from affected ruminants, this product has continuously been considered as safe. In this study, we demonstrate the presence of prions in colostrum and milk from sheep incubating natural scrapie and displaying apparently healthy mammary glands. This finding indicates that milk from small ruminants could contribute to the transmission of prion disease between animals. It also raises some concern with regard to the risk to humans associated with milk products from ovine and other dairy species

“Young Americans will learn to be shepherds.”

So says Li Edelkoort, trend forecaster with agents on five continents and more than 1,500 clients. The Dutch-born Edelkoort, 58, interviewed in New York by *Fast Company* magazine (October 2008), envisions how we'll work, live and eat in the years to come. Among her predictions:

Rural will rule: “Farmers will be the new oil barons.”

Animal husbandry will be a promising new career: “Young Americans will learn to be shepherds.”

Cities will become countrified, with parks, landscaping, and ‘vertical agriculture’ (multiple floors). “You could go to your next-door building and it will be a fresh market.”

Ed note: Since Edelkoort's usual specialty areas are fashion and architecture, you may want to sprinkle those predictions with a grain of salt. Interesting nonetheless.

Stefania's Legacy

Stefania Dignum, a longtime member and one of the first to write about her experience with OPP, passed away last year. An extensive article in the July and August 2008 issues of *The Shepherd* details the fascinating story of Stef's importation of sheep from her native Iceland — the first of that breed to arrive on this continent.

Stefania will be remembered not only for having introduced Icelandic Sheep to North America, but also for the following description of a typical OPP ewe which first appeared in *The Shepherd* magazine and which we continue to quote in various publications.

DESCRIPTION OF A TYPICAL OPP EWE

"Let's suppose that I have a good ewe lamb that I breed to lamb at two years of age. She gives me a single, a lovely strong lamb. I forgive her for giving me a single since it is her first and she is a twin herself. Next year I get twins from her. Those are also nice but not quite a good as the previous one. That is assumed natural since they are twins. Mother is now three and since she raised twins she is not in as good a condition going into breeding as she was the previous year. In next lambing—she is now four—she twins again and this time the twins are born a good size but fail to thrive. And mother is positively thin after raising these two. At this time many would decide to sell the ewe, either (hopefully) to slaughter or to someone looking for cheap breeding stock. After all, the ewe is only 4-1/2 years old. If she has been sold for breeding, (good buy, she is a twinner and should have a few years left) she will probably be dead two years later. This would be a typical OPP ewe."

STEFANIA DIGNUM (1945—2007)
Renowned Icelandic Breeder
The Shepherd magazine, 1989

NEW PROMOTIONAL ITEM

Shown below are both sides of a new info card, available now in packs of 24 — no charge. If you can help distribute these, please let us know well in advance.

Photos: Karen Kenagy (Katahdin, OR), Oogie McGuire (Black Welsh Mountain, CO), Jean Walsh (Suffolk, NY), Judy Lewman (Border Leicester, MN). Additional breeds will be considered for future editions so send us your best shots!



. . . the silent thief



Ovine Progressive Pneumonia (OPP) in sheep and **Caprine Arthritis-Encephalitis (CAE)** in goats are caused by small ruminant lentiviruses. OPPV infects 36% of flocks nationwide (USDA, 2001) and negatively impacts production. While there is no cure, both viruses can be eradicated by rigid culling or orphaning of replacement stock.

Established in 1990 with a mission to build awareness and provide education, the **OPP CONCERNED SHEEP BREEDERS SOCIETY** also serves as a support network for producers working to control or eliminate OPP and CAE. For further information, see www.OPPsociety.org

We invite you to join us! Membership — open to all — is not intended to indicate freedom from OPP or CAE, but rather active concern about the effects of these and other diseases within our own flocks/herds and within the sheep and goat industry as a whole.

YES, I WOULD LIKE TO SUPPORT THE WORK OF THE OPP SOCIETY!

NAME _____

STREET _____

CITY _____ STATE _____ ZIP _____

PHONE _____ EMAIL _____

PLEASE RETURN WITH YOUR DUES (\$15/YEAR; \$25/2 YRS; \$50/5 YRS) TO:

JEAN T WALSH, TREASURER
228 MAIN STREET
JORDANVILLE, NY 13361

"I liken OPP in the flock to having a permanent nose bleed, might not kill you in the short run, but eventually — if it begins to bleed heavier (higher percentage) — it weakens the overall system and reduces the body's ability to work at peak efficiency."

GENE SCHRIEFER
PRODUCER/EDUCATOR

"In some flocks, I think the disease has crept in so slowly and quietly that the owners don't recognize how much more production would be possible if the sheep did not have the infection."

CINDY WOLF, DVM
UNIVERSITY OF MINNESOTA

"I have observed a growing awareness of OPP, and remarkably accurate knowledge among producers as to how to eradicate this costly disease, thanks to the efforts of the OPP Concerned Sheep Breeders Society."

JANET McNALLY
PRODUCER/EDUCATOR

Genotyping, continued from cover . . .

Previous research papers showed that the Rambouillet breed had the lowest ovine progressive pneumonia virus (OPPV) seroprevalence as compared to other breeds including Columbia, Polypay, and Finnsheep cross breeds. In addition, monozygotic (identical) twins shared similar lung pathology at post-mortem after each twin was infected with a different strain of OPPV, but between the monozygotic twin sets, there were significant pathological differences in the lung. These early studies strongly suggested that there was a host genetic factor that could be affecting OPPV infection status.

Our laboratory at USDA-ARS Pullman, WA is currently evaluating several sheep genes for links to higher or lower OPP provirus levels. One host gene, Ovis aries (Ovar)-DRB1, is of particular interest since it has been described as a putative cellular receptor for OPPV and is currently being evaluated for associations to ovine progressive pneumonia (OPP) provirus levels in 383 Idaho sheep of the Rambouillet, Columbia, and Polypay breeds. In this first study, there are several Ovar-DRB1 genotypes (Y31, T32, N37, T51, Q60 or N74) that associate with lower OPP provirus levels. Five of six of these OPP provirus level-lowering Ovar-DRB1 genotypes are also predominantly found in the Rambouillet breed. In contrast, there are three Ovar-DRB1 genotypes encoding for H32, A38, or I67 that associate with higher OPP provirus levels, and these genotypes are found in all three breeds. Overall, these association results suggest that specific genotypes in Ovar-DRB1 contribute as OPP provirus level controllers especially in the Rambouillet breed. **However, prior to implementing breeding strategies, production trait analyses needs to be performed to ensure there are no links between a specific Ovar-DRB1 genotype and undesirable production traits.** Our collaborators, Dr. Michelle Mousel and Dr. Gregory Lewis, at the U.S. Sheep Experiment Station (USSES) in Dubois, Idaho are currently evaluating production traits in relationship to the Ovar-DRB1 findings.

In summary, if you are running Rambouillet sheep, you may already have lower OPP provirus levels in your flock. We are working on a high-throughput, low cost genetic test to determine the presence of these OPP provirus load-lowering genotypes. If you have flocks with some Rambouillet sheep, Ovar-DRB1 may be a future genetic tool for lowering OPP provirus load in your flock. Our study has only examined the Rambouillet, Columbia and Polypay breeds; therefore, extending these results into other breeds should not be done. Further investigations in more breeds in flocks with >50% OPPV seroprevalence will establish whether these and/or other DRB1 genotypes significantly associate with OPP provirus levels.

2009 Member List Coming Soon

ARE YOUR DUES CURRENT?

— You can check at www.OPPsociety.org —

The date in parentheses following your name on the member list (or mailing label) indicates the year through which dues have been paid. Thank you!

New and Returning Members:

We welcome the following. For more information, please see member directory at www.OPPsociety.org

Marcia Barinaga, Katahdins, California
415-663-8870, barinaga@earthlink.net

Nancy and Bill Dieterle, Dairy Goats, Pennsylvania
724-785-8916, die8036@cup.edu

Patrick and Beth Downing, Katahdins, New York
518-483-2391, downing_acres@yahoo.com

Ray & Margo Hanson, Border Leicesters, Minnesota
218-584-5545, rmhanson@arvig.net

Karen Kenagy, Katahdins, Oregon
503-266-6702, KRKenagy@hotmail.com

David and Carol Ray, Border Leicesters, Wisconsin
608-489-2329, ingreenpastures@mwt.net

EDITOR'S NOTE:

A non-shepherd friend sent the following poem awhile back, saying that it reminded her of us. While not quite sure how to interpret that, the words about thin Montana sheep brought back distant memories of well intentioned but devastating advice offered to commercial producers long before the words "Ovine Progressive Pneumonia" ever hit the popular press. Proponents arranged large imports of cull ewes off the Western range as low-cost replacements for Midwestern flocks, the theory being that the aged ewes would be productive for a few more years under more intensive management. The combination of OPPV infected animals (nearly one in two sheep on the open range carry the virus; USDA, 2001) and close confinement (i.e., winter lambing in closed barns) created the perfect storm . . . the result being that 45% of Midwestern flocks are now infected with OPPV.

A Farm in Western Minnesota

by Robt Bly, Minnesota's Poet Laureate

When I look at childhood, I see the yellow rosebush
Grandma planted near her door, the gravel
Beneath the bicycle tires, and the new legs pumping
As we raced along; and the roads that invited us
West—only a mile from home the land began to rise.

We tried those wind chargers. My father
Was open to any new idea, and one day
A thousand sheep—starving—arrived in cattle cars
From Montana—almost free. We took four
Hundred. How thin they were! Some lived for years.

Many rooms were cold at night, and the hired men
Didn't have much of a life. Sometimes they'd just leave.
I remember my father throwing dead ewes over
The edge of the gravel pit. It was efficient. There
Was work to do, but no one learned how to say goodbye.

UPDATE:**OPP/CAE Test & Control Pilot Program (MN)**

The following flocks have reached 'Test-Negative' status under the '3-Year' test protocol in the trial program offered as an add-on component of the Scrapie Flock Certification Program (SFCP) by the Minnesota Board of Animal Health in cooperation with USDA APHIS Veterinary Services and the OPP Concerned Sheep Breeders Society.

Michael Curley, DVM, Windom, MN (Suffolk)
507-822-1672, mikec@rconnect.com

Ray & Margo Hanson, Twin Valley, MN (Border Leicester)
218-584-5545, rmhanson@arvig.net

Judy & John Lewman, Minnetrista, MN (Border Leicester)
952-472-4524, JL6250@visi.com

Tom & Judy McDowell, Minnetrista, MN (Icelandic)
952-472-0883, mistymeadowicelandics@yahoo.com

Bets Reedy, Houston, MN (Clun Forest)
608-489-2329, bramble@acegroup.cc

Flocks below have selected the '5-Year' test option and are moving through the program with no positives detected to date.

Tim Reese, Minnetrista, MN (Clun Forest,
Finnsheep, Border Leicester)
763-694-2002, TReese@threeriversparkdistrict.org

Scott Wollin, Karlstad, MN (Polypay, Dorset,
Hampshire, Boer Goats)
218-436-2974, swollin@wiktel.com

Additional OPP Pilot enrolled flocks are undergoing eradication.

Ehrhardt, continued from cover . . .

Ehrhardt will also work with veterinarians in the CVM Department of Large Animal Clinical Sciences to train future professionals in ruminant care and with the Diagnostic Center for Population and Animal Health to address the diagnostic and medical issues facing sheep and goat owners.

"I am very pleased that Dr. Ehrhardt has accepted this position," says Karen Plaut, chairperson of the MSU Department of Animal Science. "He offers experience in ruminant nutrition, physiology and reproduction, and an extensive teaching and research background, and he is solidly grounded in the sheep industry as a manager and breeder. It's the perfect combination that MSU needs to move our small ruminant program into the future."

Ehrhardt holds doctoral and master's degrees in animal science from Cornell University and a bachelor's degree in animal science from the University of Wisconsin.

Ehrhardt comes to MSU from Cornell University, where he has served as a research associate in the Department of Animal Science investigating metabolic regulation in ruminants. His Extension work experience includes conducting on-farm research and offering presentations at producer events. He has also taught undergraduate courses and supervised research for undergraduate and graduate students at Cornell.

Ehrhardt will be housed in the Department of Animal Science in Anthony Hall. The department phone number is 517-355-8383.

Editor's note: Read more at — <http://ehrhartfarm.com> — or meet Dr. Ehrhardt at the MI Shepherd's Weekend, January 3-4 in Lansing.