

**FINAL REPORT 1/22/2018: American Sheep Industry Association *Let's Grow Program***  
**PROJECT TITLE: GM1 SHEEP PRODUCTION FOR HUNTINGTON'S DISEASE:  
TRAINING VIDEOS, RECORD MANAGEMENT, AND COOPERATOR  
COMMUNICATIONS**

**Project Leaders: Susan Holler and Mina Doerner**

**Organization Submitting: Dakota Lamb Growers Cooperative**

*Let's Grow Program Grant Awarded 5/15/2016*

### **Project Summary**

In December 2015, the American Sheep Industry Association's *Let's Grow Program* "Second Round of Funding" funded a joint initiative (Project Title: GM1 Sheep Production for Huntington's Disease) by GlycoScience Research, Inc. and the Dakota Lamb Growers Co-op to create a series of educational outreach videos to be used to build awareness of the GM1 production project among sheep producers. These videos are intended to grow the participating numbers of cooperators, thereby providing a safe and plentiful source of GM1 ganglioside for therapeutic use for clinical trials in Huntington's disease (a fatal progressive genetic neurologic disease). Our second project, GM1 Sheep Production for Huntington's Disease: Training Videos, Record Management, and Cooperator Communications, builds upon the previous project by providing detailed information to cooperating sheep producers (cooperators) participating in the GM1 project. Participating cooperators will be able to access training materials covering crucial techniques and record management. Potential cooperators can learn details of the GSR contract, genetic traits of the GSR rams, and care requirements of GM1 gangliosidosis-affected lambs. Record management is of particular importance to ensure the success of the GM1 project because the FDA requires strict records be kept for pharmaceutical tracking.

*Let's Grow Program* funds were used to produce a series of training videos which were widely distributed via YouTube and social media and to GM1 project cooperators via flash drive content. The training videos were designed as a series of short videos which can be viewed individually as needed for instruction on record keeping (ear tags systems and blood tube labeling), blood sample collection, and packing of samples for shipment to the genetic testing site. The American Sheep Industry Association's *Let's Grow Program* is acknowledged in each video. Flash drives all include the *Let's Grow Program* logo on one side of the case, with GSR on the reverse.

A temporary Project Coordinator (paid internship) was charged with developing an effective communication protocol to allow cooperators to coordinate blood sample collection and affected lamb deliveries to GSR for processing; this communication protocol was designed to increase efficiency and productivity by all participants in the GM1 project. The Project Coordinator was also tasked with creating a record keeping system and a robust record management tool that will be used by cooperators, DLGC and GSR in the tracking of lambs with GM1 genetics as all lambs-- normal, carriers and affected--enter the market stream after FDA approval for GM1 ganglioside use in humans. We experienced difficulty with this portion of the project as the creation of the GM1 database (the type of record management tool we focused on building) required some prior expertise with Access and database concepts; this will be addressed later.

### **Project Objectives**

Funds were used 1) to create a series of training videos primarily for use by participating cooperators and secondarily by producers who would like to learn livestock care and management details of the project; and 2) to hire a temporary Project Coordinator to develop cooperator communication protocols and a record management system, and to disseminate training videos, and evaluate the effectiveness of all three tools for use in the GM1 project going forward in anticipation of increased numbers of cooperators.

Small-scale pre-clinical trials for ovine GM1 gangliosidosis are in progress thanks in part to National Sheep Industry Improvement Center funding and fundraising by The Shepherd's Gift: GM1 for HD. At the beginning of this project, in May 2016, the number of GM1 cooperators was fourteen flocks with access to 5000 ewes. This group of GM1 cooperators served as a beta-testing group for communication and record management protocols as well as efficacy of using training videos. The need for specialized training on handling blood samples became apparent as Avanti began receiving shipments of samples from GM1 cooperators in spring 2016. The goal was to have cooperators be able to take blood samples properly and pack the samples so that they arrived at the genetic testing facility in acceptable condition, thus reducing the need to resample. Cooperator questions centered around specific details about successfully incorporating GM1 genetics into their own flocks and special care required in raising affected lambs. Using feedback from this smaller group of cooperators, training videos addressing their questions and concerns were created; communication protocols established; and the record management system tested with an eye towards quickly and efficiently scaling up once FDA Investigative New Drug Application approval is granted and the project progresses into clinical trials.

## Training Videos

The final series of cooperator training videos compliments the December 2015 American Sheep Industry Association's *Let's Grow Program*-funded education and outreach videos. Training videos include the following information (see Attachment 1, Table of Contents for flash drive, **videos in red**):

- How to sample blood for genetic testing
  - a. Using an evacuated tube
  - b. Package/seal/temp controlled shipping
  - c. Shipping instructions and explanation of timing constraints
  
- How to recognize affected lambs (See GlycoScience Research Farm Tour & History video)
  - a. Visual display of normal vs. affected lambs
  - b. Explanation of animals sent within 90 days of age.
  - c. Explanation of animals being harvested 4-6 months of age.
  
- Record keeping (carriers, affecteds) – Shearwell Data Electronic ID
  - a. Overview why record keeping is important
  - b. Offer solutions for ID – Ear tags, tattoos
  - c. Describe Shearwell Data EID ear tag identification system– possibly incorporate Shearwell Data promotional media from the company (<http://www.shearwell.co.uk/>)

Training videos were made with a combination of video and photos captured during videographer Nicole Richmond's visit to White, SD, in summer 2016 and some curated materials. The training videos are MP4 files; files have been loaded on the flash drives (proposed and funded in the 2nd round of *Let's Grow Program*) with the educational outreach materials described in the *Let's Grow Program* 2nd Round of Funding proposal (Project Title: GM1 Sheep Production for Huntington's Disease). Videos are also available on YouTube and Facebook for optimized viewing and sharing. Since travel expenses for the videographer were already covered under the 2nd round of *Let's Grow Program*, the only additional expense for creating the training videos were the planning, production, post-production, interactive and Social Media consulting services provided by the videographer. The series of training videos was therefore produced for \$4,000 by building on the work done for the previously funded educational videos.

## **Grant Funds Reallocated By Permission for Additional Video**

Unfortunately, weather and conflicting schedules conspired to prevent the video documentation of HD research efforts on-site at Massachusetts General Hospital/Harvard Medical School and the proposed joint interview of Dr. Larry Holler and Dr. Steven Hersch (funded in Project Title: GM1 Sheep Production for Huntington's Disease, awarded 12/15/2015). Reallocating these remaining funds by permission of *Let's Grow Program* director, Alan Culham, Susan and Larry Holler traveled to Indiana in April 2017 to accept a monetary award from The Bev Hartig Huntington's Disease Foundation (TBHHDF). In *Bev Hartig: Living with Huntington's Disease since 1999*, Bill Crawford of Harbor Pictures Company recorded interviews with Bev and her husband Bob, and Larry and Susan Holler prior to TBHHDF fundraiser in April 2017. Bill also interviewed Gary Dunbar, Ph.D., a GM1 researcher at Central Michigan University with whom Larry Holler made contact with during spring of 2017. These three interviews are some of the most powerful and compelling captured for this project.

Funding for the Bev Hartig video was split between this award and the *Let's Grow Program* second round of funding award (12/15/2015) (See Table 1). The first invoice from Harbor Pictures Company for filming and editing work totaled \$1786.12. The balance of this invoice (\$1317.26) was paid from reallocated *Let's Grow Program* grant funds in the GM1 Sheep Production for Huntington's Disease project (awarded on 12/15/2015). The final invoice for editing by Harbor Pictures Company totaled \$750, but Bill Crawford, owner of Harbor Pictures, gave us a \$225.26 discount on the final editing of the videos he produced (see Table 2), reducing the bill to \$524.74.

*Bev Hartig: Living with Huntington's Disease since 1999* will be added to the remaining flash drives, and is posted to YouTube as well as the GlycoScience Research website. Dr. Dunbar's interview has been recorded as a collection of 17 sound bites, and will be used strategically in social media formats to promote awareness of the project. The American Sheep Industry Association's *Let's Grow Program* funding is acknowledged in each video. Flash drives all include the *Let's Grow Program* logo on one side of the case, with GSR on the reverse.

The video presentations, along with additional paper documentation on the GM1 project, have been distributed on forty-four USB flash drives to all participating GM1 cooperators as well as selected government officials and GM1 Project supporters regionally (mailed 4/20/2017). Since the project is currently awaiting generation of supporting data for clinical trials, and funding for these trials, a decision was made to postpone distribution of the flash drives to sheep and wool producer groups until a time when the project can take on and support more sheep producers. In the meantime, we will be sending out an email to these groups with project status information and YouTube links to the videos.

### **Project Coordinator**

The Project Coordinator had three major tasks to complete during the grant period: 1) to develop a protocol to be used in effectively communicating with cooperators; 2) to create a record management system to be used by individual cooperators, GSR, and DLGC for tracking GM1 genetics within each participating flock; and 3) to disseminate training videos and evaluate their effectiveness. The Project Coordinator, Mercedes Lemke, was a student majoring in Agricultural Education and Agricultural Communications at South Dakota State University.

Working with an undergraduate student presented its own set of unforeseen challenges to GSR and DLGC staff. An inexperienced student is generally unprepared to take on the amount of responsibility and independence required to complete the tasks proposed in the *Let's Grow Program* grant proposal. The choice of record management system was also, in retrospect, quite ambitious. We built a comprehensive Access database from scratch with little prior experience with the software (the DLGC manager had the most previous experience, but it had been a while since she had used Access). Nevertheless, the project

team persisted and completed all components of the proposal satisfactorily. We now have tools which can be used as the number of cooperators participating in the GM1 program increases, and we are able to accurately provide cooperators with a comprehensive genetic inventory of their GM1 flocks, as well as track affected lambs back to their source.

## **Database**

The record management database that was created has already significantly increased organization and productivity in the genetic test processing center; the processing center is able to report lamb blood sampling results to the cooperators in the form of an easily interpreted report. As GSR gains control of the genetic testing, operation efficiency will further improve with results being provided to cooperators within 30 days. Since not all offspring will be carrier and affected lambs, producers will benefit from knowing sooner how many non-carrier lambs they have. Having these records easily searchable and available in report form will also help increase overall cooperator productivity because cooperators will know the number of stock available for the terminal market or sales (non-carrier animals) through inventory tracking and reporting. Also with this record keeping system producers will be able to know sooner which lambs carry the GM1 genetics and will be able to integrate them into their flocks at a more productive rate. The database allows GSR to search total carrier and affected animals for inventory and budgeting purposes.

The original budget included \$4000 for the Project Coordinator duties. As it became evident that we needed training in order to create a working database, we engaged the services of the Lake Area Technical Institute staff responsible for corporate education. Since the DLGC manager had a semester-long course in applied Access, and had created Access databases in previous jobs, two sessions were adequate to come up to speed on Access. Grant funds were reallocated to pay the DLGC manager for a total of 41.8 hours spent working on the database. After the database was functional and real data were loaded into the database, it became apparent that the database design could be streamlined to be more efficient and accurate. GlycoScience Research intern Hannah Hart spent an additional 17 hours aligning the original database with data collection/reporting; this expense is included as a cost-share by GSR (see Table 2). Ms. Hart also developed a number of Queries and Reports which improve communication between GSR and cooperators. Please see the accompanying Database Format and Database Report Example-Cooperator Report pdf files for details on available reports and the data uploaded and stored in the Access database created with *Let's Grow Program* funding.

## **Cooperator Communications**

Eight Constant Contact email newsletters were sent out to cooperators, potential cooperators and anyone who was interested in the project. The purpose of the newsletter was to keep all stakeholders up to date on what was happening with the project. Since many of our stakeholders are spread out throughout the Midwest we implemented the email newsletter to see if this would help improve relations and communications. We have made changes to this communication since the beginning of the grant project. One change we had to make was the email they are sent from. Originally they were being sent through a Google email account created for The Shepherd's Gift. However, we noticed when using this email that many messages were going to junk mail or not being sent. This is when we transitioned to using a GlycoScience Research email for this communication. Even now click through rates have been less than 40% since gmail accounts send the newsletter to the promotion folder. The American Sheep Industry Association's *Let's Grow Program* is acknowledged in the newsletters. (See accompanying pdf file containing copies of newsletters.)

## Conclusion

The awareness of the GM1 project has increased considerably due to the American Sheep Industry Association's *Let's Grow Program* grant support that provided for videos for training and promotion through social media. The need for tracking of all animals is essential to the success of the project in relation to FDA requirements. The lack of traceability of animals and source verification led to the demise of the bovine GM1 source. The advantage the lambs have is that each animal can be traced from farm of origin through GM1 purification and preparation for pharmaceutical use over a comparatively short period of time. Although managing these lambs involves sheep production, it is a higher level of management than practiced by most producers. Record keeping and management is more similar to a purebred registered seedstock operation. Blood sampling has also been a challenging procedure for cooperators. The potential to extract DNA from tissue samples instead of blood for genetic testing will be pursued. Additionally, reproductive techniques and efficiencies such as oocyte collection from affected ewe lambs at harvest can increase the number of affecteds through IVF and ET. Semen sorting and selection of gametes that carry the GM1 trait can be utilized for AI and IVF, thereby increasing the percent of affected lambs to 50% or even 100% of the lamb crop.

It has become evident that at least annual farm visits, by trained personnel, to cooperators will be needed to ensure a high level of animal welfare and record keeping to help producers be successful. The Dakota Lamb Growers Cooperative has been supportive and participated in the project with many of the cooperators originating from within the co-op. An organization which can coordinate communication among cooperators, and information dissemination as well as cooperator feedback, has been and will continue to be beneficial to project progress. As preclinical data continue to accumulate, the project moves closer to clinical trials. The funding provided by these grants has established training materials and a database that will facilitate a better transition as rapid sheep number expansion becomes necessary. The videos have brought more awareness to the project, helping bring in some of the necessary funding. Continued exposure will promote the potential GM1 has to improve the quality of life for patients struggling with neurological disease and their families.

The use of these GM1 gangliosidosis lambs provides a novel value added agricultural product for the sheep industry. Once GM1 is approved for pharmaceutical use, the demand for these lambs will outpace supply. There are 30,000 symptomatic HD patients and 200,000 individuals at risk in the U.S. who could benefit from GM1 treatment. There are estimated to be over 1 million Parkinson's patients, while there are an estimated 5.5 million Alzheimer's patients in the U.S. We estimate that it will take about 1 lamb to treat 1 patient for 1 year (estimating that 5 grams of GM1 can be purified per lamb). Additionally the neuroprotective and neuroregenerative properties of GM1 can be beneficial in the treatment of other neurologic diseases including spinal cord injury, stroke, traumatic brain injury and peripheral neuropathies. This list only includes conditions that have been studied thus far. The GM1 project has tremendous potential to grow the sheep industry though change.

Table 1:

<u>Grant Item</u>	<u>Submitter portion</u> (see cost share amounts in table below)	<u>ASI Portion Budgeted</u>	<u>Actual Spent</u>
<b>Production-Nicole Richmond, Videographer</b>			
Video, planning, production, post-production, interactive & social media consulting		\$4000.00	\$4000.00
<b>Project Coordinator</b>			
Intern Sadie Lemke (400 hrs @ \$10/hr)		\$4000.00	\$1305.80
<b>Constant Contact email service</b>			
6 months x \$18/month (cost shared with The Shepherd's Gift: GM1 for HD)		\$108.00	\$ 83.60
<b>Database Training</b>			
Lake Area Technical Institute		\$0	\$680.00
<b>Database Building-DLGC Manager</b>			
Creation of Access database (41.8 hrs)		\$0	\$1045.00
<b>Harbor Pictures Company-recording &amp; editing</b>			
Bev Hartig/Gary Dunbar/Hollers footage		\$0	\$ 993.60
<b>TOTALS</b>		<b>\$8108.00</b>	<b>\$8108.00</b>

Table 2:

<b>Cost Share/In Kind Contribution</b>	Amount
GSR Personnel (20 hrs @ \$25/hr)-in-kind contribution of time-training video interviews, blood collection demonstrations	\$500.00
GSR Personnel (17 hrs @ \$10/hr)-cost share-database alignment with data collection/reporting	\$170.00
DLGC Office Manager *(15 hrs @ \$25/hr)-cost-share-management of project record keeping/payments	\$375.00
Harbor Pictures Company-in-kind donation-video editing time	\$225.26
The Shepherd's Gift:GM1 for HD-cost-share-1/2 cost of Constant Contact (6/5/16 thru 3/5/17)	\$83.60
<b>TOTAL</b>	<b>\$1353.86</b>

\*Cost share of DLGC Manager time spent working on the project far exceeded the 15 hours committed.

ATTACHMENT 1

**GM1 Cooperator Information  
GlycoScience Research, Inc.  
GM1 Sheep Production for Huntington's Disease Project**

USB Drive Table of Contents (Revised 1/2018)

- **Letter of Introduction from GlycoScience Research, Director of Operations, Susan Holler**
- **Acknowledgements**
- **Participation Requirements for GM1 Production**
- **Videos** (videos will also be available at YouTube)

<i>Video Folder Name</i>	<i>Video Title</i>	<i>Video Length (minutes)</i>
<b>Folder: GM1 Scientific Presentation</b>		
	Dr. Larry Holler Presentation	60.0
	GM1 Sheep Can Treat Neurologic Disease	3.1
<b>Folder: Project Information</b>		
	GlycoScience Research Farm Tour and History	17.2
	Bev Hartig: Living With Huntington's Disease Since 1999	6.5
<b>Folder: Huntington's Disease Families</b>		
	Hilton Family	9.4
	Katelyn Sandbulte	3.2
	Oss Family	7.2
<b>Folder: Cooperating Sheep Producer Commentaries</b>		
	Heather and Mike Ludlam	5.4
	Jeff Petersen Family	3.2
	Jim Hanssen	2.3
	Pam and Greg Taylor	9.1
<b>Folder: Training Videos - IDs, Blood, Packaging</b>		
	Animal Identification Options	5.5
See ATTACHMENT 3 ►	Blood Sample Packing Summary (pdf)	N/A
	Drawing Blood Samples (All Ages)	10.1
	Packaging Blood Samples	6.1

**GM1 Sheep Production for Huntington's Disease Project**

Funded by:

In cooperation with:



## ATTACHMENT 2

### **Acknowledgements GM1 Sheep Production for Huntington's Disease Project**

This education and outreach project, *GM1 Sheep Production for Huntington's Disease*, would not have been possible without generous funding support awarded by the American Sheep Industry's *Let's Grow Through Change Program* funding committee. The *GM1 Sheep Production for Huntington's Disease* grant project received two rounds of funding for educational and training video production, and for the development of a record management database and a communication system for GM1 cooperators.



The Dakota Lamb Growers Cooperative supported the project with the cost-share of manager time devoted to managing the GM1 Sheep Production for Huntington's Disease grant project.



Thanks to Nicole Richmond, owner of Nicole Richmond Photography, for her work in conducting interviews, capturing footage, and producing most of the videos featured in the GM1 Sheep Production for Huntington's Disease grant project.

Thank you to Jace Bennett for assistance in Blood Sample videos and with the GM1 project.

Thank you to Brad Nupen and Aaron Cooley for creating the Oss Family video.

Thank you to Paul Fishback and Northern Voyage Productions for Katelyn Sandbulte's video.

Thank you to Michigan Farm Bureau, Inc. for granting permission to use the Heather and Mike Ludlam video.

Thank you to Bill Crawford of Harbor Pictures for donating editing time for *Bev Hartig: Living with HD*.

Thank you to Dr. Gary Dunbar, and Bev and Bob Hartig for their participation in project videos.

Thank you to the South Dakota Agricultural Heritage Museum for partial funding of the GM1 animated film.

Thank you to Cable Hardin and Gwen McCausland for creating the GM1 animated film.

Thank you to The Shepherd's Gift: GM1 for HD Board of Directors for participating in project videos and for partial funding of the GM1 animated film.

Thanks to the Huntington's Disease Families who continue to work towards a treatment for HD.

Thanks to the GM1 Project Cooperating Sheep Producers, without whom we could not meet the need for GM1.

**Sincerely,**  
**Susan and Larry Holler**  
**GlycoScience Research, Inc.**  
Revised 1/2018

## ATTACHMENT 3

**GM1 Cooperator Information**  
**GlycoScience Research, Inc.**  
**GM1 Sheep Production for Huntington's Disease Project**

GM1 Genetic Test Blood Sample Shipment Summary

- Refrigerate samples prior to shipping
- Place tubes upside down in original tube box to prevent breakage; cover top of tube box with plastic wrap and secure
- Pack box of samples within an insulated box to avoid freezing or overheating
- Use adequate packing materials
- Ship overnight and/or make sure adequate ice packs are included
- Include an ordered list of sample ID numbers AND email an electronic copy of list to [sueholler@glycoscienceresearch.com](mailto:sueholler@glycoscienceresearch.com)

Remember, blood samples cannot be tested if they are clotted. Follow directions for bleeding animals of all ages in the **Drawing Blood Samples (All Ages)** video. Once collected, samples must not be frozen or overheated.

Funded By:

