NRSP-8 Equine 2017 Annual Report

**Leadership:**

#### Coordinators:

Ernest Bailey, University of Kentucky

Samantha Brooks, University of Florida

Molly McCue, University of Minnesota

Workshop:

Chair: Jessica Petersen, University of Nebraska

Co-chair: Stephen Coleman, Colorado State University

2018 Equine Workshop Report

The workshop met Saturday afternoon (Jan 12) and Sunday morning (Jan 13). The first day was devoted to infrastructural development of the equine genome while the second day was devoted to applications.

**Attendees:**

January 12: 90

January 13: 45

**Posters:**

35 presented

**Station Reports** were provided by scientists from 20 laboratories including those at Colorado State University, Cornell University, University of Florida, Mississippi State University, University of Kentucky, University of Louisville, University of Minnesota, Michigan State University, University of Illinois, University of Nebraska, Texas A&M University, University of California-Davis, Argentina, Mongolia, Uppsala Sweden, Italy, Denmark and France.

**Workshop Presentations**

On January 12, 12 presentations were made and a coordinated discussion section held. Key presentations were:

1. Invited Speaker: Chongyuan Luo on Epigenomic Diversity in the Mammalian Brian
2. Samantha Brooks: Update on NRSP8 Genome to Phenome Conference
3. Edward Rice: Ecab 3.0
4. Erin Burns: Update on FAANG initiative for horse and other species

On January 13, 6 presentations were given.

**Travel support** awards were made for 24 Students from the NRSP8 Coordinator Funds. Winner of the Jorgenson Travel award was Moriel Singer-Berk from the University of California-Davis.

**Progress on the Workshop Objectives:**

**1: Advance the status of reference genomes for all species, including basic annotation of worldwide genetic variation, by broad sequencing among different lines and breeds of animals.**

The new assembly of the horse genome, Ecab 3.0, was reported to be in process at NCBI and Ensembl. The new assembly is based on the existing Sanger sequence data along with Illumina HiSeq short reads, CHiCago and Hi-C long-insert libraries, Gap-filling with PacBio and a 10x Chromium library to identify and phase variants. The final assembly has 4.5Mb contig N50, 85Mb scaffold N50, and 70Mb more sequence assigned to chromosomes.

A de novo assembly of the equine MHC was produced using the 10x GenomicsTM ChromiumTM linked read gel-bead system. The study produced six long contigs in the MHC region with very few gaps, allowing determination of the correct order of the class I and class II genes on the ELA-A3 haplotype and to obtain high fidelity full length genomic sequences for all of those genes.

To supplement the reference genome derived from a mare, an annotated assembly of the male specific region of the Y chromosome has also been completed and will be released upon acceptance of the descriptive manuscript. This resource will be made available through the NCBI and UCSC genome browsers.

**2: Develop strategies to identify and exploit genes and allelic variation that contribute to economically relevant phenotypes and traits, in part through improving functional annotation of the genomes of our species.**

A biobank of over 80 tissues, 2 cell lines, and 6 fluid types was recently established from two extensively phenotyped healthy adult Thoroughbred mares. RNA-sequencing (both mRNA and smRNA-seq) and ChIP-sequencing for four histone modifiers was initiated across 8 tissues that were prioritized in alignment with the overall across-species FAANG initiative. The biobank has led to a substantial international investment of the equine community, with 24 individuals representing 16 research institutions in 10 countries providing support for transcriptome characterization of tissue relevant to their investigations. As a result, mRNA and smRNA-seq datasets are currently available from 30 tissues to contribute to horse genome annotation. Seven laboratories also volunteered to lead other analyses, including karyotyping, centromere mapping of fibroblast cells, reduced representation bisulfite sequencing of the 8 priority tissues, fibroblast functional assays and further phenotyping through sequencing of microbiome samples. Notably, over $44,000 was contributed by individual members of the research community in addition to the funding provided by Grayson Jockey Club Foundation to support this work. ChIP-seq assays are currently being performed for two tissues and optimized for the other six prioritized, with expected completion in the Spring of 2018.  All of these data are made publically available following FAANG guidelines (8 prioritized tissues immediately available and researcher-funded tissues available after a 6 month embargo period if requested).

**3: Facilitate analysis, curation, storage, distribution and application of the enormous datasets now being generated by next-generation sequencing and related "omics" technologies with regard to animal species of agricultural interest.**

The equine community continues to add information to the [animalgenome.org](http://animalgenome.org/" \t "_blank) repository and AnimalQTL db, including new custom tracks in 2017 for CNV and SV.

[https://www.animalgenome.org/repository/horse/6\_horse-breeds\_variants/](https://www.animalgenome.org/repository/horse/6_horse-breeds_variants/" \t "_blank)

[https://www.animalgenome.org/cgi-bin/QTLdb/EC/summary](https://www.animalgenome.org/cgi-bin/QTLdb/EC/summary" \t "_blank).

ENA reports release of 932 sequences for EquCab in 2017.

[https://www.ebi.ac.uk/ena/data/warehouse/search?query=%22tax\_eq(9796)%20AND%20first\_public%3E2017-01-01%22&domain=sequence](https://www.ebi.ac.uk/ena/data/warehouse/search?query=%22tax_eq(9796)%20AND%20first_public%3E2017-01-01%22&domain=sequence" \t "_blank).

Work continues on developing a large database of genetic variants for the horse based on short-read whole genome sequences. With the release of EquCab 3.0 approximately 700-800 genomes will be re-mapped using a standard state of the art pipeline being developed in conjunction with Interval Bio (www.interval.bio). This database will allow for both open and restricted data sharing by investigators. Working with the University of Minnesota with funding from USDA NIFA Genome tools grants, Interval Bio plans to have the database, GUI, and API available in September 2018.

Several groups are working towards improving the annotation of the new EquCab 3.0 genome release. In addition to use of the RNA- and ChIP-seq data generated as part of the FAANG consortium there are on-going efforts to use RNAseq datasets from large numbers of horses in diverse tissues including using network-based approaches to functionally annotate lncRNA and small RNAs across equine tissues.

**Communication:** The coordinators maintain an email list and use it to broadcast information for USDA-NRSP8, the USDA, the Havemeyer Foundation and other information relevant to the workshop. In addition to the PAG conference, the Dorothy Russell Havemeyer Foundation International Equine Genome Mapping Workshop a meeting of the International Society for Animal Genetics are held every other year. Many of the NRSP8 members also participant in the biennial Equine Science Society Conferences.

In 2017 the Brooks lab, we continued our online extension short course designed to translate discoveries in equine genetics to application by stakeholders. 37 participants took this course from locations in four countries and included 16 participants utilizing a translation into Brazilian Portuguese provided by Laura Patterson-Rosa. Given the strongly positive evaluations of the course, we are now renovating the material to accommodate a rolling admission system better tailored to the adult professional audience.

**Summary of Funding Reported in support of Equine Genomics**

Based on 16 Stations reporting: 6 international and 10 US

|  |  |  |  |
| --- | --- | --- | --- |
| **Institution** | **Internal** | **Industry** | **Federal** |
| US | $505,693 | $918,165 | $1,094,329 |
| International | $674,009 | $243,111 | $1,533,801 |
| Total | $1,179,702 | $1,161,276 | $2,628,130 |

**Specific Industry and Federal Grants Reported**

**Finno, University of California – Davis; total for 2017 $585,064**

Center for Equine Health, The effect of alpha-tocopherol supplementation on vitamin E metabolism in healthy horses and horses with neuroaxonal dystrophy $34,244

Center for Equine Health, Validation of putative genetic variants for equine neuroaxonal dystrophy $29,795

Center for Equine Health, Validation of putative genetic variants for juvenile idiopathic epilepsy in Arabian horses, $8,452

Center for Equine Health, Genetic investigation of idiopathic persistent hypocalcemia in the Thoroughbred $12,491

Priority Partnership Collaboration Award Secrets in the bones: how functional genomics will broaden our understanding of catastrophic breakdown in racehorses $30,580

Grayson Jockey Club Foundation, Unraveling complex traits by defining genome function (Part I) $199,177

Arabian Horse Association Genetic Investigation of occipitoatlantoaxial malformation (OAAM) in Arabian Horses $6,294

NIH 1K01OD015134 Molecular pathogenesis of alpha-tocopherol associated neuroaxonal dystrophy in animal models $101,354 direct costs/year

NIH L40 TR001136 Molecular pathogenesis of alpha-tocopherol associated neuroaxonal dystrophy in animal models $70,000 direct costs/year

NIH Office of Dietary Supplements Biomarkers of alpha-tocopherol efficacy in animal models of neurodegeneration $92,677 direct costs/year

**Hill, UC Dublin/Plus Vital; total for 2017 $664, 373**

Enterprise Ireland Innovation Partnership Programme, 2017-19 (IP 2016 0503) Assessment of the Energetic Benefits of Plusvital Supplements/Nutrients on Thoroughbred Horses, €295,286

Enterprise Ireland R&D Fund grant (to Equinome Ltd.), 2015–17 (158281/RR, 158282/RF): A catalogue of genomic variation contributing to racing success in Thoroughbred horses: enabling genomic prediction for commercial genetic testing of elite performance potential. €192,270

Science Foundation Ireland Principal Investigator Career Advancement Programme, 2012-17: Integrated genomics approaches to understanding genetic contributions to system-wide exercise physiology parameters in a large animal model, €1,863,205.

**MacLeod, University of Kentucky; total for 2017 $144,490**

2016-2017.  American College of Veterinary Surgeons. Comparative chondrogenic potential of equine fetal progenitor cells and adult mesenchymal stem cells. Total direct support: $22,943

2016-2019.  Morris Animal Foundation. Developmental Progenitor Cells of Articular Cartilage. Principal Investigator, Total direct support: $121,547.

**McCue and Mickelson, University of Minnesota; total for 2017 $804,890**

Metabolomics in Equine Metabolic Syndrome: Molecular pathophysiology and biomarker discovery, American Quarter Horse Association, ME McCue and JR Mickelson, $77,556 total, 10/2016 – 10/2017. Funds for 2017 = $77,556.

Functional Prioritization of Candidate Genes and Alleles for Equine Metabolic Syndrome, Morris Animal Foundation, ME McCue, $197,000 total, 2017 – 2019. Funds for 2017 = $97,000

Integrated metabolomic and genomic approach to metabolic variation across horse breeds (2016-2018). Morris Animal Foundation Post-Doctoral Fellowship to Felipe Avila, Budget $100,000. Funds for 2017 = $50,000.

Functional Prioritization of Candidate Genes and Alleles for Equine Metabolic Syndrome (2017-2019). Morris Animal Foundation Post-Doctoral Fellowship for Elaine Norton, ME McCue Mentor. Budget for 2017 = $45,000**.**

Tools to Link Phenotype to Genotype in the Horse, USDA/NIFA/AFRI, ME McCue and JR Mickelson; $500,000 total, 2017 – 2020. Funds for 2017 = $166,667

Functional Prioritization of Genes and Alleles for Equine Metabolic Syndrome, USDA/NIFA/AFRI, ME McCue and JR Mickelson $499,000 total, 2017 – 2019. Funds for 2017 = $166,667

Discovering causal variants for complex disease using functional networks in the horse (2015-2017). USDA-NIFA Post-Doctoral Fellowship for Rob Schaefer, ME McCue Mentor, Budget $150,000. Funds for 2017 = $75,000.

Tools for Precision Medicine in the Horse (2016-2018) Minnesota Agricultural Experiment Station, Multistate Competitive Grants Program. ME McCue $68,000, funds for 2017 = $34,000

Genetic variants responsible for health and performance in the Quarter Horse (2017) American Quarter Horse Foundation, ME McCue Budget $67,171, 2017 budget = $33,000

Genetic Basis of Recurrent Exertional Rhabdomyolysis (2017-2021) NIH Office of Research Infrastructure Programs, F30 Dual-Degree Fellowship for Samantha Beeson, ME McCue Mentor, Budget $240,600. Funds for 2017= $60,000

**Bellone, UC Davis total for 2017;** **$46,106**

2016-2018 *Grant awarded from Morris Animal Foundation,*(D16EQ-820)Project Title: “Genetic Investigation of Bilateral Corneal Stromal Loss in Friesian Horses.” Funds for 2017: $10,300

2016-2019  $136,996 *Grant awarded from Morris Animal Foundation,*(D16EQ-028) “Genomic Investigation of Equine Recurrent Uveitis in Appaloosa Horses.”  Funds for 2017: $35,806 *Bellone (PI) McCue and Lassaline (Co-investigators)*

**Mienaltowski, UC Davis; total for 2017 $10,800**

Morris Animal Foundation; Grant Title: “Decoding Equine Tendon Transcriptomes to Understand Tendon Growth, Maturation, and Aging”; $10,800

**Valberg, Michigan State University; total for 2017 $141,816**

2016/2018 Morris Animal Foundation $142,909 Muscle Calcium Regulatory Proteins Unique to Horses: Implications for Exertional Rhabdomyolysis CoPI Valberg SJ coPI Thomas D, ~$47, 637/year

2016/2017 American Quarter Horse Association $19,359 Prevalence of the Mutation for Immune Mediated Myositis in the American Quarter Horse. PI CJ Finno, coPI Valberg SJ.

2017/2018 American College of Veterinary Internal Medicine $51,003 Identifying the genetic basis for a novel exertional myopathy. PI SJ Valberg

**Walner and Brem, University of Vienna; total for 2017 $305,397**

Characterisation of stallion lines in Austrian horse breeds with Y-chromosomal markers - Austrian government funded (DANFE 101184/2) Applicant: Wallner B;86.000 €

Y-chromosomale Haplotypen prähistorischer Pferde zur Analyse der Domestikation, früher menschlicher Siedlungsgesellschaften, Migrationsvorgänge und kriegerischer Auseinandersetzungen (Austrian Academy of Sciences, IF\_2015\_17) Applicant: Gottfried Brem 160.000€

**Brooks University of Florida; total for 2017: $325, 591**

6/2017-5/2018 Identification of polymorphisms for the Sunshine coat color dilution. Etalon Inc.

Funds for 2017= $1,926

5/2017 Excellence Award for Assistant Professors. UF Provost $5000

11/2016- 4/2018 Transcriptome Analysis of Supporting Limb Laminitis (AWD01050) AAEPF Funds for 2017= $95,526

10/2016 – 9/2017 Genetics of Anhidrosis in the American Quarter Horse (AWD00241) AQHF Funds for 2017= $53,247

11/2013 – 4/2017 Comparative Animal Genomics in Qatar (00092985) QNRF Funds for 2017= $169,892

**Swiderski, Mississippi State University; total for 2017 $206,045**

2015-2018.  USDA/NIFA/AFRI. Protein Networks Mediating Airway Hyper-responsiveness in Horses. Swiderski CE (PD), Bowser JE, Nanduri B, Claude A, Eddy A. Budget: $438,153. Funds for 2017= $194,345

2016-2018.  Morris Animal Foundation. Cryopreserved precision cut lung slices for investigating the regulation of airway contraction in horses. Swiderski CE (PI), Bowser JE, Lopez-Soberal. Budget: $10,800. Funds for 2017=$5,200

2017-2018. Mississippi State University Office of Research. Does Continuous Exposure to Oxygen/Carbon Dioxide Improve Viability of Isolated Bronchial Rings. Swiderski CE, Bowser JE, Dittmar W. Budget: $3,000 Funds for 2017= $ 1,500

2016-2018. College of Veterinary Medicine, Mississippi State University. Determining the Role of a Novel Ion Channel in a Severe, Neutrophilic Asthmatic Phenotype. Swiderski CE (PI), Hunter CL, Nanduri B, McCarthy F, Costa LRR. Budget: $10,000. Funds for 2017=$5,000

**Gabriella Lindgren, SLU; total for 2017 $399,000**

2017-2020. Swedish Research Council (VR), 3.475.000 SEK = 449.000 USD. Tracing the genetic origin of the horse mane: an innovative model to identify genetic factors that regulate hair growth. Main applicant: Gabriella Lindgren, SLU, Uppsala. Co-PI: Juan Negro, Donana Biological Station, Seville. For 2017: 869.000 SEK = 110.000 USD.

2017-2019. Swedish Research Council (FORMAS), 2.996.000 SEK = 379.000 USD. Genomic studies of horses lead the way to unravel genetic regulation of locomotion pattern and performance traits. Main applicant: Gabriella Lindgren, SLU, Uppsala. For 2017: 1.000.000 SEK = 126.000 USD.

2016-2018, Swedish-Norwegian foundation for equine research (Stiftelsen Hästforskning, SHF), 3.861.000 SEK = 488.000 USD. Mapping performance, genetic variation and health in the Coldblooded trotter. Main applicant in Sweden: Gabriella Lindgren, SLU, Uppsala, main applicant in Norway: Eric Strand, NMBU, Oslo. For 2017 1.287.000 SEK = 163.000 USD.

**Monika Bugno-Poniewierska,Tomasz Ząbek, Katarzyna Ropka-Molik, Tomasz Szmatoła, Klaudia Pawlina, Agnieszka Fornal, Magdalena Wojtaszek, Katarzyna Kowalska - National Research Institute of Animal Production and Monika Stefaniuk-Szmukier - Univerity of Agriculture Krakow; total for 2017 $1,980,198**

Name of Grant Agency -National Science Center; "Analysis of changes in transcriptome profile of blood and skeletal muscle in Arabian horses during training regime, using by the method based on Next Generation Sequencing - RNA-seq"; Grant identification number 2014/15/D/NZ9/05256; $206,000

Name of Grant Agency -National Centre for Research and Development; Title of Grant  "Directions of use and protection of genetic resources of livestock in conditions of sustainable development"; Grant identification number BIOSTRATEG2/297267/14/NCBR/2016

**Task1 –** $1,209,632: The use of the achievements of molecular genetics in the selection and elimination of animals affected by diseases of genetic origin

**Task 2** - $564,566: Development of new methods of preservation and selection criteria for donors of isolated genetic material for use in programs related to preserving biodiversity of breeds.

**Hamilton, University of Sydney; total for 2017 $166,157**

2017 ~ $USD 107,657 Racing Australia (Industry body) grant "Development of an assay to detect gene doping in Thoroughbred horses"

Dr. Anna Bautina (collaborator) at the National Measurement Institute

2017 $58,500 Racing Australia (Industry body) grant private genotyping consultancy.

**Publications for 2017**

1. Al Abri, M.A., König von Borstel, U., Strecker, V. and Brooks, S.A. (2017) 'Application of Genomic Estimation Methods of Inbreeding and Population Structure in an Arabian Horse Herd', *Journal of Heredity*, 108(4), 361-368, available: http://dx.doi.org/10.1093/jhered/esx025.
2. Aleman M, Finno CJ, Weich K, Penedo MCT. Investigation of known genetic mutations of Arabian horses in Egyptian Arabian foals with Juvenile Idiopathic Epilepsy. J Vet Intern Med 2017; doi: 10.1111/jvim.14873. [Epub ahead of print].
3. Balmer P, Bauer A, Pujar S, McGarvey KM, Welle M, Galichet A, Müller EJ, Pruitt KD, Leeb T, Jagannathan V. A curated catalog of canine and equine keratin genes. PLoS One. 2017 Aug 28;12(8):e0180359. doi: 10.1371/journal.pone.0180359. eCollection 2017. PMID: 28846680
4. Bauer A, Hiemesch T, Jagannathan V, Neuditschko M, Bachmann I, Rieder S, Mikko S, Penedo MC, Tarasova N, Vitková M, Sirtori N, Roccabianca P, Leeb T, Welle MM. A Nonsense Variant in the ST14 Gene in Akhal-Teke Horses with Naked Foal Syndrome. G3 (Bethesda). 2017 Apr 3;7(4):1315-1321. doi: 10.1534/g3.117.039511.
5. Bellone, R.R., Liu, J., Petersen, J.L. Mack, M., Singer-Berk, M., Drögemüller, C., Malvick, J., Wallner, B., Brem, G., Penedo, M.C., & Lassaline, M. (2017) A missense mutation in damage-specific DNA binding protein 2 is a genetic risk factor for limbal squamous cell carcinoma in horses. *International Journal of Cancer*141(2):342-353.
6. Bergmann T, Lindvall M, Moore E, Moore E, Sidney J, Miller D, Tallmadge RL, Myers PT, Malaker SA, Shabanowitz J, Osterrieder N, Peters B, Hunt DF, Antczak DF, Sette A. Peptide-binding motifs of two common equine class I MHC molecules in Thoroughbred horses. Immunogenetics. 2017 69 351-358.
7. Bordbari MH, Penedo MC, Aleman M, Mickelson JR, Valberg SJ, Finno CJ. Deletion of 2.7kb near HOX3 in an Arabian horse with occipitoatlantoaxial malformation. Anim Genet. 2017 Jun;48(3):287-294.
8. Brown J, Valberg SJ, Hogg M, Finno CJ. Effect of feeding two RRR-alpha-tocopherol formulations on serum, cerebrospinal fluid and muscle alpha-tocopherol concentrations in horses with subclinical vitamin E deficiency. *Equine Vet J*, 2017 Apr 22. doi: 10.1111/evj.12692. [Epub ahead of print]
9. Brunner MAT, Jagannathan V, Waluk DP, Roosje P, Linek M, Panakova L, Leeb T, Wiener DJ, Welle MM. Novel insights into the pathways regulating the canine hair cycle and their deregulation in alopecia X. PLoS One. 2017 Oct 24;12(10):e0186469. doi: 10.1371/journal.pone.0186469. eCollection 2017. PMID: 29065140
10. Bryan K, McGivney BA, Farries G, McGettigan PA, McGivney CL, Gough KF, MacHugh DE, Katz LM, Hill EW. Equine skeletal muscle adaptations to exercise and training: evidence of differential regulation of autophagosomal and mitochondrial components. BMC Genomics. 2017 Aug 9;18(1):595. doi: 10.1186/s12864-017-4007-9.
11. Burger D, Thomas S, Aepli H, Dreyer M, Fabre G, Marti E, Sieme H, Robinson MR, Wedekind C.Major histocompatibility complex-linked social signalling affects female fertility.Proc Biol Sci. 2017 Dec 6;284(1868). pii: 20171824. doi: 10.1098/rspb.2017.1824.PMID: 29212724
12. Canisso IF, Ball BA, Esteller-Vico A, Williams NM, Squires EL, Troedsson MH. (2017) Changes in maternal androgens and oestrogens in mares with experimentally-induced ascending placentitis. *Equine Vet J.* 49(2):244-249.
13. Carossino M, Loynachan AT, Canisso IF, Cook RF, Campos JR, Nam B, Go YY, Squires EL, Troedsson MHT, Swerczek T, Del Piero F, Bailey E, Timoney PJ, Balasuriya UBR. (2017) Equine Arteritis Virus Has Specific Tropism for Stromal Cells and CD8(+) T and CD21(+) B Lymphocytes but Not for Glandular Epithelium at the Primary Site of Persistent Infection in the Stallion Reproductive Tract. J Virol. 91e00418-17.
14. Claes A, Ball BA, Scoggin KE, Roser JF, Woodward EM, Davolli GM, Squires EL, Ball BA. (2017) The influence of age, antral follicle count and diestrous ovulations on estrous cycle characteristics of mares. *Theriogenology.* 97:34-40.
15. Dorado J., Anaya G., Bugno-Poniewierska M., Molina A., Mendez-Sanchez A., Ortiz I., Moreno-Millán M., Hidalgo M., Peral García P., Demyda-Peyrás S. 2017. First case of sterility associated with sex chromosomal abnormalities in a jenny. Reprod. Domest Anim. .52 (2) :227-234.
16. Dürig N, Jude R, Holl H, Brooks SA, Lafayette C, Jagannathan V, Leeb T. Whole genome sequencing reveals a novel deletion variant in the KIT gene in horses with white spotted coat colour phenotypes. Anim Genet. 2017 Aug;48(4):483-485. doi: 10.1111/age.12556. Epub 2017 Apr 26.PMID: 28444912
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23. Fenn, DJ, T. Raudsepp, E. G. Cothran, N.A. Hamilton and B. Haase (2017) Validation of a candidate causative mutation for white spotting in donkeys. Anim Genet 48 (1): 124 – 125
24. Fernandes CB, Loux SC, Scoggin KE, Squires EL, Troedsson MHT, Esteller-Vico A, Ball BA. Sex Steroid Receptors, Prostaglandin E2 Receptors, and Cyclooxygenase in the Equine Cervix During Estrus, Diestrus and Pregnancy: Gene Expression and Cellular Localization. *Animal Reproduction Science*. 187:141-151.
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