Joint Interbull – EAAP Session.
Session 7: Genetic defects in cattle – identification, finding the mutation and managing it in breeding plans (with Interbull)
Chair: Hossein Jorjani
Date/Time: Monday 28 August 2017/14:00-18:00

Abstract number: 25867 / accepted / order: 1 / pres.means: Theatre / time: 15
Implications of mosaicism for deleterious de novo mutations in artificial insemination bulls
H. Pausch[1,2], C. Wurmser[1], S. Ammermueller[1], D. Segelke[3], A. Capitan[4], R. Fries[1]
[1]Animal Breeding, TU Muenchen, Liesel-Beckmann Str. 1, 85354 Freising, Germany, [2]Animal Genomics, ETH Zurich, Tannenstr. 1, 8092 Zurich, Switzerland, [3]vit w.V., Heinrich-Schroeder-Weg 1, 27283 Verden, Germany, [4]INRA, Allée de Vilvert, 78352 Jouy-en-Josas, France; hubert.pausch@usys.ethz.ch

Animals that carry known disease-causing alleles can be detected using haplotype information or direct gene tests from custom genotyping arrays. However, the early identification of carriers of deleterious de novo mutations is barely possible because whole-genome sequencing of breeding animals is not routinely performed and the prediction of phenotypes associated with new sequence variants is difficult. Within a short time, breeding consultants noticed a high proportion of calves with lethal congenital malformations among the descendants of two young sires from the Fleckvieh (FV) and Holstein (HOL) breeds. The analysis of 442 and 275 calving records revealed that 140 (32%) and 57 (21%) calves sired by the FV and HOL bull, respectively, were stillborn or perished within 48 hours of birth. Clinical and pathological findings of affected calves were similar to those described for osteogenesis imperfecta and lethal chondrodysplasia (bulldog). Because the disorders were detected in such a high proportion of the paternal half-sibs and both sexes were affected, autosomal dominant inheritance of deleterious mutations with mosaicism in the sires was likely. The whole-genome sequencing of both bulls, affected calves and healthy half-sibs revealed that a frameshift and a missense mutation in the COL1A1 and COL2A1 genes segregated with osteogenesis imperfecta and chondrodysplasia, respectively. The mutations were heterozygous in affected calves while healthy half-sibs and 1577 animals from the 1000 bull genomes project were homozygous for the reference alleles. Sanger- and pyrosequencing of DNA extracted from blood and semen samples confirmed mosaicism in both sires indicating that the mutations occurred early in development. Our findings show that mosaicism for deleterious mutations in artificial insemination bulls may result in a high number of paternal half-sibs with congenital malformations, particularly when mosaic bulls are used for thousands of inseminations before the birth of their first progeny.

Abstract number: 26444 / accepted / order: 2 / pres.means: Theatre / time: 15
Genotype prediction for a structural variant in Brown Swiss cattle using Illumina Beadchip data
F.R. Seefried[1], P. Von Rohr[1], C. Drögemüller[2]
[1]Qualitas AG, Chamerstr. 56, 6300 Zug, Switzerland, [2]University of Bern, Institute of Genetics, Bremgartenstr. 109a , 3001 Bern, Switzerland; franz.seefried@qualitasag.ch

Generally Brown Swiss (BSW) cattle are characterised by solid brown coloured coat, which is devoid of white spotting. However, two hypopigmented coat colour phenotype variants exist at low frequencies. One of these is colour sidedness (Cs), where animals have pigmented sectors on the flanks, ears and snout combined with unpigmented areas on head, legs and spine. In breeding history, colour sided animals have been excluded from the national herdbook since complete pigmentation was declared as a major breed characteristic. Nonetheless, due to dominant inheritance colour sided animals still occur. Homozygous (Cs/Cs) and heterozygous (Cs/+) animals differ by the extent of pigmentation, explaining why colour sidedness represents a semi-dominant trait. Colour sidedness in BSW cattle is caused by a complex structural copy number variant (Cs6), namely by a serial translocation of hundreds of kb-sized chromosome segments between BTA6 encompassing the KIT gene and BTA29. In total the Cs6 allele encompasses two duplicated fragments on BTA6 and BTA29 of 3.87 Mb (Durkin et al. 2012). Illumina Infinium assay provide genotypes and signal intensities for each assayed SNP. Structural variants are easily seen in log R ratio data. Log R ratio values are calculated by the binary logarithm of the ratio between normalized vs. expected intensity values. Increased log R ratios relative to the base value represent higher signal intensity due to increased copy number variants in the genomic sequence. A Support Vector Machine (SVM) classification algorithm on Log R ratios from Illumina BovineHD SNPs located within the 3.87 Mb fragment was used to predict BTA6/BTA29 Cs6-genotypes in BSW. Confirmed Cs6-genotypes were available for a total of 2003 animals, including 37 heterozygous and 7 homozygous colour-sided animals. Leave-One-Out cross validation with 2000 replicates resulted in an estimated error-rate of 0.22%. Therefore, Illumina Beadchip data together with a SVM-based classification algorithm seem to be applicable for genotype prediction of larger structural variants. Limiting factors may be SNP-density and size of

the structural variant.

Abstract number: 27144 / accepted / order: 3 / pres.means: Theatre / time: 15
Chasing deleterious recessives in Italian Holstein dairy cattle
P. Ajmone Marsan[1], M. Milanesi[1], S. Capomaccio[2], L. Colli[1], S. Biffani[3], J.T. Van Kaam[4], R. Finocchiaro[4], R. Negrini[1], C.J. Rubin[5], A. Nardone[6], N.P.P. Maciotta[7], J.L. Williams[8]
[1]Università Cattolica del Sacro Cuore, Zootechnics, Via Emilia Parmense 84, 29122 Piacenza, Italy, [2]Università degli Studi di Perugia, Dipartimento Medicina Veterinaria, Via San Costanzo, 06123 Perugia, Italy, [3]Associazione Italiana Allevatori, Via Molini 36, Roma, Italy, [4]Anafi - Associazione Nazionale Allevatori Frisona Italiana, Via Bergamo, 26100 Cremona, Italy, [5]Science for Life Laboratory Uppsala, Uppsala University , Husargtan,, Uppsala, Sweden, [6]Universita della Tuscia, Department for innovation in biological, agro-food and forest systems (DIBAF), Via de Lellis, Viterbo, Italy, [7]Università degli studi di Sassari, Dipartimento di Agraria, Via Enrico de Nicola,, Sassari, Italy, [8]University of Adelaide, School of Animal and Veterinary Sciences, Faculty of Sciences, Roseworthy, Roseworthy, Australia; paolo.ajmone@unicatt.it

Deleterious recessive variants have been searched in Italian Holstein dairy cattle combining High Density SNP genotypes from more than 1000 progeny tested bulls and exome sequence data from 18 animals sampled from the extremes of the male and female fertility effective daughter performance deregressed proof (EDP) distribution. SNP data were used to identify high linkage disequilibrium haplotype blocks. Haplotypes significantly lacking one class of homozygotes, compared to HWE expectation were classified as Homozygous Haplotype Deficient (HHD). In parallel, variants with a putative deleterious effect were identified from exome data. Candidate deleterious variants mapping within HHD were identified and further investigated in silico to assess their conservation across vertebrates and gene function. Thirteen candidate deleterious variants resided in nucleotides or genomic regions highly conserved across vertebrates and occurred in genes functionally linked to fertility or defects in mouse and human. These are pursued as candidates to influence fertility and fitness in Italian Holstein animals and are being validated to evaluate their use in genome-informed breeding programs.

Abstract number: 26808 / accepted / order: 4 / pres.means: Theatre / time: 15
Reverse genetics to describe a recessive defect in different breeds
C. Grohs[1], P. Michot[2], S. Chahory[3], M.C. Deloche[2], S. Barbey[4], M. Boussaha[1], C. Danchin-Burge[5], S. Fritz[2], D. Boichard[1], A. Capitan[2]
[1]GABI, INRA, AgroParisTech, Université Paris Saclay, 78350 JOUY-EN-JOSAS, France, [2]Allice, 149 rue de Bercy, 75595 Paris, France, [3]ENVA, Université Paris-Est, Ophtalmology, 7 Avenue du Général de Gaulle, 94704 Maisons-Alfort, France, [4]INRA, Domaine Expérimental du Pin, 61310 Exmes, France, [5]Idele, 149 rue de Bercy, 75595 Paris, France; cecile.grohs@inra.fr

Cattle breeds have a narrow genetic basis favoring emergences of recessive defects. In recent years, detection of cases by dedicated observatories (e.g. ONAB in France) combined with homozygosity mapping based on high density SNP genotyping data have proven to be efficient tools, leading to the characterization of more than 130 genetic defects in cattle. However, considering that more than 4900 defects have been identified in human, this might be only the tip of the iceberg. Indeed, this approach relies on the observation of affected animals with distinctive symptoms, and mutations resulting in non-specific symptoms or symptoms with little economic importance are likely to be missed. The increasing availability of whole-genome sequences has opened new research avenues such as reverse genetics for the identification of mutations impacting animal's health. Recently, using this top-down strategy, we described 2489 putative deleterious mutations in 1923 genes, segregating at a minimal frequency of 5 % in at least one of 15 breeds studied. The genes observed to be enriched in this study were mainly associated with nervous, visual and auditory systems, suggesting that those genes have not been taken into account for production purposes. Among them, we identified an ancestral deleterious variant in retinitis pigmentosa-1 (RP1) gene causing progressive retinal degeneration in several breeds. ONAB used the well-established and motivated network of partners to investigate the phenotypic consequences of the frameshift candidate variant. Clinical and functional analysis were performed and permit us to validate the causal mutation. Large scale genotyping showed that the mutated variant is very frequent in Normande breed (27%) but also segregates in other breeds at lower frequency (1.5% in Holstein). The conserved sequence haplotype suggests that the mutation is around 3800 years old.

Abstract number: 26844 / accepted / order: 5 / pres.means: Theatre / time: 15
Identification and management of recessive genetic defects in Belgian Blue beef cattle
T. Druet[1], A. Sartelet[2], X. Hubin[3], N. Tamma[1], M. Georges[1], C. Charlier[1]
[1]Unit of Animal Genomics, GIGA-R, 11 avenue de l'Hôpital B34 , 4000 Liège, Belgium, [2]Clinical Department of Production Animals, FARAH, Avenue de Cureghem 3, 4000 Liège, Belgium, [3]Association Wallonne de l'Elevage,

Rue des Champs Elysées 4 , 5590 Ciney, Belgium; tom.druet@ulg.ac.be

The Belgian Blue cattle breed has been intensively selected for extreme muscular development, causing a reduction of its effective population size. Several outbursts of recessive genetic defects have been observed in recent years. With the availability of high-density SNP panels, the Unit of Animal Genomics developed highly effective mapping and identification methods. Causative variants for two recessive defects (congenital muscular dystonia 1 & 2) were identified in a early pilot study (2006) and five more subsequently (crooked tail syndrome, dwarfism, gingival hamartome, prolonged gestation, lethal arthrogryposis syndrome). To improve genome-wide association studies (GWAS), we developed a haplotype-based GLMM suited for binary trait, effective for different scenarii (recessive, dominance, heterogeneity) and robust to isolated misclassifications. Surprisingly, some of the defects segregated at high frequency in the population. Based on segregation analysis and GWAS for selected traits, we provided strong evidence that at least two recessive defects were under balancing selection. More recently, with the reduction of costs for whole genome sequencing, an alternative strategy based on reverse genetic screen was developed to identify defects and embryonic lethal variants. That strategy is particularly important for small populations where screens for depletion in homozygous haplotypes lack of power. Five putative embryonic lethal variants were validated by carrier by carrier crosses. Genetic tests were rapidly implemented and massively used by the breeders (only bulls free of all defects were selected). As a result, a desirable drastic reduction of calf peri-natal mortality was observed but this imposes new constraints affecting genetic diversity. Currently, tools are tested to reduce the risk of mating two carriers of the same recessive defect, either based on genotypes from bulls (sire, maternal grand-sires, etc.) or based on segregation analysis for cows. First results indicate that this can be done effectively.

Abstract number: 27171 / accepted / order: 6 / pres.means: Theatre / time: 30

A review of bioinformatic methods to locate a new recessive mutation on the genome

G.E. Pollott
Royal Veterinary College, Royal College Street, London, NW1 0TU, United Kingdom; gpollott@rvc.ac.uk

The advent of a new recessive Mendelian condition can be critical if it is associated with a lethal or disease phenotype. Such a scenario has several challenges such as little information, few cases and a general fear amongst breeders that their breed will get a bad reputation if word gets out, causing a drop in prices for breeding stock. One might expect that the introduction of molecular genetic technologies would make the situation more tractable but, if the literature reports are anything to go by, this appears not to be the case. Two major contrasting bioinformatic approaches have been suggested to find the location of such novel recessive genetic diseases using molecular genetic markers. The first is based on the use of chi-squared tests (CST) at each marker location and the second utilises runs of homozygosity (ROH). Other candidate gene methods have been used in certain circumstances but this relies heavily on a well-annotated genome and some preliminary information on the likely candidate genes. Methods based on CST may be useful under certain circumstances but suffer from significant locations only being found when one allele segregates with the new mutation and is found at a relatively low allele frequency. Mutations in a ROH in both cases and controls will never be found by this method. There has been much debate about the efficacy of certain ROH methods. The most reliable seem to be those based on measuring ROH in cases using bp lengths and taking into account any similar ROH in controls. Phenotypic permutation allows some degree of probability to be attached to identified regions. Such methods are extendable from SNP to WGS approaches and only require ~10 cases and ~10 controls to detect the region containing the mutation. If this ROH method is used with NGS data there should not be any need for further resequencing to locate the exact position of the mutation. Apart from DNA quality control issues and reliance on a good reference genome these methods also critically depend on good phenotyping at the field level, which is not necessarily as accurate as geneticists would like. This presentation will use real examples to illustrate these methods.

Abstract number: 26388 / accepted / order: 7 / pres.means: Theatre / time: 15

Managing lethal alleles using genomic optimum contribution selection

L. Hjortø[1], J.R. Thomasen[1,2], P. Berg[1,3], M. Kargo[1,4], M. Henryon[5,6], H. Liu[1], A.C. Sørensen[1]
[1]Aarhus University, Department of Molecular Biology and Genetics, Blichers Allé 20, DK-8830, Denmark, [2]Viking Genetics, Ebeltoftvej 16, DK-8960 Randers SØ, Denmark, [3]NordGen Husdyr, Postboks 115, NO-1431 Ås, Norway, [4]Seges, Agro Food Park 15, DK-8200 Aarhus N, Denmark, [5]The University of Western Australia, School of Animal Biology, 35 Stirling Highway, CRAWLEY WA 6009, Australia, [6]Seges, Axeltorv 3, DK-1609 København V, Denmark; AChristian.Sorensen@mbg.au.dk

We tested the hypotheses that (i) culling animals that carry a recessive lethal allele reduces genetic gain when animals are truncation selected on genetic merit, and (ii) optimum-contribution selection (OCS) reduces the frequency of lethal alleles without reducing genetic gain. We tested these hypotheses by simulating rates of

genetic gain realized by three selection strategies that reduce the frequency of a single lethal allele: truncation selection, OCS penalising average-genetic relationship based on pedigree information, and OCS penalising average relationship based on genomic information. In each strategy, carriers of the lethal allele were either culled or not culled prior to selection. The strategies were simulated at 1% rate of increase in identity-by-descent averaged across a 30 M genome. We simulated breeding schemes with 10 discrete generations of selection for a single trait with a heritability of 0.2. Only females were phenotyped, all animals were genotyped prior to selection, and genetic merit was predicted using GBLUP. We found that when selection was by truncation selection, culling carriers reduced initial genetic gain by up to 15% compared to no culling of carriers. Genetic gain in subsequent generations was unaffected by culling strategy. On the other hand, when selection was by OCS, culling carriers reduced the frequency of lethal alleles without reducing genetic gain. The reason was that culling carriers distorted the desired distribution of parental contributions in the remaining selection candidates. OCS was able to restore the desired genetic contributions in the selected animals. Truncation selection did not have this tidying function and allowed the distorted distribution to persist. This implies that OCS should be used in breeding schemes, where carriers of lethal alleles are culled prior to selection.

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Using a MQTL matrix to test for pleiotropic effects of Mendelian trait loci on quantitative traits.

C. Scheper, S. König
Justus-Liebig-University Gießen, Ludwigstr. 21b, 35390 Gießen, Germany; carsten.scheper@agrar.uni-giessen.de

Genotypes for Mendelian trait loci can be used to set up a MQTL relationship matrix to enhance variance component estimations. The approach allows to test for pleiotropic QTL-effects of favorable Mendelian traits (e.g. polledness in cattle) or Mendelian inherited detrimental genetic disorders on quantitative traits. The present study aimed on i) the validation of a MQTL matrix approach to test for pleiotropic QTL-effects of Mendelian trait loci via simulation, and ii) the application of this approach to real data, i.e. considering pleiotropic QTL-effects of the polled locus on quantitative production and reproduction traits. Via stochastic simulations, a Mendelian trait locus with a pleiotropic QTL-effect on a simulated quantitative trait was generated. The MQTL matrix approach successfully detected the simulated pleiotropic QTL-effects using bivariate models, but with the tendency for slight overestimation of QTL-effects. The real data considered 48,046 test day and 3,834 calving and insemination records from 1,746 German Simmental cows kept in 12 herds. The pedigree traced back to five generations, and included 8,624 animals with known polled pheno- or genotypes. The MQTL matrix was constructed considering reliable reconstructed polled marker genotypes. Results for model comparisons based on likelihood values indicated generally better model fits for bivariate models including the QTL-effects compared to base models without QTL-effects. For milk yield, fat percentage, somatic cell score, non-return-rate 56, days to first service and days open, the proportion of additive genetic variance explained by a QTL-effect of the polled locus was negligible. However, the QTL-effect of the polled locus explained 2.7% of the additive genetic variance for protein percentage, whereas the corresponding genetic correlation of -0.005 for MQTL matrix based random effects indicated no genetic antagonism. We conclude that the reported inferiority of polled animals in quantitative traits is not due to inevitable detrimental effects of the polled locus. Furthermore, the presented approach allows for further integration of polledness in present breeding goals using estimated (co)variance components in selection indexes.

Abstract number: 26907 / accepted / order: 9 / pres.means: Theatre / time: 15

Bovine Genetic Disease and Trait Frequencies in Ireland: >85 causative alleles in >1M animals

M.C. Mcclure[1], P. Flynn[2], R. Weld[2], T. Pabiou[1], M. Mullen[3], J.F. Kearney[1], J. Mcclure[1]
[1]Irish Cattle Breeding Federation, Bandon, Cork, Ireland, [2] Weatherbys Ireland, Johnstown, Kildare, Ireland, [3]Athlone Institute of Technology, Athlone, Westmeath, Ireland; mmcclure@icbf.com

On the International Dairy and Beef (IDB) custom Illumina bovine SNP chip we have included diagnostic probes for as many disease and trait causative alleles available. The current build, IDBv3, includes 238 diagnostic probes, of which 86 have been validated. Via multiple national Department of Agriculture, Food, and the Marine schemes over 1 million Irish cattle have now been genotyped and have had their data deposited in the ICBF database. These include AI sires, pedigree cattle, and a large number of commercial and crossbred animals. Most studies that report the allele frequencies in a breed or national population are only able to include data from AI or pedigree animals, a few are able to include a small amount of commercial animals. Given the size of our dataset we are able to show that the frequency of undesirable alleles is often lowest in the AI population, highest in the commercial population, and that the frequencies between them to be highly variable. This trend is understandable as traditionally only animals with a high economic value were tested for genetic diseases as their value, or sale price, offset the cost of multiple genetic diagnostic tests. By incorporating all of the causative alleles on the IDBv3 we are able to provide carrier status information for all animals tested, although some traits do require an additional royalty fee for individual reporting. By having the animal's genomic status known Ireland will be able to reduce its genetic disease risk by advising against carrier x carrier matings. To aid the farmers and advisors we

also developed a booklet that describes each trait in plain language. The booklet lists known carrier ancestors, for example top AI sires, and pictures of affected animals when possible. For scientists we have developed a second booklet which expands on the first and include flanking DNA sequence, HSPC information, a more in depth trait description, and references. Both booklets are available via the ICBF website at https://www.icbf.com/wp/?page_id=2170

Abstract number: 26774 / accepted / order: 10 / pres.means: Theatre / time: 30
Management of Mendelian traits in breeding programs by gene editing
J.B. Cole
Agricultural Research Service, USDA, Animal Genomics and Improvement Laboratory, 10300 Baltimore Avenue, Beltsville, MD 20705-2350, USA; john.cole@ars.usda.gov

SNP genotypes have been used to identify several new recessive mutations that adversely affect fertility in dairy cattle, and to track conditions such as polled. Recent findings suggest that the use of sequential mate allocation strategies that account for increases in genomic inbreeding and the economic impact of affected matings result in faster allele frequency changes than those which do not. However, the effect of gene editing on selection programs also should be considered because it has the potential to dramatically change allele frequencies in livestock populations. Computer simulation was used to study the effect of clustered regularly interspaced short palindromic repeat, transcription activator-like effector nuclease, and zinc finger nuclease technologies for gene editing on dairy cattle breeding programs. A hypothetical technology with a perfect success rate was used to establish an upper limit on attainable progress, and a case with no editing served as a baseline for comparison. Technologies differed in the rate of success of gene editing, as well as the success rate of the embryo transfer step, based on literature estimates. Number of alleles edited was assumed to have no effect on success rate. The two scenarios evaluated considered only the horned locus, or 12 recessive alleles segregating in the US Holstein population. The top 1, 5, or 10 % of bulls were edited each generation, and either no cows or the top 1 % of cows were edited. Inefficient editing technologies produced less cumulative genetic gain and lower level of inbreeding than efficient ones. Gene editing was very effective at reducing the frequency of the horned haplotype (increasing the frequency of polled animals in the population), and allele frequencies of the 12 recessives segregating in the US Holstein population decreased faster with editing than without. These results suggest that gene editing can be an effective tool for reducing the frequency of harmful alleles or increasing the frequency of desirable alleles in a dairy cattle population even if only a small proportion of elite animals are modified. The source code for the simulation and scripts used to analyze the data are available on GitHub: https://github.com/wintermind/gene-editing.

Abstract number: 27290 / accepted / order: 11 / pres.means: Theatre / time: 30
International registration and management of genetic defects: General discussion
H. Jorjani
Department of Animal Breeding & Genetics, Box 7023, 75007 Uppsala, Sweden; hossein.jorjani@slu.se

Discussing national and intrernational initiatives to standardize the nomenclature, register and manage the genetic defects.

Abstract number: 26852 / accepted / order: 12 / pres.means: Poster
APOB associated cholesterol deficiency in Holstein cattle is not a simple recessive disease
U. Schuler[1], M. Berweger[1], B. Gredler-Grandl[1], S. Kunz[1], S. Hofstetter[2], T. Mock[3], T. Mehinagic[4], M. Stokar-Regenscheit[4], M. Meylan[3], F. Schmitz-Hsu[5], F.R. Seefried[1], C. Drögemüller[2]
[1]Qualitas AG, Chamerstr. 56, 6300 Zug, Switzerland, [2]University of Bern, Institute of Genetics, Bremgartenstr. 109a, 3001 Bern, Switzerland, [3]University of Bern, Clinic for Ruminants, Bremgartenstr. 109a, 3001 Bern, Switzerland, [4]University of Bern, Institute of Animal Pathology, Längasstr. 122, 3012 Bern, Switzerland, [5]Swissgenetics, Meielenfeldweg 12, 3052 Zollikofen, Switzerland; urs.schuler@qualitasag.ch

Cholesterol deficiency (CD) has been reported for the first time in 2015 as a new recessive inherited genetic defect in Holstein cattle. It was initially mapped on BTA11 and subsequently a causative loss of function mutation in APOB was identified by whole genome sequencing. Affected homozygous mutant calves showed poor development, intermittent diarrhea and hypocholesterolemia. Usually heterozygous carriers did not show any clinical signs of maldigestion but had in general lower cholesterol and lipoprotein concentrations, suggesting a codominant effect of the APOB mutation on lipid homeostasis. In the meantime we collected 15 CD affected animals heterozygous for the APOB mutation indicating a more complex inheritance compatible with a dominant disease with incomplete penetrance. We have also analysed possible effects on additional traits and used routine phenotypes and official models from Swiss Holstein genetic evaluation for fertility,

birth, conformation and beef traits. A fixed effect decoding the risk status for CD-homozygosity was fitted in genetic evaluation models. Since dams are usually not genotyped, nine subclasses were defined for three possible conditions of each sire / maternal grandsire status. Interestingly, effects were found on non-return rate and on interval from first to last insemination in both, heifers and cows. Furthermore, negative effects on birth weight and stillbirth could be identified whereas effects on beef traits have not been detected. In conclusion, as beyond malabsorption of dietary lipids, deleterious effects of APOB deficiency can be expected on hepatic lipid metabolism, steroid biosynthesis, and cell membrane function. Therefore the APOB mutation may also explain unspecific symptoms of reduced fertility.

Abstract number: 26814 / accepted / order: 13 / pres.means: Poster

Associations between a causal mutation for Mulefoot and production traits in Holstein Friesian cows

M.P. Mullen[1], J. Mcclure[2], F. Kearney[2], M. Mcclure[2]

[1]Bioscience Research Institute, Athlone Institute of Technology, Athlone, Co. Westmeath, Ireland, [2]Irish Cattle Breeding Federation, Highfield road, Bandon, Co. Cork, Ireland; mmullen@ait.ie

The impact of causal mutations with undesirable effects on animal growth and development are of particular interest to the livestock breeding industry. In dairy cattle, a doublet substitution mutation (NG1621KC) in LRP4 is attributed to the fusion or non-division of the functional digits of the hoof, termed syndactyly or Mulefoot. The identification and exclusion of Mulefoot carriers from breeding is a desirable goal, however, strategic mating may be considered in the case of otherwise high genetic merit animals. Estimation of the possible pleiotropic effects of such mutations would enable more informed strategic mating decisions. The objective therefore of this study was to estimate the effects of the NG1621KC causal mutation for Mulefoot in LRP4 on milk, fertility, carcass and health traits (n=16) in dairy cows in Ireland. Genotypes and phenotypes on 10,707 dairy cows were obtained through the Irish cattle breeding federation (ICBF). Phenotypes were expressed as predicted transmitting abilities (PTAs). PTAs were deregressed following the removal of parental contributions. Only animals with an adjusted reliability of >10% were included in the analysis which included n=6876, 1198, 264, 4566, 8564, 152, 2280, 3194, 518, 360, 1374, 5747 cows for milk traits (n=5), calving interval, survival, gestation length, calf mortality, maternal calving difficulty, carcass weight, carcass conformation, carcass fat, cull cow weight, and somatic cell score, respectively. The association between NG1621KC and deregressed PTAs were analysed in ASREML using a weighted mixed animal model. The NG1621KC mutation was associated with increased calving difficulty (3.41, s.e. 1.56, $p<0.05$) and decreased maternal calving difficulty (-4.24, s.e. 1.85, $p<0.05$), however, there was no association ($p>0.05$) identified with any of the other milk, carcass or health related traits examined. Assuming average genetic merit the results of this study provide no evidence to support the maintenance of carriers of the NG1621KC mutation on farm or in the national herd in relation to the production traits analysed.

Abstract number: 26910 / accepted / order: 14 / pres.means: Poster

Relationships between mutations responsible for Holstein Haplotype 1, 3 and 4 and Bovine Leukocyte A

M. Mcclure[1], J. Mcclure[1], L. Ratcliffe[2], J.F. Kearney[1], M. Mullen[2]

[1]Irish Cattle Breeding Federation, bandon, cork, Ireland, [2]Athlone Institute of Technology, Bioscience Research Institute, Athlone, Westmeath, Ireland; mmcclure@icbf.com

Identification of carriers of mutations with lethal effects in cattle populations enables more informed decision making by the farmer be it elimination from breeding stock or management through strategic mating schemes for high genetic merit carriers. In order to best advise farmers on the use of this information, estimation of the effects of these mutations on routinely recorded production traits in carrier animals is needed. Therefore, the objective of this study was to estimate if the mutations associated with HH1, 3, 4 or BLAD showed any evidence of effects across any production traits (milk, fertility, carcass and health traits (n=16)) in dairy cows. Genotypes and phenotypes (expressed as predicted transmitting abilities (PTAs)) on 10,707 dairy cows were obtained from the Irish Cattle Breeding Federation (ICBF) database. Only animals with an adjusted reliability of >10% were included in the analysis which included n=6876, 1198, 264, 4566, 8564, 152, 2280, 3194, 518, 360, 1374, 5747 cows for milk traits(n=5), calving interval, survival, gestation length, calf mortality, maternal calving difficulty, carcass weight, carcass conformation, carcass fat, cull cow weight, and somatic cell score, respectively. The association between each SNP and PTA (deregressed) was analysed in ASREML using weighted mixed animal models. BLAD carriers were associated with increased somatic cell score ($p<0.05$) and calf mortality ($p<0.05$), however, there was no association ($p>0.05$) with any of the other milk, fertility or carcass traits analysed in this study. No association ($p>0.05$) was observed between HH1 and any of the traits examined. Cows with a HH2 allele were associated ($p<0.05$) with decreased gestation length with no other effects identified. Cows with a HH3 allele were associated ($p<0.05$) with increased calving interval with no other effects observed. Unless carriers of either BLAD, HH1, HH3 or HH4 are of otherwise high genetic merit these results provide no evidence to support the maintenance of

carriers on farm or in the national herd.

Abstract number: 27032 / accepted / order: 15 / pres.means: Poster
A region on BTA5 is significantly associated with Brachygnathia inferior in dairy cattle
C. Flury[1], H. Signer-Hasler[1], M. Frischknecht[1,2], A. Lussi[1], F.R. Seefried[2], C. Drögemüller[3]
[1]Bern University of Applied Sciences, School of Agricultural, Forest and Food Sciences HAFL, Länggasse 85, 3052 Zollikofen, Switzerland, [2]Qualitas AG, Chamerstrasse 56, 6300 Zug, Switzerland, [3]University of Bern, Institute of Genetics, Bremgartenstrasse 109a, 3001 Bern, Switzerland; christine.flury@bfh.ch

Brachygnathia inferior (BI) in cattle is considered as a heritable condition. However the mode of inheritance and underlying genes still remain unclear. Braunvieh cows being affected from BI are recognized during linear type classification in the first lactation and penalized in their overall type note. At 1.1.2014 104 living cows with BI were registered by Braunvieh Schweiz. Out of these, hair samples of 81 cows were collected and genotyped for the 80k-GGHDP. These genotypes were combined with 440 HD-genotypes from unaffected cows. After filtering data from 81 cases and 440 controls and 50'864 SNP were used in a genome wide association study. 17 SNP located in a 4.2 Mb interval on BTA5 were significantly associated with BI. The interval is positioned between 29.1 and 33.3 Mb and contains several genes. Subsequently runs of homozygosity (ROH) were calculated and their distribution was compared between cases and controls. More than 70% of the cases had SNP between 29.9 and 33.5Mb on BTA5 in a ROH, while the same holds only for less than 16% of the controls. For SNP on all other autosomes the deviations between the two groups were much less pronounced.

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Genetic basis of the intrauterine growth restriction (IUGR) in cattle
K. Rutkowska, M. Lukaszewicz, J. Oprzadek
Institute of Genetics and Animal Breeding of the Polish Academy of Sciences, Department of Animal Improvement, Postepu 36A, Jastrzebiec, 05-552 Magdalenka, Poland; k.rutkowska@ighz.pl

Foetal growth is a process which largely depends on sustainable communication between placenta, foetus and mother of the foetus. The aim of this paper is to demonstrate the actual state of the art about intrauterine growth restriction (IUGR) in cattle. IUGR remains a significant problem in animal agriculture. IUGR animals are often culled because of their increased susceptibility to the onset of pathology/disease, permanent impaired growth, and sub-optimal carcass quality. In cattle, 115kb deletion of the 3`end of the bovine non-protein coding MIMT1 gene, when inherited from the male parents, causes IUGR, late abortion and stillbirth. The deletion removes exons 3rd and 4th of the gene at 3`UTR. Mutation causes loss of MIMT1 expression in the brain and cotyledon in all carrier foetuses. This mutation for the first time was identified in offspring of Finnish Ayrshire bull – YN51. The semen of the YN51 bull was commercially used in 2006 and 2007 to artificially inseminate 1.900 Finnish Ayrshire cows. In offspring of YN51 bull late gestation abortions and stillbirth were observed. Cattle genetic model provides a powerful new resource and a unique opportunity to systematically investigate IUGR. Although cattle is not a standard model to investigate IUGR, however may be useful in examinating stillbirth in large mammalian organisms without any surgery or other invasive methods. This is the first time when was reported foeto-maternal specific regulation in the placenta of IUGR large animals. Described in the text state of knowledge about genetically conditioned IUGR in cattle indicate that the need for testing IUGR in animals still exists. Animal studies about IUGR will provide valuable knowledge to improve livestock management systems during the progression of pregnancy and to identify foetuses at risk. Molecular studies will be useful in increasing the number of live-born individuals what, in the future, will reduce production cost and improve welfare of animals.

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Screening for missing homozygosity in a local Swiss dual purpose breed
F.R. Seefried[1], M. Berweger[1], B. Gredler-Grandl[1], S. Kunz[1], C. Drögemüller[2]
[1]Qualitas AG, Chamerstr. 56, 6300 Zug, Switzerland, [2]University of Bern, Institute of Genetics, Bremgartenstr. 109a, 3001 Bern, Switzerland; franz.seefried@qualitasag.ch

However the population size of the autochthonous Swiss dual-purpose breed Original Braunvieh (OB) is rather small, genomic selection has been implemented. Therefore large-scale SNP genotype data became available and enables an identification of haplotypes with reduced or missing homozygosity that may harbour deleterious recessive mutations. Genome-wide scans for missing homozygosity were applied based on 1'379 animals genotyped at of at least 50K density level. Sliding window approach using windows sizes between 0.5 and 10 Mb was applied for inferring haplotypes. FImpute software was used for phasing, and expected numbers of homozygous animals were calculated assuming random mating. Phenotypes were taken from routine genetic

evaluations for fertility-, birth- and beef traits. Official models were adjusted by adding a fixed effect decoding the risk of homozygosity. Since dams are usually ungenotyped, nine subclasses were defined for three possible conditions of each sire / maternal grandsire status. In summary, haplotype analyses detected a single genome region at significant level: a 2 Mb segment on BTA11. Additional seven genome regions located on BTA1, BTA5, BTA13, BTA14, BTA17 and BTA20 were identified slightly below significance threshold. Subsequent phenotypic analyses were performed for all identified genome regions revealing that an increased risk of homozygosity for the BTA11 region is associated with a reduced birth weight. Effects on fertility traits, in detail reduced non-return rate and extended interval from first to last insemination, were detected for regions on BTA1, BTA5, BTA17 and BTA20. Interestingly, regions on BTA1 and BTA20 exhibited effects on beef traits either. Based on further analyses, one may assume a co-segregation of the growth-related and recessive FH2-disorder originally reported in Simmental behind the observations made for the haplotype region at the telomeric end of BTA1 in OB.

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Searching for, finding, and fixing genetic diseases: We can't afford not to

J. Mcclure[1], P. Flynn[2], S. Waters[3], F. Kearney[1], M. Mullen[4], T. Pabiou[1], R. Schnabel[5], J. Taylor[5], R. Weld[2], M. Mcclure[1]

[1]Irish Cattle Breeding Federation, Highfield House, Shinagh, Bandon, County Cork, Ireland, [2]Weatherby's DNA Laboratory, Johnstown, Co. Kildare, Ireland, [3]AGRIC, Teagasc, Grange, Co. Meath, Ireland, [4]AIT, Department of Life and Physical Sciences, Faculty of Health and Science, Athlone, Co. Westmeath, Ireland, [5]University of Missouri Columbia, Animal Sciences, UMC, Columbia, Missouri 65211, USA; jmcclure@icbf.com

Genetic diseases cost the livestock industry millions every year. It is estimated that every animal carries 20-100 genetic disease causing alleles and that every animal born carries 50 spontaneous mutations, though not all are detrimental to the viability or productivity of the animal, in fact, some may be beneficial. Since 2013, 650,000 Irish cattle have been genotyped and allele frequencies were analysed to calculate carrier frequency on 33 different diseases using the International Dairy and Beef (IDB) SNP Chip. Economic losses and gains will be calculated for disease and trait genes tested on the IDB SNP chip. Genotyping costs have shrunk dramatically and made developing a "Breed Smarter Strategy" realistic for the Irish population. Implementation of this strategy, will allow the industry to retain high value animals even if they carry known adverse traits through mating them with animals that do not carry those genes. The idea behind the program has incentivised ICBF to seek out new disease SNP in the population. A survey was developed allowing farmers and veterinarians to report genetic defects and provide samples to identify diseases causing economic loss. The limitations in a program like this are removing the stigma linked with having an atypical animal, and identifying diseases that are genetic. While implementation of this program has been slow, articles online and in popular press have increased the frequency of reports every year. After a few key diseases were identified, DNA from affected animals was sent off for whole genome sequencing and analysis of the genomes will commence to identify candidate causal mutations. This is a constant process as new genetic diseases appear every year. Success of the program will save the industry millions of euros annually once new SNP are identified and added to the next version of the IDB chip.
