Changes in bull breeding during the years

– A comparison between 50s and 80s/90s

Förändringarna i tjuravel genom tiderna- en jämförelse mellan 50 talet och 80/90 talet.

Moa Hagelberg

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Swedish University of Agricultural Sciences, SLU
Faculty/Department, Husdjursgenetik (HGEN)
Programme/Education, Animal science
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Supervisor: Anna Maria Johansson, Swedish University of Agricultural Science, Department of Animal Breeding and Genetics (HGEN)

Examiner: Sofia Nyman, Swedish University of Agricultural Science, Department of Animal Breeding and Genetics (HGEN)

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Swedish University of Agricultural Sciences
Faculty Institution of animal genetics (HGEN)
Department of animal breeding and genetics

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Abstract

Breeding on bulls have occurred during many decades in the same way as it has for dairy cattle. Both the sire and dams that are being used during the selection breeding have been tested through genomic selection to see their value for each trait, for the dams this has been started more recently than for the bulls. The breeding bulls are being progeny tested to see how good parents they are and if they should be continued to be bred on. Single- nucleotide polymorphs (SNPs) are variable base pairs in the genome. 150 000 SNPs were analysed for 81 SRB bulls and 83 SLB/Holstein bulls in this study and compared to other quantitative trait loci regions and SNPs from previous studies to find the associations to genes/traits. Many of the SNPs were associated to production and health. The SNPs found for the SLB/Holstein bulls had changed more than for the SRB bulls. The production traits were found to have a negative correlation to fertility and also some diseases for example mastitis. Between 1950 and 1980/1990 the production traits such as milking speed and protein yield have changed in the dairy bulls. When breeding for a specific gene/trait it is important to know that the traits can be correlated with other genes/traits that can be unfavourable for both the farmer economy and for the animal welfare.

Keywords: Bull, breeding, SNP, traits, decades, production, health, SLB, Holstein, SRB

Sammanfattning

Tjuravel har genomförts under många decennier på samma sätt som för mjölkkor. Både tjurarna och korna som används har testats genomiskt för att se deras värde för varje egenskap. För kor har detta börjat testas senare jämfört med tjurar. Avelsdjur testas för att se hur bra föräldrar de är och om de ska fortsätta att avlas på. Singel- nucleotide polymorphs (SNPs) är olika baspar i genomet. 150 000 SNPar analyserades hos 81 SRB tjurar och 83 SLB/Holstein tjurar och jämfördes med andra quantitative trait loci regioner och SNPar från tidigare studier för att hitta kopplingar till gener/egenskaper. Många av SNParna var förknippade med produktion- och hälsoegenskaper. Det visade sig att SNP för SLB/Holstein-tjurarna hade förändrats mer än för SRB-tjurarna. Produktionsegenskaperna hade en negativ korrelation till fruktsamhetsegenskaperna och sjukdomar som t.ex. mastit. Inom tjuraveln har förändringar skett för produktionsegenskaper som bland annat mjölkningshastighet och proteininnehåll. När man avlar på en specifik gen/egenskap att det viktigt att veta att egenskapen kan ha ett genetiskt samband till andra gener/egenskaper som kan vara ogynnsamma för både lantbrukarnas ekonomi och djurens hälsa.

Nyckelord: Tjurar, avel, SNP, egenskaper, årtal, produktion, hälsa, SLB, Holstein, SRB.

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Abbreviations

AI Artificial insemination
BLUP Best linear unbiased prediction
cM Centimorgan
DNA Deoxyribonucleic acid
EBV Estimated breeding value
GEBV Genomic estimated breeding value
GS Genomic selection
MAS Marker assisted selection
Mb Million base pair
SLB Svensk låglandsboskap
SNP Single -nucleotide polymorphism
SRB svensk rödbrokig boskap
QTL Quantitative trait locus

1. Introduction

Cattles have been important production animals during several decades. The number of farms has during the recent decades decreased from 300 000 farms in 1950 to 50 000 in 1990 (Jordbruksverket 2016). The cattle population has also decreased during the last decades from 2700 000 during the 1950 to 1700 000 during 1990 (Jordbruksverket 2016). During these decades the average dairy cattle herd size has expand from 15 dairy cattle on the 1980 to 65 during 2011 (Jordbruksverket 2016).

Through the years the breeding goal for the Swedish dairy cattle has changed as the population in Sweden has increased. Dairy cattle are being bred for different traits such as milk yield, health, fertility (Delaval 2004), where the main focus is a high milk yield (Björklund et al. 1999; Morell & Myrdal 2011). The most common dairy breeds in Sweden are Swedish red dairy cows (SRB) and Swedish Holstein (SH; Delaval 2004). In contrast to the increased milk production in dairy cattle, the fertility started to decline because these two traits have a negative correlation (Hill et al. 1997).

In the same time to be able to get the cattle to produce milk they need to get an offspring to stimulate the milk production (Nygård & Wramner 2012). It is not only the mother that the offspring inherits its genes/traits from, the father also contributes with their genetic genes/traits (Gordon 2004). A few decades ago, the farmers used their own farm bull to produce offspring's (Nygård & Wramner 2012). In the modern dairy cattle production, the most common way to get an offspring is through artificial insemination (AI; Gordon 2004). As the farms got bigger and the cattle populations increased new breeding techniques were introduced (Phillips 2009).

The bulls and dams are selected with help from different selections methods and one common technique today is genomic selection (GS;Goddard et al. 2016). Today candidate bulls in different breeds are being chosen through GS or marker-assisted selection (MAS) and they get progeny tested. This is one way to know which bulls will give the best wanted results in the offspring, either getting a well producing cow or knowing that the bull calves that are being born will be a good breeding bull (Hallerman et al. 1990). To be able to do analyses for the marker data, the bull's DNA is extracted from either a blood sample or from the semen. It is shown that some quantitative trait loci from bulls has effects of the female fertility, but it also affects other traits and it can be caused by pleiotropic effects (Guldbrandtsen et al. 2009).

The dairy cattle's traits have changed over the decades to fit the market requirements. The purpose of this thesis was to investigate how the traits of the dairy bulls have changed during the decades. Which are the traits that has changed the most between the 50^{th} comparing to 80^{th}/90^{th}?. How have the allele frequencies changed over time and how did they affect the traits bred for.

2. Genetic terms and methods

2.1. Genetic terms

Deoxyribonucleic acid (DNA) is the molecule that works as the genetic material in living cells. DNA is a copy of the parent's DNA which is passed on to the offspring when the offspring inherits a trait from their parents. The DNA carries information that is necessary to be able to build up an offspring organism (Perona 2013). The DNA consists of four different nucleotides adenine; A, guanine; G, cytosine; C and thymine; T where A is paired with T and G is paired with C.

The chromosome function as a carrier for the genes. It consists of DNA and associated proteins. Bacteria's have one circular chromosome while eukaryotes have linear chromosomes. The chromosomes differ in numbers and size depending on species (Lee & Orr-Weaver 2013). Cattles have 60 chromosomes that contributes to 30 chromosome pairs (Meo & Iannuzzi 1995), while e.g. humans have 46 chromosomes that contributes to 23 chromosome pairs (Trask 2002).

Alleles are alternative forms of a gene. All individuals inherit one allele from the dam and one from the bull. If the alleles that are inherited from the parent are identical the individual will be called a homozygote for this gene. If the alleles are different it will be called heterozygote (Anderson 2013). In all populations each allele contributes to a specific role and is more or less common, this constitution of alleles contributes to allele frequency. The allele frequency changes during time and is affected by e.g. selection and genetic drift (Hedayat & Rezaei 2013).

Genetic drift is a factor that is causing the gene pool to change through generations. The genetic drift focus on two different types of alleles, e.g. A and a, where A (q) is dominant and a (p) is recessive. The allele frequency can change over time. One example is described in Table 1 where the allele frequency in generation 1 equals 0.4 (q) and 0.6 (p). In generation 2 a genetic drift may have occurred and the frequency can become equal between the alleles (q=0.5 and p=0.5). The genetic drift has a larger effect in a small population compared to a bigger population. This is due to the fact that a smaller population have fewer animals which leads to a larger total change in the allele frequency in the population. This will result in a higher percentage of a certain allele frequency in the smaller population compared to a larger population (Honnay 2013).

Table 1. An example of changes in a population due to genetic drift

	Generation 1	Generation 2	Generation 3
P	0.6	0.5	0.4
Q	0.4	0.5	0.6

Centimorgan (cM) is the distance between two markers on the same chromosome (Stahl 2013). cM is connected to the expected recombination distance per million base pair (Mb) where the recombination distance is calculated from the expected genetic length (measured in cM) divided by the corresponding chromosomes physical length (measured in Mb ;Garrick et al. 2014). Recombination is when an exchange of DNA between homologous chromosomes occurs (Garrick et al. 2014). The number of recombination's per chromosome depends on the length, for example a longer chromosome tend to have more recombination's compare to a shorter chromosome (Garrick et al. 2014). As an example chromosome 1 has an expected recombination distance of 1.07 while chromosome 19 has an expected recombination distance on 1.58 (Aries et al. 2009).

A single- nucleotide polymorphism (SNP) is a variation at a single position in a DNA sequence among individuals. It is during the SNP were individuals in a population can look different by the sequence of a single base pair. The nucleotides can differ between animals which will result in different traits (Darvasi & Lencz 2013). Table 2 shows an example of 3 individuals where individual 1 and 3 have the same SNP sequence while individual 2 differs for SNP 1 and SNP 2.

Table 2. Example of differences in SNP sequence between individuals

	SNP 1	SNP 2	SNP 3
Individual 1	A	C	A
	T	G	T
Individual 2	C	A	A
	G	T	T
Individual 3	A	C	A
	T	G	T

A quantitative trait loci (QTL) is a specific chromosomal region or genetic locus in which sequence of bases in DNA markers are statistically associated with variation in the trait (Hall 2005).

2.2. Genetic methods

Animal breeding has been going on for many decades where farmers have bred for important traits. In the beginning selection of breeding animals were based on phenotypic recordings.

Artificial insemination (AI) is when frozen or fresh semen from selected bulls are inseminated in cows. AI has been used since 1933 when the first cooperative dairy AI organization began. It is being used a lot, in country's like Denmark AI is used for 90 % of the times to get the cow pregnant also it has given big genetic effects for example on milk yield (Ombelet & Robays 2015). During AI it is important to know when the cow is in estrus to get a high accuracy for pregnancy (Foote 2002).

In the begging breeding were based on the phenotypic recordings and with help of best linear unbiased prediction (BLUP) that combined the individual's recordings to the relative's recordings, it was possible to be able to get the estimated breeding value (EBV) for the animal (Goddard et al. 2016). EBV are calculated from the phenotypes and family relationships and are based on the animal's pedigree (Goddard et al. 2016).

Using phenotypic records have been proven to give good results, but it was discovered that using DNA information would improve the genetic gain even more. Marker-assisted selection (MAS) has been used since late 1990 and includes two steps; 1) to detect and find genes of interest and 2) include this information to the BLUP-EBV equation (Goddard et al. 2016). The problem with MAS was that only larger QTL were detected, and the smaller ones were ignored (Goddard et al. 2016).

Genomic selection (GS) is the latest technique where DNA markers is used to gain genetic improvement (Bowman et al. 2009). When applying GS, breeding values from a reference group with genotyped and phenotyped animals. Based on the reference group breeding values for selected genotyped cows/bulls can be estimated even though they have no phenotypes. The possibility to find good breeding animals are good when applying GS science because of that the accuracies are quite high (Goddard et al. 2016). For example, accuracies from GS exceeds 0.8 for milk yield and 0.7 for fertility (Cooper et al. 2011; De Roos et al. 2011). Genomic selection decreases the generation intervals and increases the predication accuracy and selection intensity, and can be used for animals without phenotypes (Allan et al. 2015). Comparing to the traditional BLUP method the genomic estimated breeding values (GEBV) in genomic BLUP (GBLUB), are estimated by the phenotypes and genomic relationship instead of a pedigree relationship (Goddard et al. 2016).

The bull's merit is an important aspect in the dairy cattle's genetic process. The ranking of the bull's that is getting a merit depends on several factors, such as pedigree merit of the parents, number of bulls sampled, speed and accuracy of the progeny test (Norman et al. 2003). Progeny testing is a commonly used method in animal breeding and depends on the offspring's estimated phenotypic value. In progeny testing several offspring's is being analyzed from a one selected animal. If

the analyzes gives good results for the wanted trait the selected animal will continue as a breeding animal. If the population has a lot of tested offspring the accuracy for the selected animal is high. Progeny testing is used on males and is mostly used for traits that has a medium heritability, e.g. milk yield (Ruvinsky 2001).

3. Method

The bulls that were used in this study were 81 SRB and 83 SLB/Holstein. For each bull 150 000 SNP were analyzed. The samples that contained the SNP's were from frozen semen that Viking Genetics had collect. The DNA were extracted at the Swedish University of Agricultural Science, Uppsala (Sweden) and then sent to Neonen for genotyping.

Table 3. Number of animals per breed and decade.

Decade	SRB[1]	SLB[1]/Holstein
1950	4	7
1960	27	27
1970	35	23
1980	15	21
1990	0	5
Total	81	83

[1]*SRB=Swedish Red and White, and SLB= Swedish Lowland*

The bulls were categorized depending on when they were born and what breed they were. The bulls were of two breeds, Swedish red and white (SRB) and Swedish lowland cattle (SLB)/Swedish Holstein. Table 3 shows the number of bull per breed born in the different decades.

For this thesis the programs R and PLINK were used to calculate the allele frequency.
R is a program for statistical computing and graphics, and was used in the beginning and in the end of the programing. PLINK is a program for whole genome data analysis and this program were used to estimate allele frequencies and to be able to see which SNP that changed the most.

The different breeds were first put into R independent on what year they were born but dependent on the breed. Later on the breeds were put into R depending on which breed and decade they were born respectively. All different decade and breeds groups were compared to see which chromosome differed the most. The main focus was to compare the allele frequency change between SLB/Holstein and SRB-bulls (all individuals), the 50th SLB/Holstein-bulls compared to the 90th SLB/Holstein-bulls and the 50th SRB-bulls compared to the 80th SRB-bulls.

To see how the allele frequencies has been changing and which chromosomes that has been changing the most during the years PLINK was used. To compare different groups of animals these were separated by putting one of the groups as cases (2) and the other ones as controls (1). Table 4 shows an example of a fam file needed for estimations in PLINK. This file was used to compare the different breeds and decade groups. Since only bulls were included in this study the gender column in Table 4 was set to 1 for all animals.

Table 4. An example of a fam file needed for estimations in PLINK

Animal ID	Animal ID	Father ID	Mother ID	Gender[1]	Control or case[2]
AJSE-1	AJSE-1	0	0	1	1
AJSE-2	AJSE-2	0	0	1	1
AJSE-11	AJSE-11	0	0	1	1
AJSE-53	AJSE-53	0	0	1	2
AJSE-55	AJSE-55	0	0	1	2
AJSE-58	AJSE-58	0	0	1	2

[1.] *1=male*
[2.] *1= control and 2=case*

To investigate the largest changes between the breeds and decades (1950 until 1990) we wanted to find the SNPs that had changed the most throughout the years. This was performed by using PLINK. In the file from PLINK it was possible to see which SNP's that had changed the most between the 1950 and 1990. Table 5 shows the chromosome the SNP were located, the name of the SNP and also the p-value for the SNP. The top 10 changed SNPs during the years were chosen for further studies.

Table 5. How the tables from PLINK looked like with the most changed SNP in the top. Table 5 are only showing the top three most changed SNP from the table of 150k SNP.

Chromosome	SNP	p-value
26	BovineHD2600014487	2.727e-0.6
2	ARS-BFGL-NGS-109852	1.854e-0.5
2	BovineHD0200023624	1.854e-0.5

.

The next step was to investigate what associations the SNP had to different traits. This were done by both searching for the top 10 SNP in scientific articles, and search for genes in scientific articles where positions for other QTL or SNPs that wee associated to a gene/trait, had a nearby laying position in the chromosome as the relevant SNP investigated study. Then another research was done to find facts about each trait if it were a favorable or unfavorable trait for the animals and the production. It was shown why this gene has been chosen to select on or if it has changed a lot caused to that it had a genetic correlation to another gene that has been chosen in the selection step.

The frequency that were given from PLINK were used for the plot diagram in R. The different frequencies from each SNP and decade were put into R in order to get the plot diagram.

The Mb values from the PLINK file were converted to cM values to be comparable with results from earlier studies. The result in Mb were multiplied with the relevant chromosome recombination extracted from Aries et al. (2009) for the chromosome. The equation used was: $cM = \left(\frac{cM}{Mb}\right) x\ Mb$

4. Results

Table 6 shows the top 10 SNPs on chromosomes that changed the most between the 50th SLB/Holstein group and 90th SLB/Holstein group. The SNP that changed most was found on chromosome 26 and the SNP that lays on this chromosome is BovineHD26000014487, this SNP has the lowest p-value which means that it has the highest significant change during the years. Position in Mb shows were on the chromosome the SNP are located. On chromosome 2 we found two SNPs which both has the same p-value and has therefore changed the same amount during the years. The same thing can also be seen for chromosome 19 which also has two SNP that has the same p-value. It can be seen that some of the SNP's has the same p-value and therefore has changed the same.

Table 6. The top ten SNPs that changed most between 1950 and 1990 for SLB/Holstein bulls

Chromosome	SNP	Position (Mb)[1]	p-value
26	BovineHD2600014487	50	2.727e-06
2	ARS-BFGL-NGS-109852	61	1.854e-05
2	BovineHD0200023624	82	1.854e-05
0	Hapmap48635-BTA-118353	-	1.854e-05
9	BovineHD0900010333	37	1.854e-05
1	BTB-01210202	21	1.854e-05
7	BovineHD0700013592	46	1.854e-05
19	ARS-BFGL-NGS-103353	25	1.854e-05
19	BovineHD1900007499	25	1.854e-05
6	BTA-77154-no-rs	93	1.854e-05

[1.] Where on the chromosome the SNP are located.

Figure 1 and 2 shows how the allele frequencies have changed for each SNP in SLB/Holstein bulls born between 1950s and 1990s. All the top 10 SNPs were found to slowly decrease in frequency. All SNP are decreasing from a high frequency in the 1950s to very, close to zero in the 1990s.

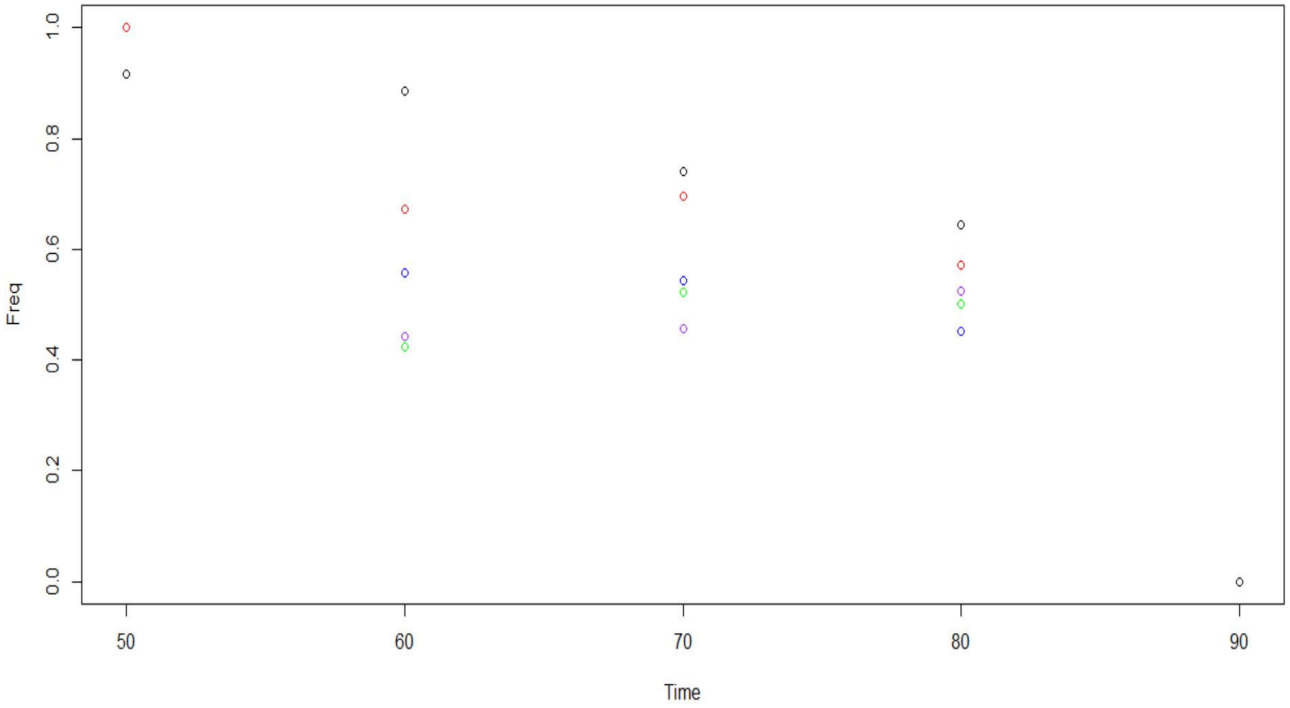

Figure 1. The frequencies changes for SNP 1-5 for SLB/Holstein bulls between 1950 and 1990s. Freq is the allele frequency and time is years. The colors represent the different SNPs, where red is the SNP BovineHD2600014487, blue ARS-BFGL-NGS-109852, green BovineHD0200023624, purple Hapmap48635-BTA-118353 and black BovineHD0900010333.

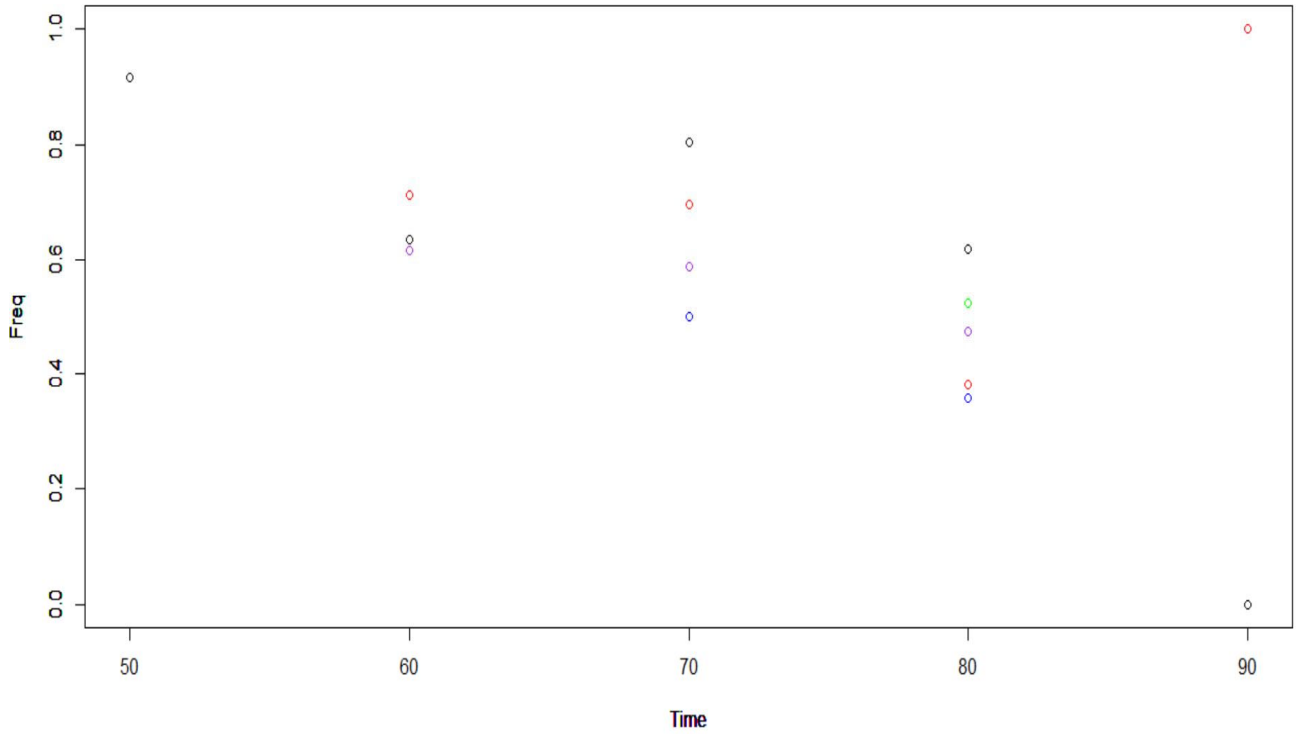

Figure 2. The frequencies changes for SNP 6-10 for SLB/Holstein between 1950 and 1990s. Freq is the allele frequencies and time is years. The colors represent the different SNPs. Where red is BTB-01210202 blue BovineHD0700013592 green ARS-BFGL-NGS-103353 purple BovineHD1900007499 and black BTA-77154-no-rs.

The top 10 SNP that changed the most for the comparison between the 50th group and 80th group in SRB can be seen in table 7. Many of the changed SNPs were found on chromosome 2 which indicates that this is a chromosome that has changed a lot during these years for the SRB. Other SNP that had changed for SRB lays on chromosome 16 and 0. The SNP that are located in the top of the table are the one that has changed the most during the years, the p-value shows the highest significant change for the SNP which means that the SNP in the top is the one that has changed most significant during the years.

Table 7. The top ten SNPs that changed most between 1950 and 1980 for SRB bulls

Chromosome	SNP	Position (Mb)[1]	p-value
0	ARS-BFGL-NGS-115075	-	2.353e-07
2	Hapmap25231-BTA-120294	70	1.768e-06
2	BovineHD0200020260	70	2.79e-06
0	BovineHD0200020246		3.383e-06
2	ARS-BFGL-NGS-65317	79	3.383e-06
2	BovineHD0200015240	53	3.383e-06
0	BovineHD2000005508	-	9.733e-06
0	BovineHD1600007201	-	1.013e-05
16	ARS-BFGL-NGS-110702	4	1.013e-05
0	BovineHD1600007200	-	1.013e-05

[1] Where on the chromosome the SNP are located

In figure 3 and 4 shows the allele frequencies for SRB bulls born between 1950s and 1980s have changed for each SNPs. For all the top 10 SNPs were slowly decreased in allele frequency. The trend for all SNPs were found to be decreasing from a high frequency in the 1950s to very low/close to zero in the 1980s.

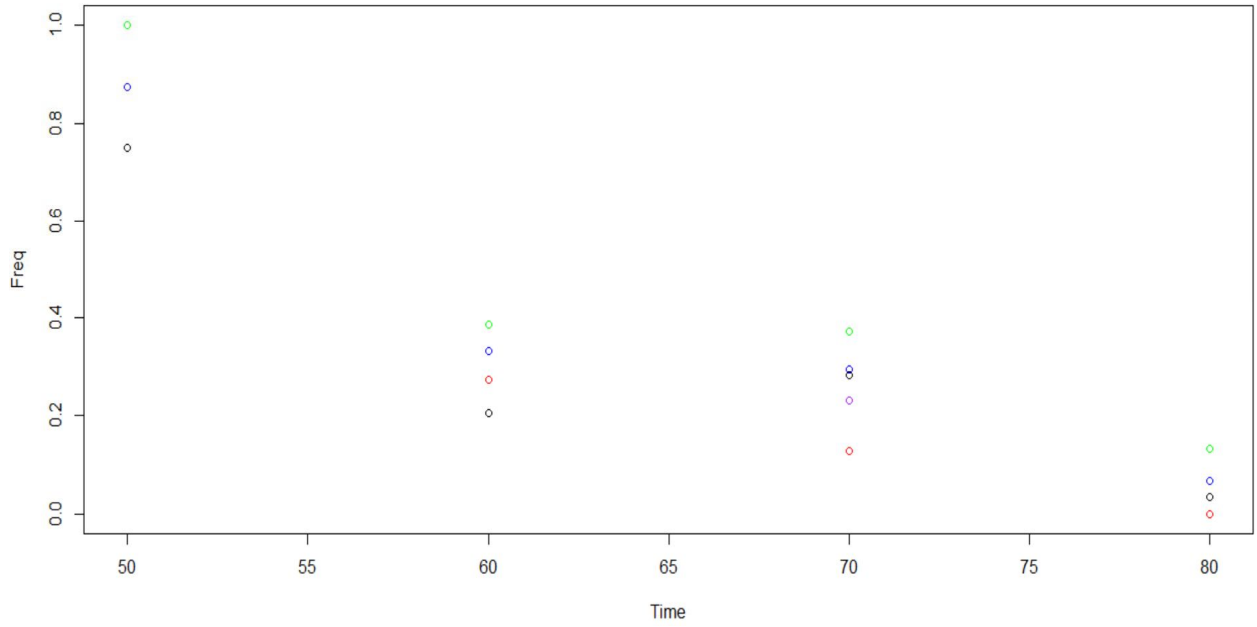

Figure 3. The frequencies changes for SNP 1-5 for SRB between 1950 and 1980s. Freq is the allele frequencies and time is years. The colors represent the different SNPs, where red is ARS-BFGL-NGS-115075, blue HAPMAP25231-BTA120294, green BovineHD0200020260 purple BovinHD0200020246 and black ARS-BFGL-NGS-65317.

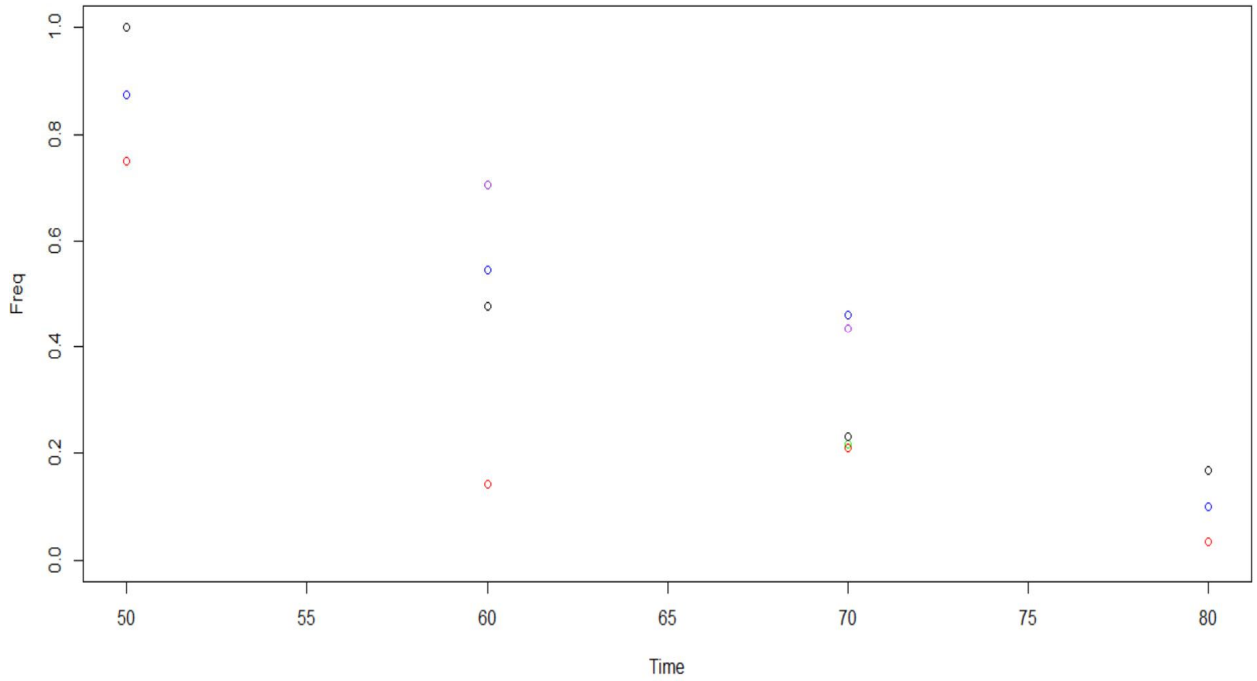

Figure 4. The frequencies changes for SNP 6-10 for SRB between 1950 and 1980s. Freq is the allele frequencies and time is years. The colors represent the different SNPs, where red is BovineHD0200015240 blue is BovineHD2000005508, green is BovineHD1600007201 purple is ARS-BFGL-NGS-110702 and black is BovineHD1600007200.

The top 10 SNPs that changed the most for the comparison between the breeds independent of the years can be seen in table 8. It is shown that the chromosomes 27, 16 and 8 have two SNP that are in the top 10 most changed SNPs and therefore these chromosomes have changed more compared to the other SNPs in table 8. Table 8 also show that SNP BovineHD2700003000 on chromosome 27 is the most changed SNP between the breeds regarding to the p-value, and this SNP has the highest significant change between 1950s and 1980s.

Table 8. Differences in SNP on chromosomes between the breeds independent on decade.

Chromosome	SNP	Position (Mb)[1]	p-value
27	BovineHD2700003000	13	4.846e-41
15	BovineHD1500016904	79	1.264e-40
27	BovineHD2700010708	37	3.659e-39
16	BovineHD1600013344	48	2.599e-38
8	BovineHD0800002964	9	6.942e-38
16	ARS-BFGL-NGS-32498	48	4.894e-37
8	BTB-01098498	18	5.708e-37
14	BTB-01119200	34	2.378e-36
0	BovineHD1400011446	-	9.136e-36
26	ARS-BFGL-NGS-115002	39	9.136e-36

[1] *Where on the chromosome the SNP are located*

5. Discussion

5.1. The changes in chromosomes and SNP

When the SNPs that changed the most were identified, and it was time to connect them to a gene/trait is was shown that the chosen SNP were not connected to any traits yet. This is why we had to investigate where genes for specific traits were located on the chromosomes. By doing this it was possible to find close QTL regions or SNPs that were connected to a specific gene/trait. In this way it was possible to make associations between the discovered SNPs and genes/traits.

In the SRB groups there was a lot of SNP on chromosome 0 that were changed, the expression chromosome 0 in this situation means that it is not known on which chromosome the SNPs were located. Therefore, it was not possible to find the traits that were connected to these SNP's.

During the study it was discussed what a closely located trait, SNP or QTL region were. It was decided that everything within a target of 10 000 Mb were a closely located trait, SNP or QTL region, but it was preferred if it laid closer.

5.2. Traits located near the identified positions

5.2.1. SLB/Holstein group

The SNP BovineHD0200023624 are located on a position of 82 Mb (87 cM) on chromosome 2. This is quite near the marker BMS1987 which has a position a bit above 90 cM and is associated to birth weight (Grosz & MacNeil 2001). It was shown that for Holstein cows, that are both heavier and larger, had easier calving's and needed less assistance. Calf birth weight was found to have a positive correlation with calving assistance (Freeman et al. 1989).

The SNP BovineHD0700013592 were found to be located on a position of 46 Mb (51 cM) on chromosome 7. This SNP was quite close to the QTL region (at 55 cM) that is important for fat depth (Casas et al. 2003a). It was shown that Holstein hade a lower fat depth than both Friesian and Charolais (Caffrey et al. 2005).

It was also found that the SNPs BovineHD1900007499 and ARS-BFGL-NGS-103353 located at position 25Mb (39cM) on chromosome 19 were close to the QTL region associated with somatic cell score (SCS) at 32 cM (Averdunk et al. 2003).

By looking at the study from Bishop *et al*., 1998 it is shown that the QTL region for SCS begins to peak around 50 cM and reaches its peak around 70 cM. This

region is close to the SNP BovineHD2600014487 at the position of 50 Mb (67 cM) on chromosome 26. With an an increasing milk yield has a positive genetic correlation with SCS which means an increase in milk yield also increases the level of SCS (Dekkers et al. 1998). Regarding to Berger et al (1978) selection for a high milk yield therefore also results in diseases. In the comparison between SLB/Holstein sires from the 50th and 90th it is shown that chromosome 6 has changed a lot. On this chromosome the SNP BTA-77154-no-rs was the SNP that had changed most. Recording to Kent et al (2011) the genes for clinical mastitis 1, clinical mastitis 4, clinical mastitis 6 are located in the interval between 90 and 96 Mb. We found that SNP BTA-77154-no-rs on the chromosome 6 that had a position of 93 Mb and could therefore be associated to this trait. Mastitis has a strong positive correlation (0.7) with production traits, where while SCS has a strong positive correlation of 0.8 with production traits (Carlén et al. 2004)

The SNP BovineHD0900010333 on chromosome 9 located at position 37 Mb (38 cM) is near the SNP BTA9 located at position around 40 cM. BTA9 has an association to non-return on day 56 in both SLB/Holstein and SRB cows. This mean that SNP BovineHD0900010333 may affect non-return on day 56 in dairy cattle (Andersson-Eklund et al. 2007). Breeding for higher milk yield gives fertility problems because there is a negative correlation between fertility traits and production traits (Garnsworthy et al. 2004).

The SNP BTB-01210202 has a position around 21 Mb (21 cM) on chromosome 1 are located near BMS2263. This SNP is associated to the gene CD18, which is the gene for Bovine leukocyte adhesion deficiency (BLAD) syndrome in cattle (Amigues et al. 2002). BLAD is a common disorder that is truly world spread. Calves often dies during their first year in life. BLAD causes immunodeficiency in older cattle (Agerholm & Windsor 2009).

ARS-BFGL-NGS-109852 has a position on chromosome 2 at around 61 Mb (65 cM) and is quite near to the QTL region (located between 45 and 70 cM) that has an impact on milking speed (Casas et al. 2003b). According to Blöttner et al. (2011) purebred Hoslteins have higher milking speed compared to other breeds.

5.2.2. SRB group

SNP BovineHD0200015240 was located at 53 Mb (56 cM) on chromosome 2. This is near the SNP ETH121−BM4440 that is associated with milking speed that are located on a position of 57 cM (Bovenhuis et al. 2000). In the study by Carlström *et al*. (2013) SRB was found to have a longer milking time and longer box time compared to SLB/Holstein.

The SNP ARS-BFGL-NGS-110702 was located at 4 Mb (6cM) on chromosome 16: This is quite near the QTL region for EUROP body score which has a position of 12 cM (Burton et al. 2009). It was shown that cows that were considered thin or below 3 on the body condition score (BCS) scale had a higher milk yield production than the moderate BCS cows (Akbulut et al. 2012).

The SNPs Hapmap25231-120294 and BovineHD0200020260 were located at 70 Mb (72 cM). These SNPs are located near the SNP BMS1866 that are associated with birth weight located at a position around 72 cM (Grosz & MacNeil 2001). The SNP ARS-BFGL-NGS-65317 are also located at a position around 79 Mb (84 cM) on chromosome 2 which is quite near the marker BMS1987 (at 90 cM) associated with birth weight (Grosz & MacNeil 2001). According to Freeman et al (1989) there is a positive correlation between calf birth weight and assistance at birth (Freeman et al. 1989).

5.2.3. Between the breeds

The SNP BovineHD0800002964 was located at a position of 9 Mb (9 cM) on chromosome 8. This SNP is quite near a QTL region associated with pigment concentration, moisture content and pH in the meat 24 hours postmortem (Burton et al. 2007). Dark, firm and dry (DFD) meat is when there is a high pH in the meat over pH 6.2. For Holstein this has been found more frequently during the summer compared to the winter (Weglarz 2010).

The SNP BovineHD2700003000 was located at a position around 10 Mb on chromosome 27 which is near a QTL region associated with persistency of milk yield which are located around 13 Mb.

The SNP BTB-01098498 was located on chromosome 8 at a position of 18 Mb and was found to be near the QTL region associated with persistency of milk yield (Grant et al. 2008). The study by Carlström *et al*. (2013) showed the differences in milking between the breeds. The average flow rate during milking was found to be higher for SLB/Holstein cows compared to SRB cows, the peak flow was also higher, and the milking time shorter for SLB/Holstein cows compared to SRB cows (Carlström et al. 2013).

The SNP BTB-01119200 was located at position 34 Mb on chromosome 14 which is quite close to the QTL region for clinic mastitis which are located on a position 42 Mb (Kent et al. 2011). It was shown that Swedish Holstein cows had a higher frequency of veterinary-treated clinical mastitis compared to SRB cows (Bengtsson et al. 2009).

The SNP ARS-BFGL-NGS- 115002 was located at a position of 39 Mb (53 cM) on chromosome 26. Barcelona *et al*. (2005) found a QTL region with a peak for protein yield between 50 and 70 cM. SRB cows were found to have higher protein content in the milk compared to SLB/Holstein cows (Andrén et al. 2008).

The SNP BovineHD1500016904 was located on chromosome 15 at a position of 58 Mb (79 cM). this SNP are located quite near the position for protein percent and fat percent in the milk which is at 84 cM (Amigues et al. 2002). It is shown that SRB cows have a higher fat and protein percentage in their morning milking compared to SLB/Holstein cows. It was also shown that the difference between SLB/Holstein and SRB cows were greater for the fat and protein percentage if the SRB cows were selected for high fat percentage (Andrén et al. 2008).

The SNPs BovineHD1600013344 and ARS-BFGL-NGS-32498 were located on chromosome 16 at a position around 48 Mb (60 cM) and the gene for estimated kidney, heart and pelvic fat are located at a position of 62 cM. Both these have positions close to each other and there is a chance that these SNPs have large effects on kidney, heart and pelvic fat (Casas et al. 2003). It has been shown that Holstein cows have a percent of 3% kidney, heart and pelvic fat which were around 8 kg (Aydin et al. 2013; Aydin et al. 2016). Kidney, heart and pelvic fat are related to fat cow syndrome which often occurs in loose housing stable, where all cows eat together independently on which lactation state they are in. The cows that dies caused by fat cow syndrome often have large amounts of fat around the kidney, heart and pelvic canal (Morrow 1976).

BovineHD2700010708 had a position of 37 Mb (46 cM) on chromosome 27 which is close to INRAMTT183 associated to teat length (Amigues et al. 2002). Closely placed teats have a positive correlation to more interrupted milking times and short and thin teats was found to be associated with better milking. Carlström et al. (2016 also found that SRB cows have shorter teats compared to SLB/Holstein cows, and SLB/Holstein cows had closer placed rear teats (Carlström et al. 2016).

The SNP ARS-BFGL-NGS- 115002 on chromosome 26 has a position of 39 Mb (52 cM) is close to the SNPs TGLA429 and BMS882 which are associated with SCS located at 50 cM and 51 cM, respectively (Longeri et al. 2006). Swedish Holstein has a higher frequency of SCS compared to SRB (Bengtsson et al. 2009)

5.3. General Discussion

It has been shown that many different SNP and genes/traits have changed during the observed years for bulls in both breeds, and some traits that have changed more for one of the breeds compared to the other one and vice versa. In the figures we could identify that different SNPs have the same frequencies, and therefore they are hard to identify in the figures since they are overlapping each other. Some SNPs affected the same traits but was located on different chromosomes.

It was interesting to find out that most of the SNP that changed the most during the years, are associated to traits that are known to have been breed on during the years. It was also interesting to see how these were correlated to other unfavorable traits such as SCS, mastitis and that it was shown that these SNP has changed a lot too.

As discussed above Carlén et al (2004) found that both SCS and mastitis has a positive correlation to the production traits. In this case it results that not only the positive traits changes but also the negative traits change a lot at the same time. The problem with this is that it is unfavorable both for the farmer economy as well as it effects the animal health and lower the animal welfare.

Non-return rate is a fertility trait and has a negative correlation to the production traits. This may have been affected during the decades in the way that when the milk production has increased the fertility has decreased. A low non-return rate leads to more tries before the animal gets pregnant. In this way it also costs more for the farmer than it was expected in the beginning. Therefore, it is important to consider, when breeding, that there might be some unfavorable correlations between some traits.

SLB/Holstein bulls had a SNP that had changed a lot that were associated to BLAD syndrome. BLAD is a serious disease were death can occur if to young animals gets it, and it gives serious problems for the older animals when it comes to their immune system. BLAD is associated to a high feed intake which can occur in free housing systems. This might be one of the reason why this SNP has changed during the years is because of with help from breeding it might have decreased the risk for the cattle to get BLAD.

It was also shown that SLB/Holstein had a SNP that were associated to birth weight that had changed. One reason why this SNP have changed is that heavy calves brings more complications to the birth and needs a larger assistance during birth (Freeman et al. 1989). Breeding towards smaller calves have decreased this problem, which also would decrease the work and costs for the farmer during the birth process. Two SNPs that had changed in SRB were also associated to BCS and birth weight. A moderate BCS of the cattle gave a lower milk yield compared to cattle that had a BCS lower than 3 (Akbulut et al., 2012).

It was found that the meat from Holstein had a high risk to develop DFD especially during the summers this is as discussed when pH in the meat reaches 6.2. It was more common to find articles about Holstein when it comes to this problem, therefore it seems like it is a trait that has been a bigger problem in this breed. It might be a reason why this trait has been worked on in SLB/Holstein more than in SRB. One other reason can be that Holstein is a more global breed and is therefore more studied.

Even though SRB had a lower milk yield compared to SLB/Holstein, the milk content for SRB was higher in protein and fat compared to the SLB/Holstein. This might conclude that the breeding has been focused on a higher protein and fat concentrations in SRB instead of a high milk yield.

When it comes to heart, kidney and pelvic fat on SRB it was not possible to find any articles about this problem, it might be the reason that it has already been treated and that it was breed to fix this problem for SRB during the earlier decades.

It has been interesting to see how the different SNP has changed over the years in bull breeding and many of these traits are more correlated to the female side than the male side. At the same time this is also interesting because it really shows the truth in that the sire and dams genes contributes in the same amount to the offspring, and that our breeding bulls also is selected and breed to increase the production and health in dairy cattle.

It is important to be aware of the correlations between traits and also how the feeding and management factors have an effects on the breeding. Too focused breeding selection for a specific or a lower number of chosen traits may cause unhealthy animals. This because of that other favorable traits can decrease in frequency when the breeding only focus on specific traits. Unhealthy animals result in lower production and profitability. It is important to reach a balance between the traits for production, health and fertility to get the best possible milk production.

Some of the identified SNP are more close located to different genes/traits in the genome than others. Further research is needed to get a deeper knowledge about how close the studied SNP's are to the specific traits/genes.

6. Conclusion

It was shown that by breeding on the bulls during the decades has resulted in big changes on some of the identified SNPs. There have been big changes for both breeds but on different traits. SLB/Holstein had changed a lot when it comes to the udder health indicators such as mastitis and SCS, while SRB has changed a lot when it comes to production traits as milking speed and fat & protein content. It was shown that production traits had a positive correlation to diseases like mastitis and SCS and a negative correlation to fertility traits such as non-return rate. Therefore, it is important that the farmers and breeding advisors are aware of these correlations and continue to have a balanced breeding.

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