Impact of the mitogenome inheritance on the milk production traits in Holstein cows
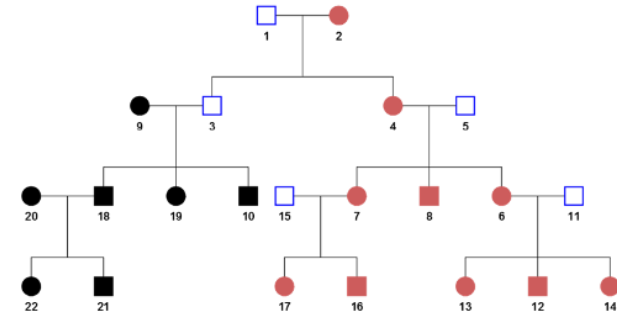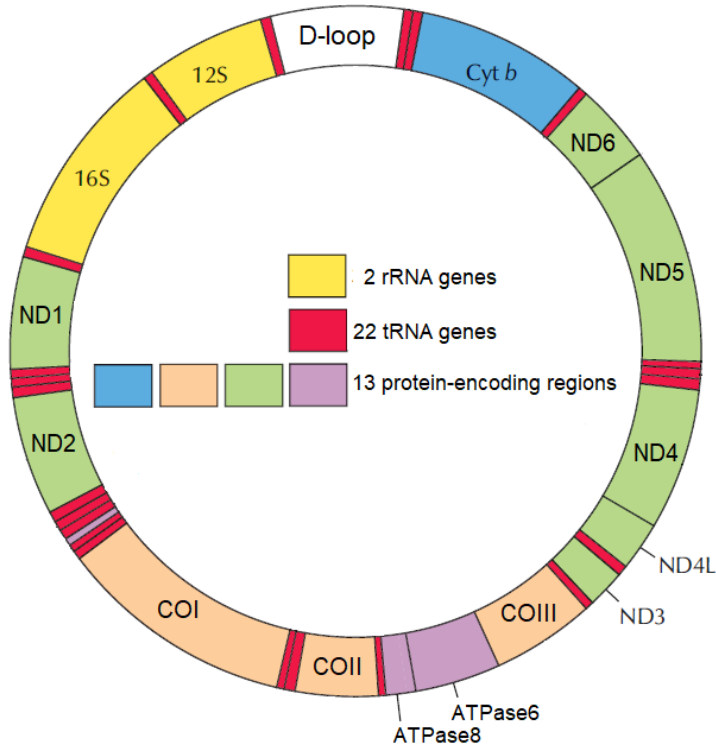
Vladimir Brajkovic, Maja Ferenčaković, Marija Špehar, Dinko Novosel, Vlatka Cubric-Curik, Ivica Međugorac, Elisabeth Kunz, Stefan Krebs, Johann Sölkner, Ino Curik

Background

Mitogenome

- maternal transmission ♀

- small circular molecule (mtDNA≈**16,472** bp : nDNA≈$3*10^9$ bp)

- coding of 37 genes (13 of ~ 85 OXPHOS components → **cell energy**)

Mitogenome impact on the phenotypic variability

Analyses with maternal lineage and D-loop mtDNA :

→ 0 to 4-5% phenotypic variability

Bell et al., 1985; maternal lineage

Kennedy 1986; maternal lineage

Schutz et al., 1994; mtDNA D-loop

Boettcher et al., 1996; mtDNA D-loop, rRNA

Boettcher and Gibson 1997; maternal lineage

Roughsedge et al., 1999; maternal lineage

Špehar et al., 2017; maternal lineage

milk production traits in cattle

→ estimation of **mitogenome polymorphism** contribution to the **total variance for milk traits in first three lactations**:

- **milk yield - MY**

- **fat yield - MY**

pedigree of Holstein cows ← HPA
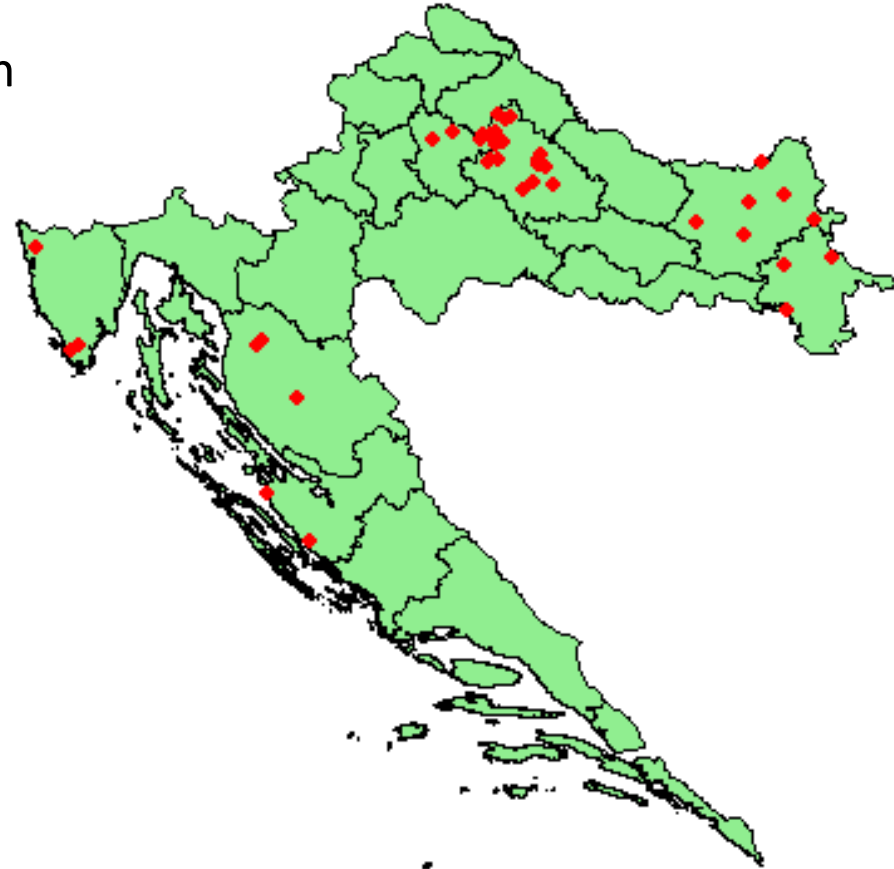
↓

295 349 individuals – phenotypic information

↓

20 973 lactating individuals in 2016.

↓

Stat	N
Samples	**109**
- milk	86
- tissue	1
- hair	22
Regions	7
Places	39
Farms	40

Pedigree analysis and imputation

Maternal lineages

↓

foun**de****rs** = 109

indi**vidu****als** = 2373

indi**vidu****als** = 109

ML1 ML2 ML3

GSE Genetics Selection Evolution

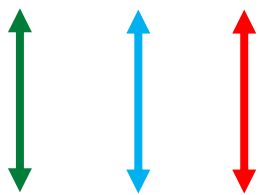**SOFTWARE**   **Open Access**

MaGelLAn 1.0: a software to facilitate quantitative and population genetic analysis of maternal inheritance by combination of molecular and pedigree information

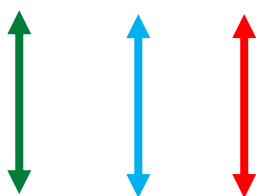Strahil Ristov[1*], Vladimir Brajkovic[2], Vlatka Cubric-Curik[2], Ivan Michieli[1] and Ino Curik[2]
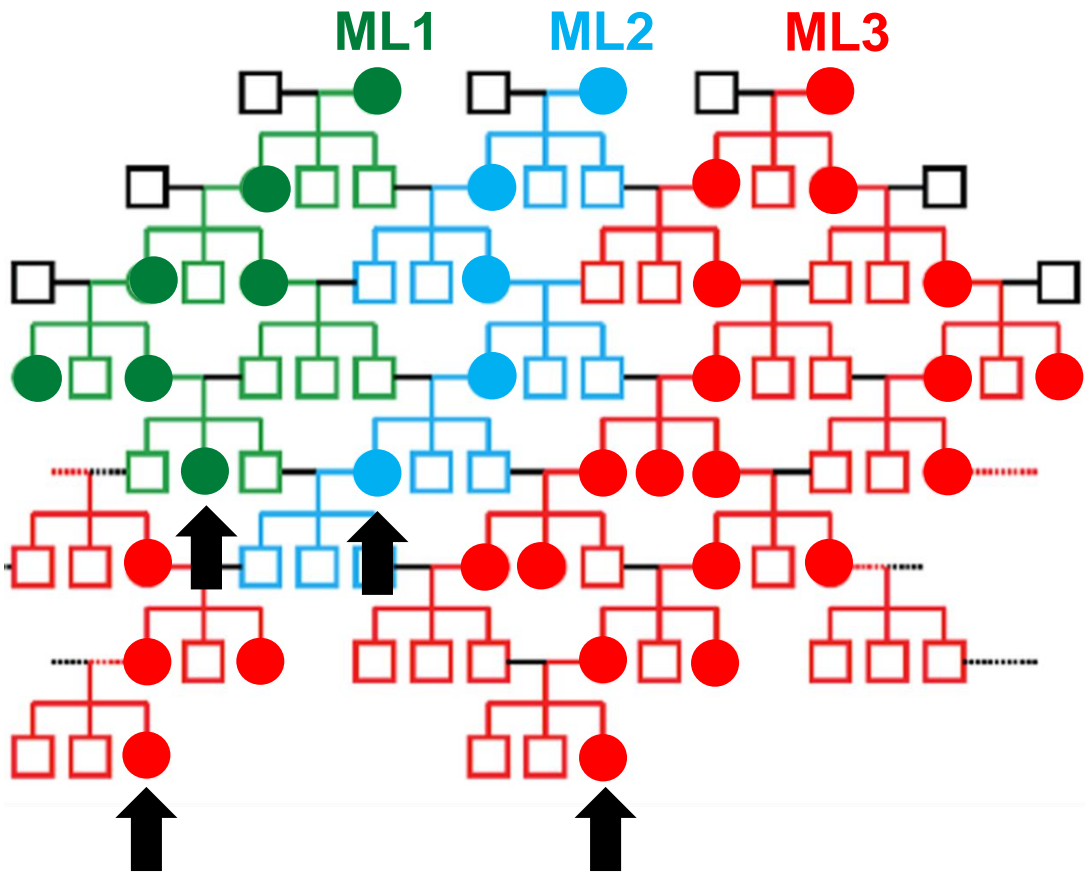
"Maternal inheritance without recombination"

MaGelLAn (Maternal Genealogy Lineage Analyser)
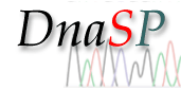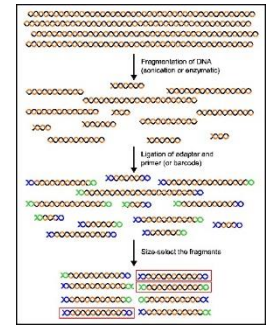
Part of mitogenome	Number of variable sites	Length bp	Position bp
ND1	7	957	3104-4060
ND2	5	1044	4269-5312
COX1	2	1545	5691-7235
COX2	1	684	7380-8063
ATP8	2	201	8135-8335
ATP6	4	681	8296-8976
COX3	7	804	8976-9779
ND3	2	357	9829-10185
ND4L	1	297	10245-10541
ND4	6	1425	10535-11959
ND5	11	1821	12115-13935
ND6	1	528	13919-14446
CYTB	10	1140	14520-15659
	59	**11484**	

↓

A T G T T C A T T A A C C G C T G A C T A T T C T C A A C C A A

↓

AIDIYVVATVVSIAMLIAIYTIIMMMPMLALTVVIYMFTYDSVIVVIIVSAVFSVLDMV

↓

48 aminoacid haplotypes

**Mitogenome
16345 bp**

↓

363 variable sites

↓

96 sequence haplotypes

Methods – statistical model

- mitogenome impact on the phenotypic variability
- linear mixed model – animal model:

MTDFREML

$$Y_{klmop} = \mu + b1(x_{klmop} - \mu_{\bar{x}}) + s_{kl} + h_{mo} + a_o + e_{klmop}$$

Milk yield; (y_{klmop})
Fat yield; (y_{klmop})
} dependent variable → first three lactation

Age at first calving (x_{klmop})
} covariate

Herd_Year_Season - HYS (s_{kl});

Cytoplasmatic effect (h_{mo})::

  - maternal lineage (Lineage)

  - sequence haplotype (Sequence)

  - aminoacid haplotype (Aminoacid)

Direct additive genetic effect (a_o)
} random effects

Lactation	N	Lineage	Sequence	Aminoacid	Regions	Herd	HYS
1st	2373	109	96	48	7→16	40→202	1285
2nd	1975	109	96	48	7→16	40→191	1195
3rd	1332	109	96	48	7→16	40→171	904

Results

Lactation	Variable (kg)	N	Mean	SD	Min	Max
1st	MY	2373	6761.90	1549.01	3022.20	11980.20
	FY	2372	258.31	63.22	109.00	500.20
2nd	MY	1975	7462.48	1841.52	3067.70	11960.10
	FY	1975	288.74	78.42	102.10	597.50
3rd	MY	1332	7497.19	1899.16	3103.10	11982.30
	FY	1332	290.77	80.65	94.10	585.90

Results - variance components ratios (± SE) for milk yield (kg)

Lactation	Model	Heritability	"Mito-effect"	HYS	ΔAICc
1st	Lineage	0.39±0.04	0.07±0.02	0.15±0.02	26.9
	Sequence	0.40±0.04	0.07±0.02	0.15±0.02	0.0
	Aminoacid	0.42±0.04	0.09±0.03	0.15±0.02	35.1
2nd	Lineage	0.28±0.04	0.07±0.02	0.19±0.03	0.2
	Sequence	0.29±0.04	0.07±0.02	0.19±0.03	0.0
	Aminoacid	0.31±0.04	0.09±0.03	0.18±0.03	1.4
3rd	Lineage	0.31±0.06	0.07±0.02	0.26±0.04	0.2
	Sequence	0.31±0.05	0.07±0.02	0.26±0.04	0.0
	Aminoacid	0.32±0.05	0.10±0.04	0.25±0.04	0.2

Herd_Year_Season - HYS

Results - variance components ratios (± SE) for fat yield (kg)

Lactation	Model	Heritability	"Mito-effect"	HYS	ΔAICc
1st	Maternal lineage	0.38±0.05	0.10±0.04	0.12±0.02	39.2
	Sequence hap	0.38±0.05	0.10±0.04	0.15±0.03	0.0
	Aminoacid hap	0.38±0.04	0.07±0.03	0.16±0.03	37.8
2nd	Maternal lineage	0.30±0.04	0.08±0.02	0.15±0.03	0.0
	Sequence hap	0.30±0.04	0.08±0.02	0.15±0.03	0.0
	Aminoacid hap	0.32±0.04	0.07±0.03	0.16±0.03	5.0
3rd	Maternal lineage	0.28±0.06	0.08±0.02	0.23±0.04	2.2
	Sequence hap	0.29±0.06	0.06±0.02	0.24±0.04	0.0
	Aminoacid hap	0.32±0.06	0.11±0.05	0.20±0.04	13.8

Herd_Year_Season - HYS

Conclusion

- **Significant contribution of mitogenome on milk production traits in Holstein cows in Croatia:**

$$\left.\begin{array}{l}\text{milk yield} \rightarrow \text{7 – 11\%}\\ \text{fat yield} \rightarrow \text{6 – 10 \%}\end{array}\right\}$$ **of phenotypic variabilitiy**

IN PROGRESS:

- **nucleotide polymorphism**
- **coding regions** (or mini haplotpyes)

↓

contribution to **the total variance on milk traits**

WORK IN PROGRESS

Acknowledgement

MitoTAUROmics: "Utilisation of the **whole mitogenome** in cattle **breeding** and **conservation** genetics - "

Miroslav Kaps

Strahil Ristov

Nikola Raguž and Boris Lukić

Thank you for your attention!