

KNOWLEDGE ON CAMEL MILK GENOMICS: STATE OF ART AND PERSPECTIVES

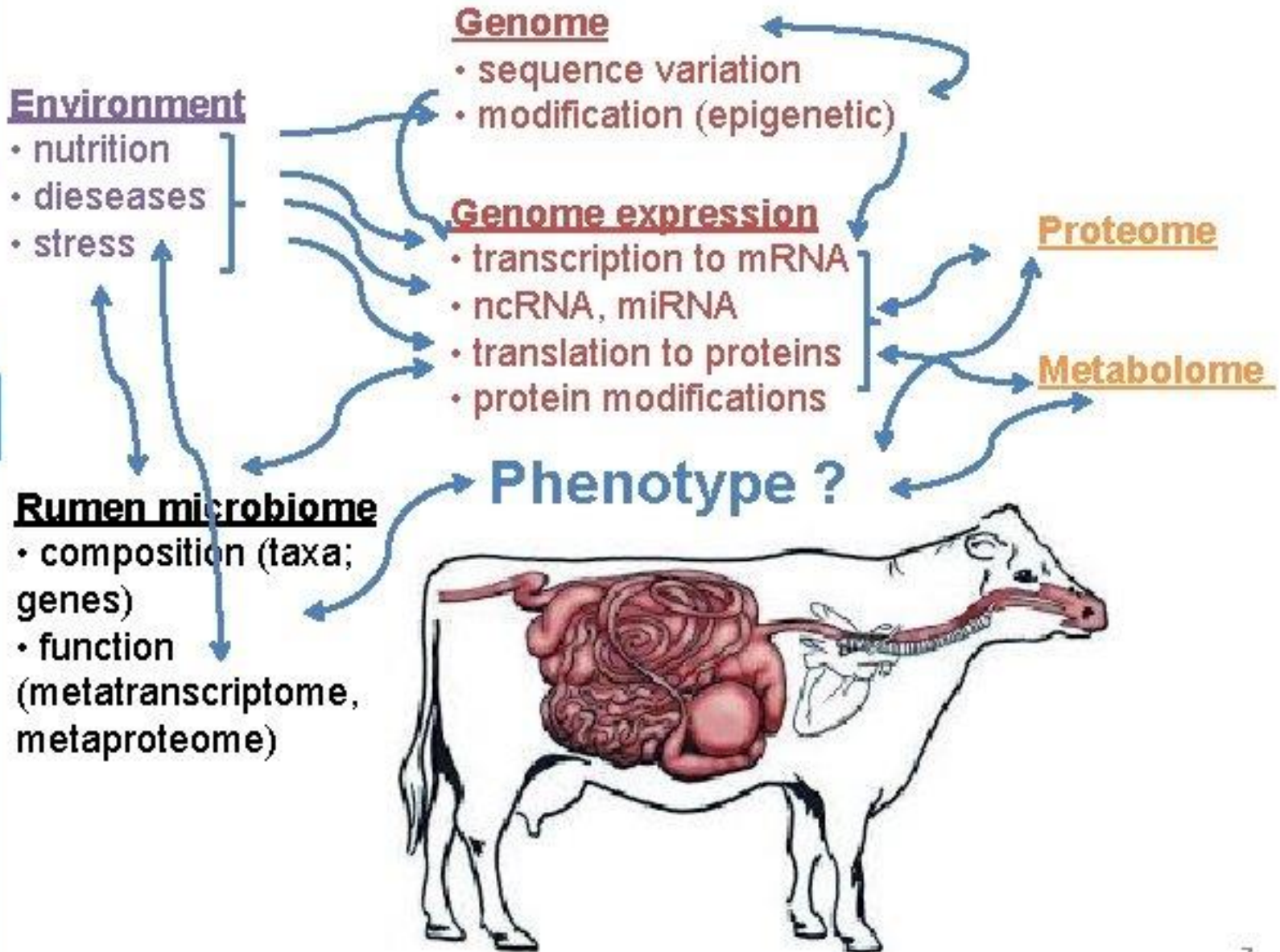
Elena Ciani

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RUMINOMICS

The systems biology challenge



...some tools are more innovative and disruptive than others...



*'Give me a lever ...
and I shall move the world.'*

Archimedes

CamDro3

Organism name: [Camelus dromedarius \(Arabian camel\)](#)

Infraspecific name: Breed: African

Isolate: Drom800

Sex: female

BioSample: [SAMN03252735](#)

BioProject: [PRJNA269274](#)

Submitter: Vetmeduni Vienna

Date: 2019/10/07

Assembly level: Chromosome

Genome representation: full

RefSeq category: representative genome

GenBank assembly accession: GCA_000803125.3 (latest)

RefSeq assembly accession: GCF_000803125.2 (latest)

RefSeq assembly and GenBank assembly identical: no ([hide details](#))

- Only in RefSeq: chromosome MT (in non-nuclear assembly-unit)
- Data displayed for RefSeq version

WGS Project: [JWIN03](#)

Assembly method: ABySS v. 1.3.6; HiRise v. MAY-2017; PBJelly v. 15.8.24; Pilon v. 1.22; ABySS Sealer v. 2.0.2; HiRise v. MAY-2018; PBJelly v. 15.8.24; BBMAP-CallVariants v. 38.12; ABySS Sealer v. 2.1.0

Expected final version: yes

Genome coverage: 65.0x

Sequencing technology: Illumina HiSeq; Dovetail Hi-C and Chicago; PacBio Sequel



Camelus dromedarius

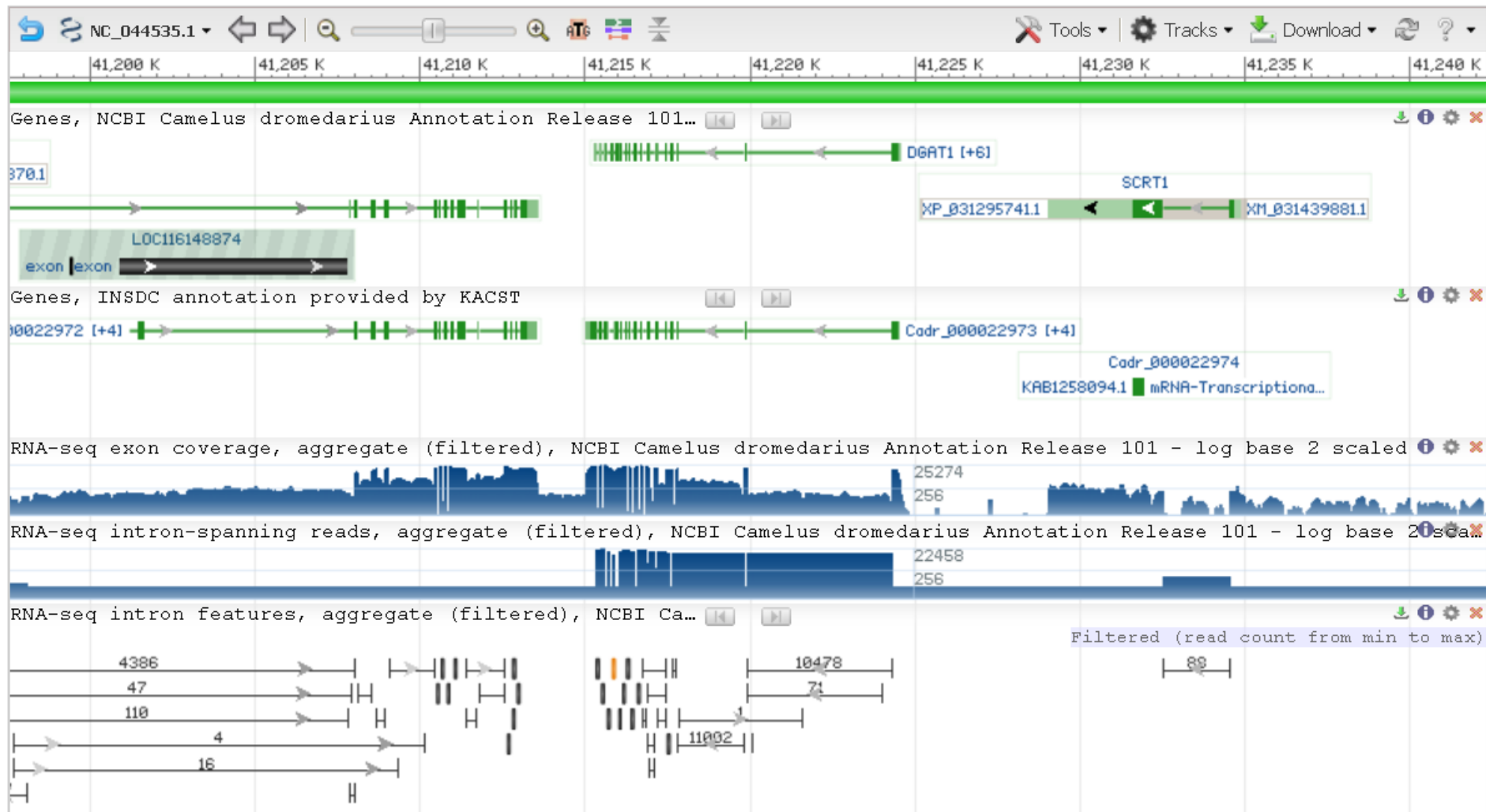
REFERENCE GENOME

The Genome Sequence is not *THE* answer!

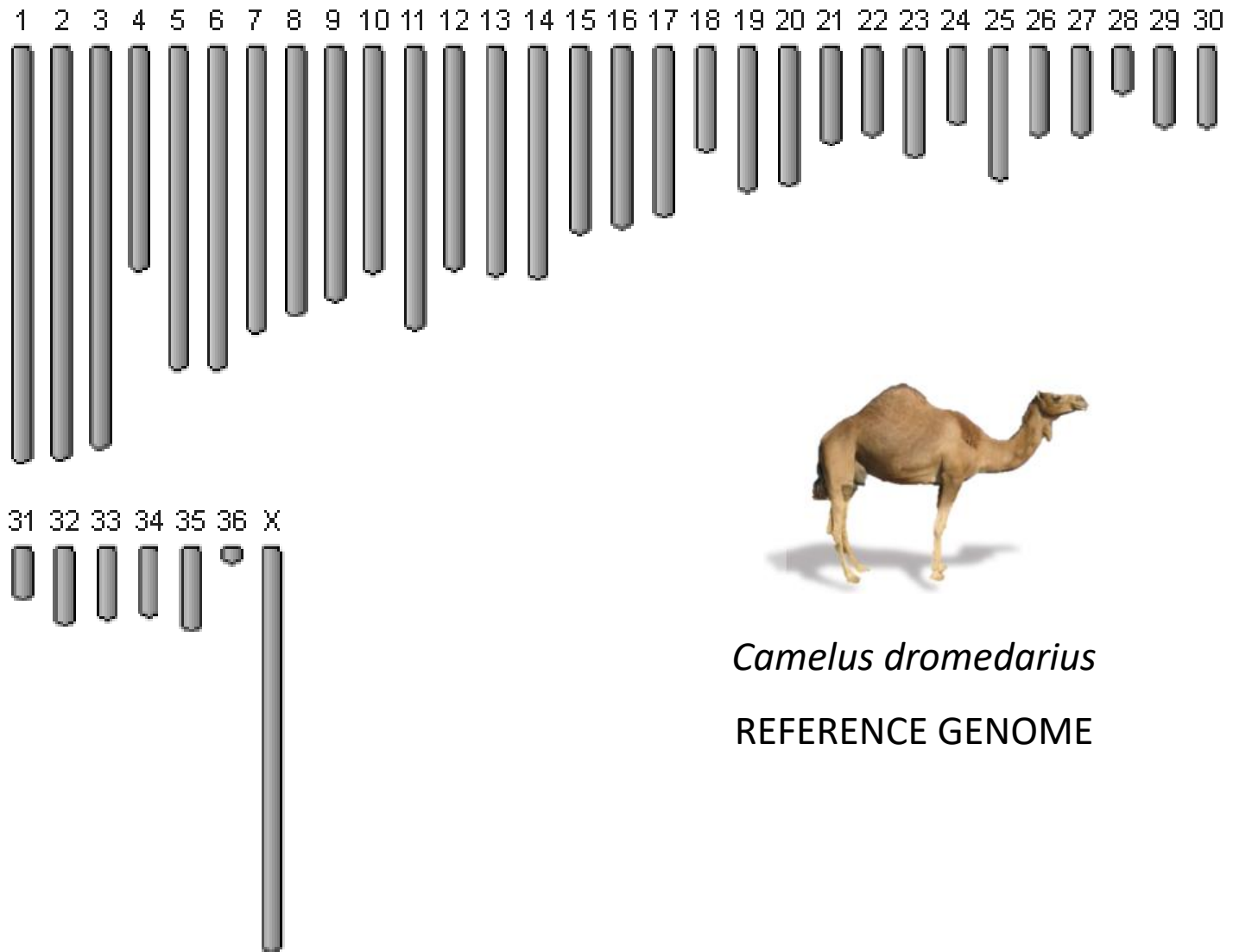


CamDro3 is ANNOTATED

(gene positions, sequence & structure are known)



CamDro3 sequence is now organized into **CHROMOSOMES**

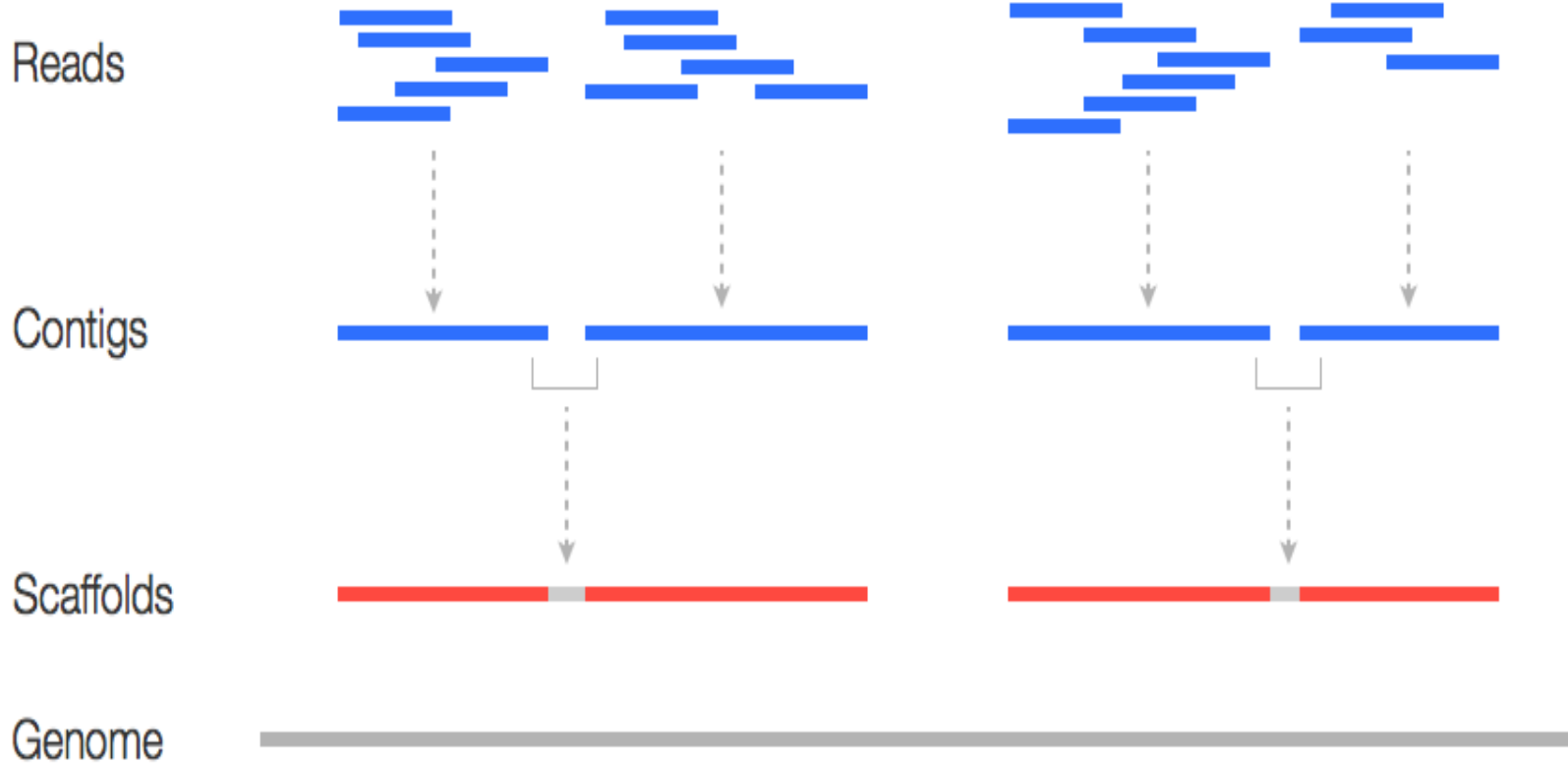


DE NOVO ASSEMBLY

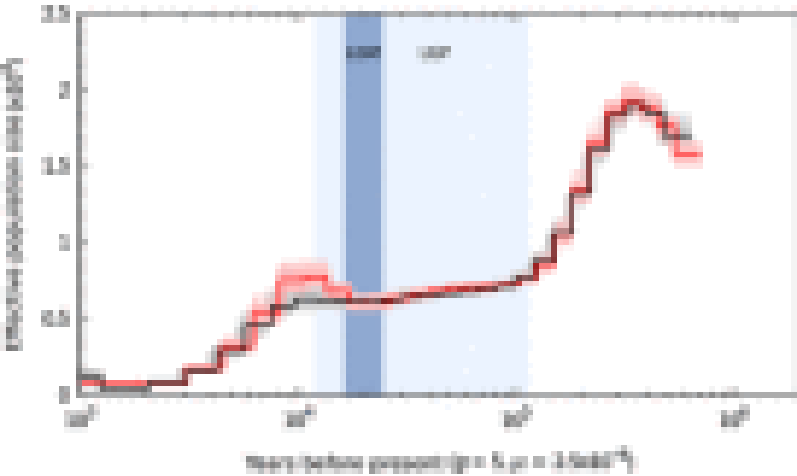


Camelus dromedarius
REFERENCE GENOME

BEFORE: Scaffold level



CamDro3 is a **TREASURE TROVE** of information



Historical effective population size

Further data mining?



COMPARATIVE GENOMICS

ORIGINAL RESEARCH article

updates

Front. Genet., 23 March 2021 | <https://doi.org/10.3389/fgene.2021.662609>

Comparative Genomics, Evolutionary and Gene Regulatory Regions Analysis of Casein Gene Family in *Bubalus bubalis*

 Saif ur Rehman^{1†},  Tong Feng^{1†},  Siwen Wu¹,  Xier Luo¹,  An Lei²,  Basang Luobu³,  Faiz-ul Hassan^{4*}
and  Qingyou Liu^{1*}

¹State Key Laboratory for Conservation and Utilization of Subtropical Agro-Bioresources, Guangxi University, Nanning, China

²National Engineering Laboratory for Animal Breeding, Key Laboratory of Animal Genetics, Breeding and Reproduction of the Ministry of Agriculture, College of Animal Science and Technology, China Agricultural University, Beijing, China

³Shannan Animal Husbandry and Veterinary Terminus, Xizang, China

⁴Faculty of Animal Husbandry, Institute of Animal and Dairy Sciences, University of Agriculture, Faisalabad, Pakistan

Comparative Genomics, Evolutionary and Gene Regulatory Regions Analysis of Casein Gene Family in *Bubalus bubalis*

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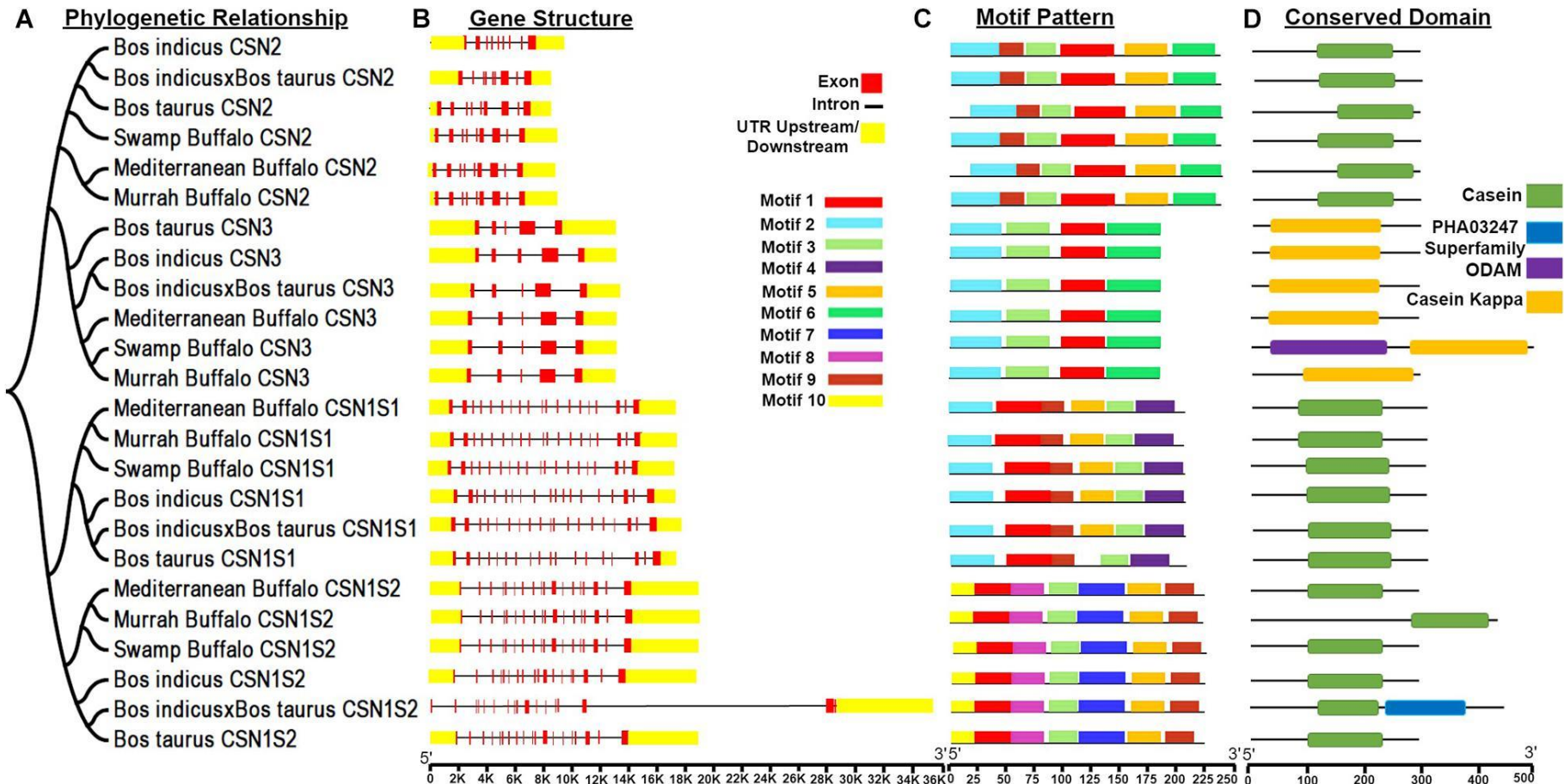
¹State Key Laboratory for Conservation and Utilization of Subtropical Agro-Bioresources, Guangxi University, Nanning, China

²National Engineering Laboratory for Animal Breeding, Key Laboratory of Animal Genetics, Breeding and Reproduction of the Ministry of Agriculture, College of Animal Science and Technology, China Agricultural University, Beijing, China

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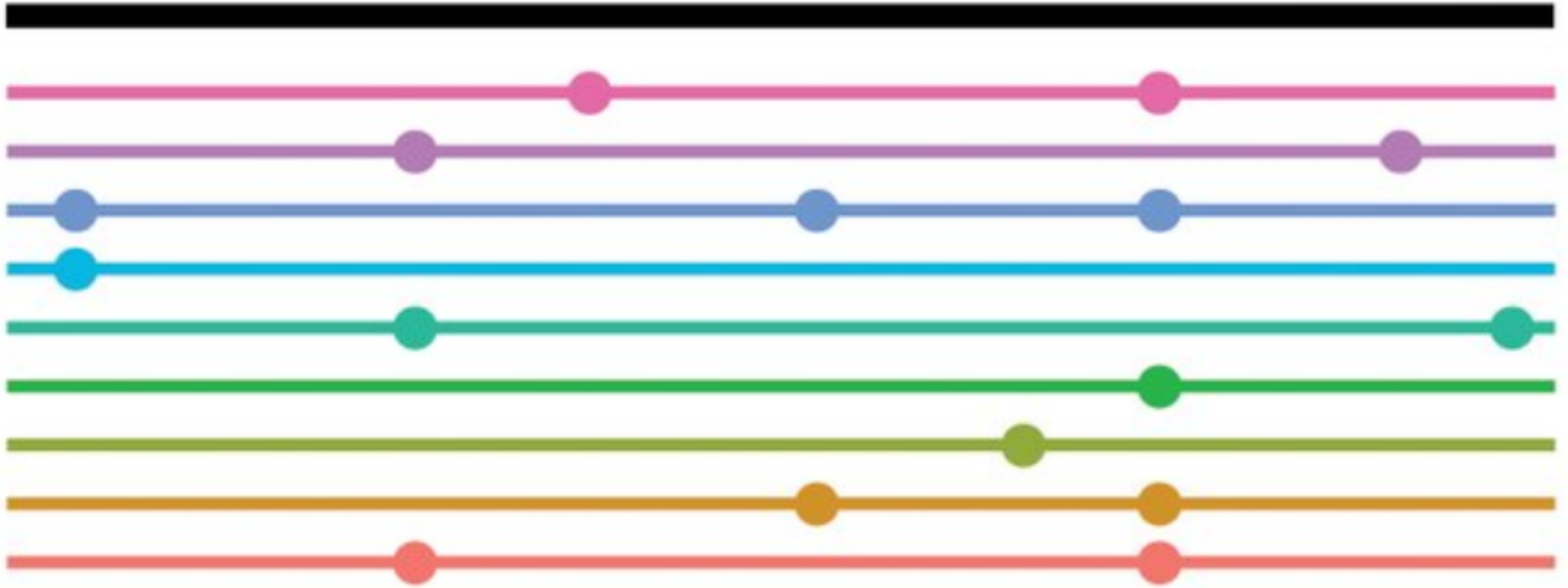
*Faculty of Animal Husbandry, Institute of Animal and Dairy Sciences, University of Agriculture, Faisalabad, Pakistan

- Comparative & structural genomics
- In silico* protein properties prediction
- In silico* transcription factor prediction



RE-SEQUENCING & POLYMORPHISM DETECTION

Reference



NOT ONLY SNPs (Single Nucleotide Polymorphisms),
also structural variations, including CNVs (Copy Number Variations)

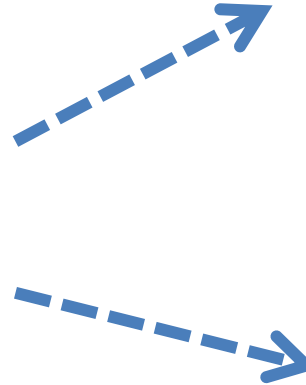
RE-SEQUENCING & POLYMORPHISM DETECTION

Targeted	Untargeted
<p data-bbox="401 601 884 701">Resequencing of specific genes or regions</p> <p data-bbox="413 772 873 872">(also in a genome-wide fashion, e.g. SPET)</p>	<p data-bbox="1078 601 1495 701">Whole-genome (WG) resequencing</p> <p data-bbox="1051 772 1522 986">Randomly skimmed WG resequencing (eg. RAD & DDRAD sequencing)</p>

RE-SEQUENCING & POLYMORPHISM DETECTION



Targeted	Untargeted
Resequencing of specific genes or regions (also in a genome-wide fashion, e.g. SPET)	Whole-genome (WG) resequencing Randomly skimmed WG resequencing (eg. RAD & DDRAD sequencing)



COLLABORATION AMONG UNIBA, VETMEDUNI, UFLORIDA; KFU & ILLUMINA: **14 millions SNP** LOCI FROM > 170 DROMEDARIES FROM 18 COUNTRIES

COLLABORATION AMONG UNIBA, VETMEDUNI, IGA: **50K SNP** LOCI FROM >100 DROMEDARIES FROM 18 COUNTRIES

(MORE ADVANCED) EVOLUTIONARY & COMPARATIVE/STRUCTURAL GENOMICS



ARTICLE



<https://doi.org/10.1038/s42003-020-1098-7>

OPEN

Genome-wide diversity and global migration patterns in dromedaries follow ancient caravan routes

Sara Lado¹, Jean Pierre Elbers¹, Angela Duskocil¹, Davide Scaglione², Emiliano Trucchi³,
Mohammad Hossein Banabazi⁴, Faisal Almathen^{5,6}, Naruya Saitou⁷, Elena Ciani⁸ & Pamela Anna Burger¹

(MORE ADVANCED) EVOLUTIONARY & COMPARATIVE/STRUCTURAL GENOMICS



ARTICLE

<https://doi.org/10.1038/s42003-019-0734-6>

OPEN

Whole-genome sequencing of 128 camels across Asia reveals origin and migration of domestic Bactrian camels

Liang Ming et al.[#]



ARTICLE

Received 6 Feb 2014 | Accepted 9 Sep 2014 | Published 21 Oct 2014

DOI: 10.1038/ncomms6188

Camelid genomes reveal evolution and adaptation to desert environments

Huiguang Wu^{1,*}, Xuanmin Guang^{2,*}, Mohamed B. Al-Fageeh^{3,*}, Junwei Cao^{1,*}, Shengkai Pan^{2,*}, Huanmin Zhou^{1,*}, Li Zhang¹, Mohammed H. Abutarboush³, Yanping Xing¹, Zhiyuan Xie², Ali S. Alsharqeti³, Yanru Zhang¹, Qulin Yao², Badr M. Al-Shomrani³, Dong Zhang¹, Jiang Li², Manee M. Manee³, Zili Yang¹, Linfeng Yang², Yiyi Liu¹, Jilin Zhang², Musaad A. Altammami³, Shenyuan Wang¹, Lili Yu², Wenbin Zhang⁴, Sanyang Liu², La Ba⁴, Chunxia Liu¹, Xukui Yang², Fanhua Meng¹, Shaowei Wang², Lu Li¹, Erli Li², Xueqiong Li¹, Kaifeng Wu¹, Shu Zhang², Junyi Wang^{2,*}, Ye Yin², Huanming Yang², Abdullaziz M. Al-Swailem³ & Jun Wang^{2,5,6}

Comparative approach

SCIENTIFIC REPORTS

OPEN

Mitogenome Sequencing in the Genus *Camelus* Reveals Evidence for Purifying Selection and Long-term Divergence between Wild and Domestic Bactrian Camels

Received: 8 March 2017
Accepted: 14 July 2017
Published online: 30 August 2017

Elmira Mohandesan^{1,2,3}, Robert R. Fitak⁴, Jukka Corander^{5,6}, Adiya Yadamsuren⁷, Battsetseg Chuluunbat⁸, Omer Abdelhadi⁹, Abdul Raziq¹⁰, Peter Nagy¹¹, Gabrielle Stalder¹, Chris Walzer^{1,12}, Bernard Fave¹³ & Pamela A. Burroer¹



TARGETED GENE RE-SEQUENCING

Article

Genetic Diversity in Casein Gene Cluster in a Dromedary Camel (*C. dromedarius*) Population from the United Arab Emirates

Abdullah Al Mutery ^{1,2,3,*}, Naushad Rais ⁴, Wala KE Mohamed ⁵ and Tlili Abdelaziz ^{1,2,3}

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 - ⁴ School of Life Sciences, Manipal Academy of Higher Education, Dubai P.O. Box 345050, United Arab Emirates; naushad@manipaldubai.com
 - ⁵ Department of Genetics and Microbiology, Universitat Autònoma de Barcelona, P.O. Box 08193 Barcelona, Spain; walaakamal87@outlook.com
- * Correspondence: aalmutery@sharjah.ac.ae; Tel.: +971-6-5053860



Targeted

Resequencing of specific genes or regions

Structural organization of the casein cluster

Table 2. Summary of organization of CSN cluster in *C. dromedarius* as adopted from Pauciullo et al. [22].

Gene	Position	Size (bp) (A)	Intergenic Distance (bp) (B)	Total Size (bp) (A+B)	Exons
CSN1S1	242,112 to 258,587	16,476		16,476	20
CSN2	265,187 to 273,094	7908	6600 (CSN1S1→CSN2)	14,508	9
CSN1S2	321,355 to 335,898	14,544	48,261 (CSN2→CSN1S2)	62,805	17
CSN3	421,597 to 430,955	9359	85,699 (CSN1S2→CSN3)	95,058	5
Total		48,287		188,847	51

PREDICTION OF (FUNCTIONAL) EFFECT OF POLYMORPHISMS

(a first step toward connecting genetic variation with phenotypic variation)







Table 3. Summary of total number of variants identified in the casein gene cluster.

Gene	Variant Type	Impact	Total Variants
CSN1S1	Intron variant	Modifier	76
	Missense variant	Moderate	2
	Splice region variant & intron variant	Low	1
	Synonymous variant	Low	1
	Upstream gene variant	Modifier	5
CSN1S2	3 prime UTR variant ¹	Modifier	1
	5 prime UTR variant ²	Modifier	1
	Intron variant	Modifier	34
	Splice acceptor variant & splice region variant & intron variant	High	1
	Splice region variant & intron variant	Low	2
	Upstream gene variant	Modifier	3
CSN2	Downstream gene variant	Modifier	45
	Intron variant	Modifier	37
	Splice region variant & intron variant	Low	1
	Synonymous variant	Low	1
	Upstream gene variant	Modifier	7
CSN3	5 prime UTR variant ²	Modifier	1
	Intron variant	Modifier	66
	Upstream gene variant	Modifier	9

¹ 3' UTR is the portion of an mRNA from the 3' end of the mRNA to the position of the last codon used in translation. ² 5' UTR is the portion of an mRNA from the 5' end to the position of the first codon used in translation.

FROM (1st time) SNP DETECTION TO ROUTINE GENOTYPING

<p>ARRAYS</p> 	<p>LOW DENSITY</p>	<p>MEDIUM DENSITY</p> 	 <p>HIGH DENSITY</p> 
<p>GBS</p>	<p>AMPLICON RESEQUENCING</p>	<p>RAD/DDRAD</p>	<p>WHOLE GENOME</p>



FROM TENS OF SEQUENCED ANIMALS TO HUNDREDS/THOUSANDS OF GENOTYPED ANIMALS

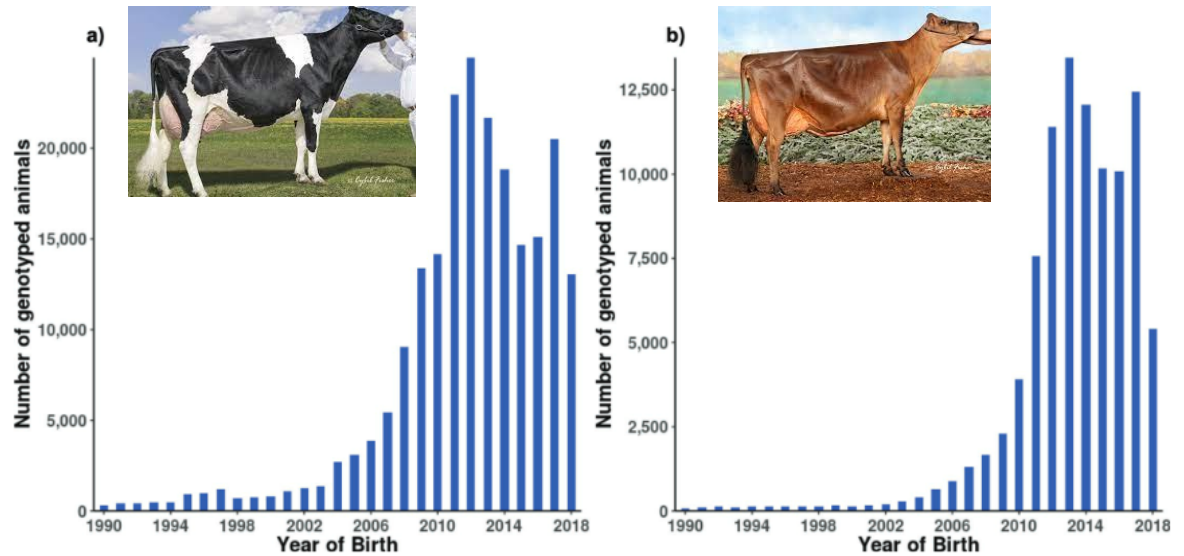


Figure 1. Distribution of genotyped animals per year of birth from 1990 to 2018. (a) Holsteins; (b) Jerseys.

A total of 205,755 and 89,238 pedigreed and **genotyped** animals born between 1990 and 2018 were available for Holsteins and Jerseys, respectively.

ASSISTING BREEDING AND GENETIC MANAGEMENT OF POPULATIONS

□ INBREEDING ASSESSMENT



J. Dairy Sci. 103:5183–5199
<https://doi.org/10.3168/jds.2019-18013>

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Effect of genomic selection on rate of inbreeding and coancestry and effective population size of Holstein and Jersey cattle populations

Bayode O. Makanjuola,¹ Filippo Miglior,^{1,2} Emhimad A. Abdalla,¹ Christian Maltecca,^{1,3} Flavio S. Schenkel,¹ and Christine F. Baes^{1,4*}

¹Centre for Genomic Improvement of Livestock, Department of Animal Biosciences, University of Guelph, Guelph, ON, N1G 2W1 Canada

²Ontario Genomics, ON, M5G 1M1 Canada

³Department of Animal Science and Genetics Program, North Carolina State University, Raleigh 27607

⁴Institute of Genetics, Vetsuisse Faculty, University of Bern, Bern 3001, Switzerland

Table 2. Within-breed averages of pedigree inbreeding (F_{PED}), genomic inbreeding ($F_{ROH_SNP1101}$, F_{ROH_PLINK} , F_{GRM}), pedigree coancestry (f_{PED}), and genomic coancestry (f_{SEG}) coefficients for genotyped animals born between 1990 and 2018

Item	Inbreeding (%) ± SD	
	Holstein	Jersey
F_{PED}	7.74 ± 2.22	7.20 ± 2.48
$F_{ROH_SNP1101}$	13.61 ± 3.41	21.16 ± 3.46
F_{ROH_PLINK}	15.64 ± 3.38	22.54 ± 3.39
F_{GRM}	31.40 ± 2.72	42.62 ± 2.55
f_{PED}	8.33 ± 3.13	9.23 ± 3.69
f_{SEG}	15.84 ± 4.48	23.46 ± 4.49



**INBREEDING
ESTIMATED VIA
GENOMIC DATA**

ASSISTING BREEDING AND GENETIC MANAGEMENT OF POPULATIONS

☐ INBREEDING ASSESSMENT



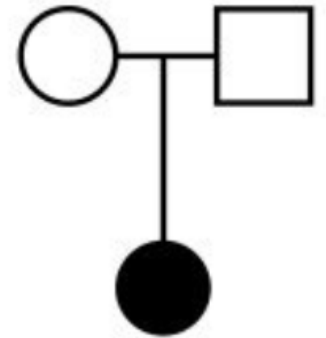
illumina®

Take
Note

No positive F values in 161 animals typed at 800K SNP loci when considering them as a single population (preliminary results)

ASSISTING BREEDING AND GENETIC MANAGEMENT OF POPULATIONS

□ PEDIGREE VERIFICATION



illumina®

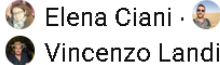
ASSISTING BREEDING AND GENETIC MANAGEMENT OF POPULATIONS

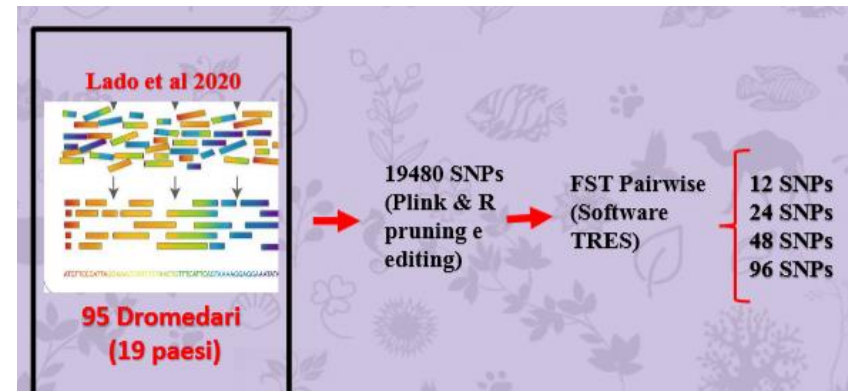
□ PEDIGREE VERIFICATION

Efficienza di un set ridotto di marcatori SNPs come strumento per il controllo genealogico e per l'identificazione individuale nella specie *Camelus dromedarius*

September 2021

Conference: XIII Convegno Nazionale sulla Biodiversità - Foggia


 Elena Ciani · Gabriele Senczuk · Salvatore Mastrangelo · [Show all 5 authors](#) · Vincenzo Landi



N LOCI	PNE	PNI*
12	0.54	0.22
24	0.34	0.06
48	0.15	0.007
96	0.029	0.000099

* Assuming one parent putative & the other known

FROM REMOTE EVOLUTIONARY HISTORY TO DOMESTICATION & POST-DOMESTICATION HISTORY

Ciani *et al. Genetics Selection Evolution* (2015) 47:64
DOI 10.1186/s12711-015-0139-z



GSE Genetics Selection Evolution

RESEARCH ARTICLE

Open Access

Merino and Merino-derived sheep breeds: a genome-wide intercontinental study



Elena Ciani^{1*}, Emiliano Lasagna², Mariasilvia D'Andrea³, Ingrid Alloggio¹, Fabio Marroni^{4,5}, Simone Ceccobelli², Juan V. Delgado Bermejo⁶, Francesca M. Sarti², James Kijas⁷, Johannes A. Lenstra⁸, Fabio Pilla³ and the International Sheep Genomics Consortium

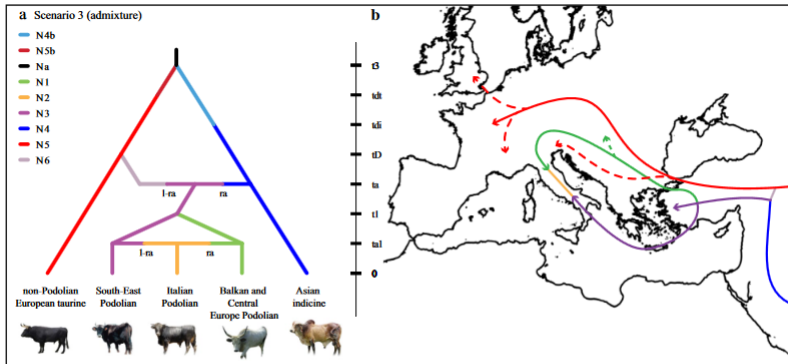
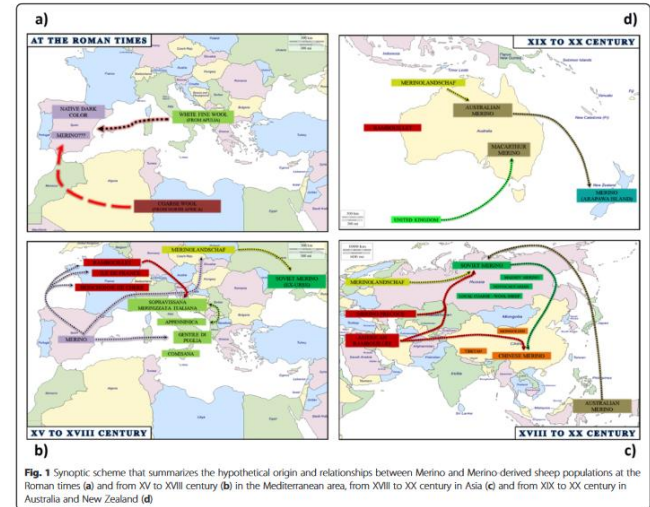


Fig. 1 a Schematic representation of the most voted scenario of colonization. The model predicts a first separation between taurine and indicine (t3) followed by independent domestication events (tdt and tdi) that took place in the Fertile Crescent and the Indus Valley, respectively. An early non-Podolian taurine migration (td) occurred before the admixture event between taurine and indicine (ta). This scenario, simulates an admixture event (ta1) between the Balkan and Central Europe Podolian and the South-East Podolian leading to the formation of the Italian Podolian breeds. b A geographic map indicating the presumed migration routes as inferred for Scenario 3. Arrows and dotted arrows indicate the assumed or alternative (Mediterranean or Danube) migration routes

Senczuk *et al. Genet Sel Evol* (2021) 53:48
<https://doi.org/10.1186/s12711-021-00639-w>



GSE Genetics Selection Evolution

RESEARCH ARTICLE

Open Access

On the origin and diversification of Podolian cattle breeds: testing scenarios of European colonization using genome-wide SNP data

Gabriele Senczuk^{1*}, Salvatore Mastrangelo², Paolo Ajmone-Marsan³, Zsolt Becskei⁴, Paolo Colangelo⁵, Licia Colli³, Luca Ferretti⁶, Taki Karsli⁷, Hovirag Lancioni⁸, Emiliano Lasagna⁹, Donata Marletta¹⁰, Christian Persichilli¹, Baldassare Portolano², Francesca M. Sarti⁹, Elena Ciani¹¹ and Fabio Pilla¹



POST-DOMESTICATION HISTORY



CAMELSHIELD

MULTIFONCTIONNALITÉ DE L'ÉLEVAGE CAMELIN
DANS LES SOCIÉTÉS SAHARIENNES

TARGET AREAS: ALGERIA AND MOROCCO

DISENTANGLING THE GENETIC ARCHITECTURE OF “MILK” TRAITS

(complex quantitative traits)

STUDY SAMPLE TYPE	PHENOTYPE MEASUREMENT AVAILABILITY	APPROACH	NOTES
POPULATION	NO	SELECTION SIGNATURES	-within pop (homozygosity) -between pops (FST-outlier) - among pops (HAPFLK)
POPULATION	YES	•A PRIORI TARGETED CANDIDATE GENE • GWAS	
FAMILY (PEDIGREE)	YES	QTL MAPPING	

DISENTANGLING THE GENETIC ARCHITECTURE OF “MILK” TRAITS (complex quantitative traits)

GWAS – Genome-wide Association Studies

scientific reports

OPEN Genomic prediction for growth
using a low-density SNP panel
in dromedary camels

Morteza Bitaraf Sani^{1,2,3}, Javad Zare Harofte¹, Mohammad Hossein Banabazi²,
Saeid Esmailkhanian³, Ali Shafei Naderi¹, Nader Salim⁴, Abbas Teimoori⁴, Ahmad Bitaraf¹,
Mohammad Zadehrahmani⁵, Pamela Anna Burger⁶, Vincenzo Landi⁷, Mohammad Silawi⁸,
Afsaneh Taghipour Sheshdeh⁸ & Mohammad Ali Faghihi^{8,9}



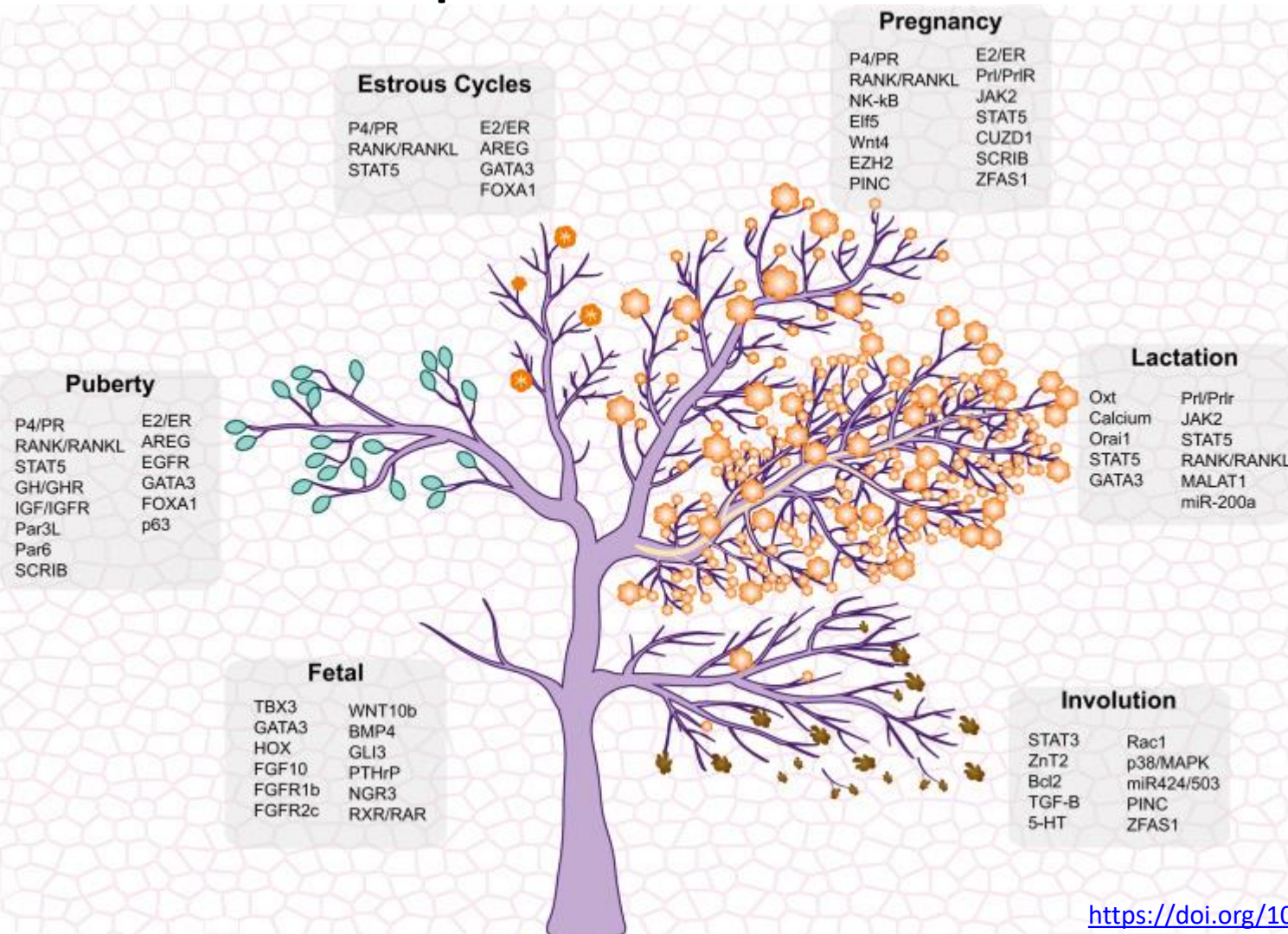
Growth traits...but not (yet) milk traits: more difficult to be collected
(monthly test-day milk records)

Trait	Chromosome	pos	MAF	$-\log_{10}$ (p-Value)	Candidate gene
Birth weight	7	82,483,685	0.09	3.29	<i>ACTR3B, RPL32, XRCC2</i>
	7	82,483,675	0.08	3.10	
	8	72,594,633	0.11	3.81	<i>SERAC1</i>
	8	72,594,548	0.09	3.77	
	8	72,594,549	0.09	3.77	
	8	72,594,593	0.13	3.51	
	8	72,594,639	0.08	3.12	
	9	22,550,930	0.15	3.47	<i>TBX15</i>
	11	81,210,420	0.06	3.07	<i>mRNA-hypothetical protein and KAB1271495.1</i>
	19	10,237,661	0.05	3.21	<i>RNF114, IFNLI, SPATA2, SNAI1</i>
	19	10,237,641	0.05	3.18	
	34	6,774,561	0.06	3.54	UNKHOWN
	Gain/day	10	13,892,353	0.06	3.41
16		34,483,240	0.39	3.38	<i>EFCAB5, NSRP1, Slc6a4</i>
12		5711	0.02	3.34	<i>ITGA7, OR6C2</i>
19		9,631,630	0.17	3.32	<i>RIPOR3, PTPN1, PARD6B, BCAS4, MOCS3</i>
14		31,371,259	0.11	3.29	<i>TRAPPC9</i>
14		30,865,065	0.23	3.23	
14		30,854,110	0.37	3.07	
Body weight	11	72,356,401	0.30	3.76	<i>EMX2, mRNA-hypothetical protein and KAB1271709.1</i>
	8	43,104,525	0.30	3.42	<i>FAM184A, MCM9, ASF1</i>
	19	10,894,226	0.34	3.38	<i>CSE1L, ARFGEF2</i>
	X	78,141,509	0.43	3.30	<i>TSR2, WNK3</i>
	X	78,141,514	0.43	3.30	<i>TSR2, WNK3</i>
	X	60,452,363	0.08	3.16	<i>LPAR4, RTL3, PEG10</i>
	X	62,116,802	0.06	3.12	<i>PBDCL1, TRAPPC13</i>
	4	40,844,257	0.16	3.13	UNKNOWN
	18	29,958,631	0.06	3.08	<i>DEX1, TSPYLA, CIITA</i>

Table 4. Genome-wide association studies (GWAS)-identified significant single-nucleotide polymorphisms (SNPs) ($-\log p$ value > 3), associated traits, and candidate genes.

“OMIC” DATA INTEGRATION

The molecular basis of mammary gland development and epithelial differentiation



GENOMIC EVALUATION/PREDICTION

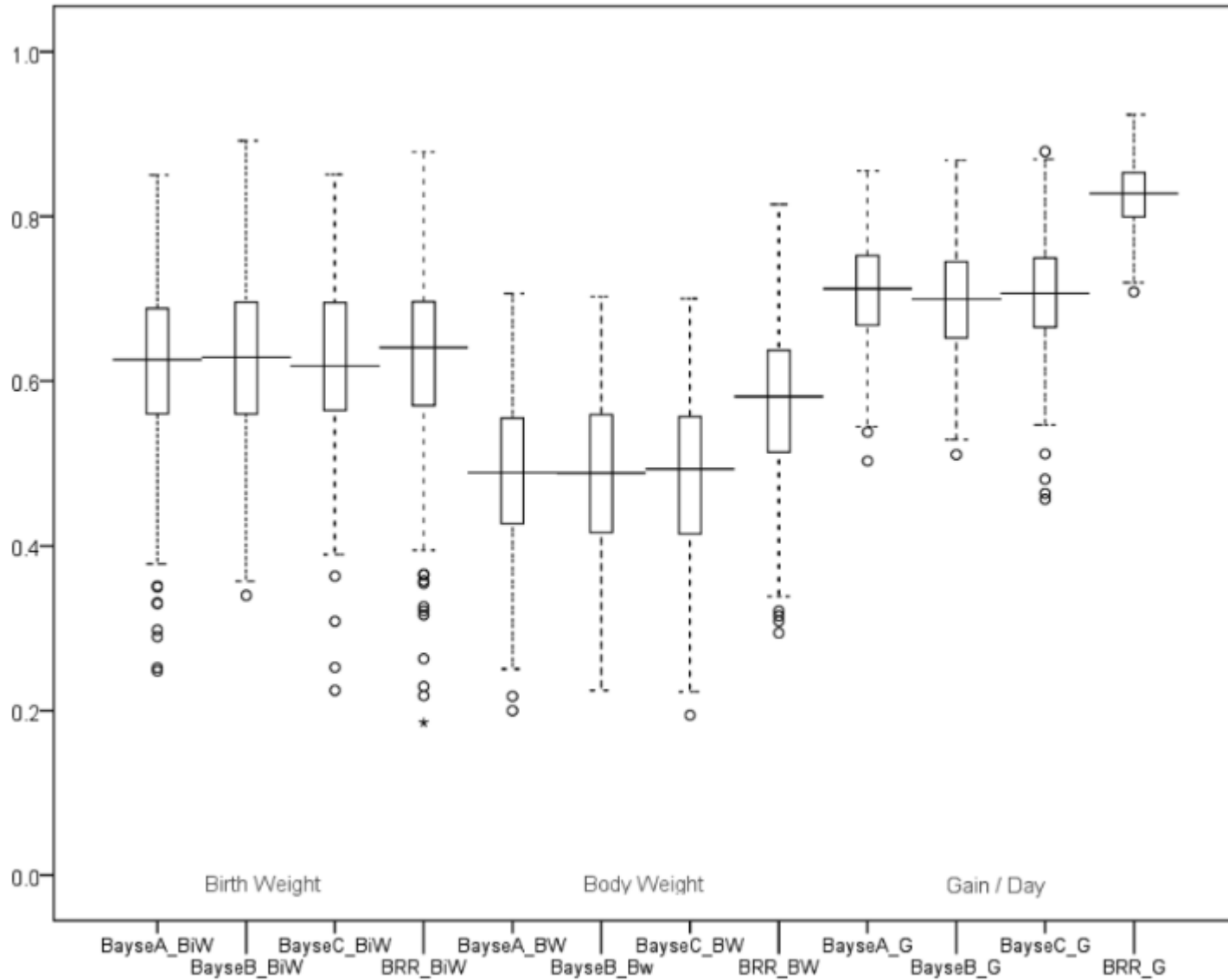
scientific reports

OPEN Genomic prediction for growth using a low-density SNP panel in dromedary camels

Morteza Bitaraf Sani^{1✉}, Javad Zare Harofte¹, Mohammad Hossein Banabazi², Saeid Esmailkhanian³, Ali Shafei Naderi¹, Nader Salim⁴, Abbas Teimoori⁴, Ahmad Bitaraf⁴, Mohammad Zadehrahmani⁵, Pamela Anna Burger⁶, Vincenzo Landi⁷, Mohammad Silawi⁸, Afsaneh Taghipour Sheshdeh⁸ & Mohammad Ali Faghghi^{8,9}



GENOMIC EVALUATION/PREDICTION



Predicted
GEV
estimation
accuracy

Figure 8. The accuracy of predicted GEVs from the 99 SNPs using BGLR package.

MILK TRAITS

MILK TRAIT
MILK YIELD
MILK GROSS COMPOSITION
MILK FATTY ACID PROFILES
MILK PROTEIN PROFILES
MILK SOMATIC CELL COUNT/SCORE
UDDER CONFORMATION TRAITS

**LEARN
FROM PAST
MISTAKES**

- ✓ Negative correlations!!!
- ✓ Genetic erosion!!!

OTHER (NEW) FUNCTIONAL TRAITS:

- ✓ FERTILITY
- ✓ HEALTH (mastitis, ketosis..)
- ✓ ENVIRONMENTAL IMPACT (climate resilient cattle, low-methane emissions..)

ACROSS “BREEDS” EVALUATION: INTERNATIONAL EFFORTS



Multiple Country and Breed Genomic Prediction of Tick Resistance in Beef Cattle

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OPEN CHALLENGES

- ❑ MILK PHENOTYPING IS COMPLEX (although some techniques are automated. Validation is needed for the dromedary species)

- ❑ LOWER HEREDITABILITY THAN MEAT TRAITS (lower expected genetic progress, not at the beginning but in the long-term)

- ❑ CAVEATS:
 - Negative correlations with fertility and adaptive traits (learn from past mistakes)
 - Poor genetic variability in this species = poor genetic gain
 - Further genetic erosion: fitness and adaptation???

WHERE WE ARE?

STATUS	STEP
YES	REFERENCE GENOME ANNOTATED & CHROMOSOMES
YES	RESEQUENCING VIA WGS
YES	RESEQUENCING VIA GBS
YES (more expected)	EVOLUTIONARY/STRUCTURAL GENOMICS
YES (more expected)	COMPARATIVE GENOMICS
YES (more expected)	IN SILICO FUNCTIONAL PREDICTION
YES	SNP ARRAY - MEDIUM DENSITY
COMING SOON	SNP ARRAY – HIGH DENSITY
YES (more expected)	GENOTYPE-PHENOTYPE ASSOCIATION STUDIES
NO	ROUTINE GENOTYPING
NO	ROUTINE PHENOTYPING
COMING SOON	SNP-BASED PATERNITY TESTS
NO	MOLECULAR-ASSISTED BREEDING & SELECTION
NO	MOLECULAR-BASED MILK ADULTERATION ASSAYS

DO WE REALLY WANT TO TRANSFORM A SHE-CAMEL INTO A HIGH-PRODUCING DAIRY COW?



THANK YOU