

A photograph of a desert landscape with sand dunes under a clear blue sky. In the foreground, a person wearing a brown robe and a dark cap is walking across the sand, leading a line of camels. The camels are carrying loads on their backs. The scene is bathed in warm, golden light, suggesting late afternoon or early morning. The title text is overlaid on the upper half of the image.

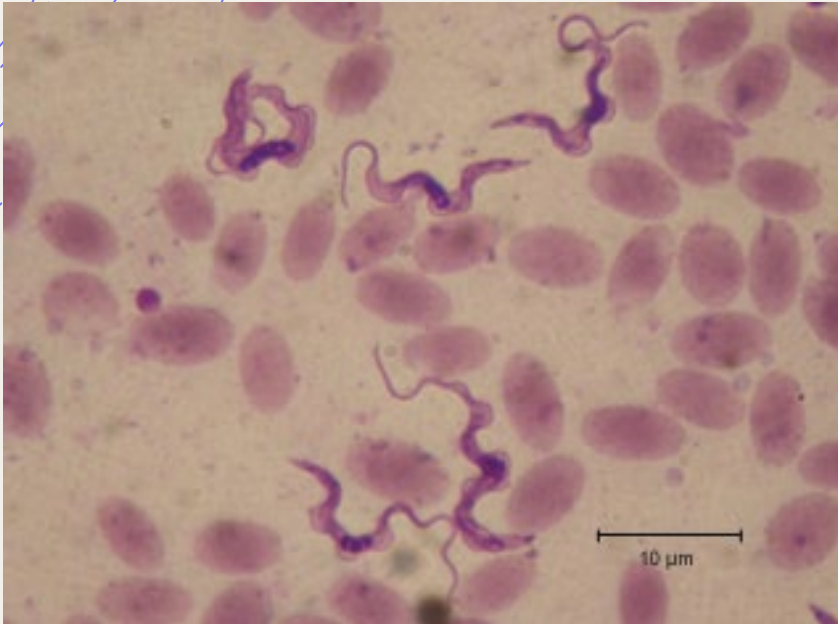
Case/Control Association Study on Trypanosome Infection in Algerian Dromedaries: Unraveling Genetic Determinants

Silvia Bruno
silvia.bruno@uniba.it
University of Bari

Department of Biosciences, Biotechnologies and Environment

BACKGROUND

Desquesnes et al., 2013



Giemsa-stained camel blood smear where the typical morphology of *T. evansi* can be observed.



***Trypanosoma evansi*:** first pathogenic mammalian trypanosome to be described in the blood of dromedary camels.



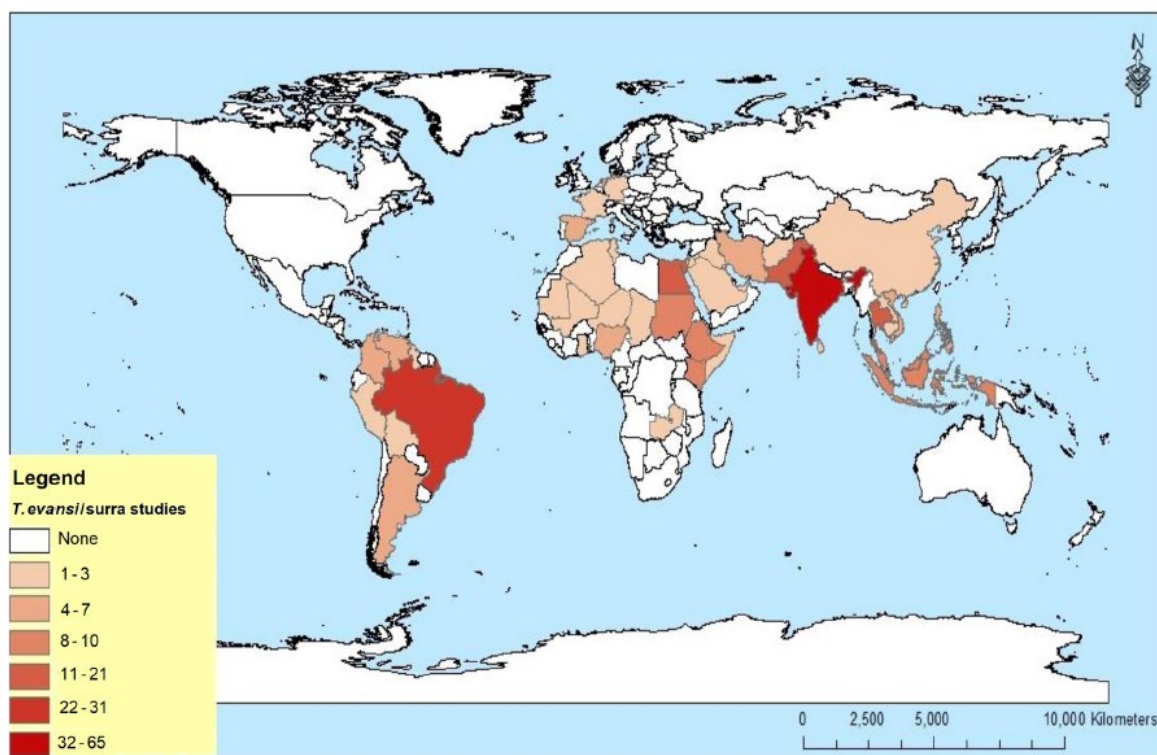
Transmission: mechanically transmitted by the biting of hematophagous flies (e.g. *Tabanidae*, *Stomoxys*).



Host: the principal host is the dromedary. Affects a wide variety of animals worldwide (e.g. horses, cattle, etc).

BACKGROUND

Aregawi et al., 2019



Global distribution of *T. evansi* based on studies published between 1906 and 2017.



Distribution: Asia, Africa, the Middle East, the Canary Islands, Central and South America. Also identified in Spain and France.



Trypanosomiasis: complex zoonotic disease.



«**Surra**»: the course of infection ranges from an acute disease with high mortality to a chronic form with different signs (intermittent fever, anemia, body weight loss, decrease milk production, abortion, infertility, and muscular atrophy). Clinical signs of neurological disorders reported in dromedaries.

The disease has a severe impact on the productivity, health, and working capacity of dromedaries and causes mortality and extensive economic losses.

AIM OF THE STUDY

Grech-Angelini, Sébastien, 2008



Zaitoun et al., 2016



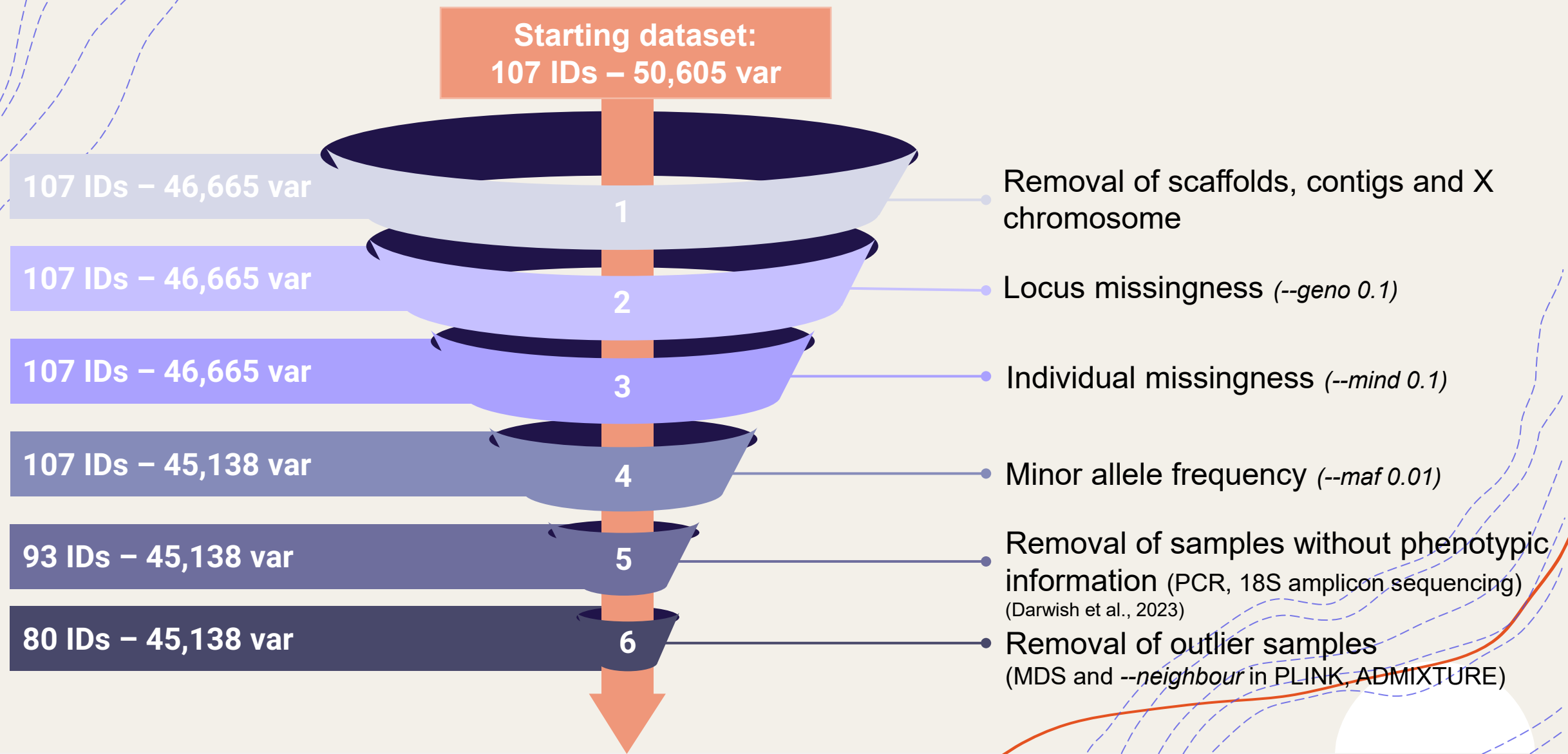
Pictures showing dromedaries infected by *T. evansi*.

Investigate the genetic association between SNP markers and the presence of trypanosome infection in a cohort of dromedaries from **Algeria** through a case/control association study approach.

N = 107



MATERIALS AND METHODS



MATERIALS AND METHODS

Working dataset for
Case/Control Association Study
80 IDs – 45,138 var

PHENOTYPE

POSITIVE TO TRYP.	NEGATIVE TO TRYP.
20	60

1. Unbalanced (20 vs 60)
2. Balanced 1 (20 vs 20)
3. Balanced 2 (20 vs 20)
4. Balanced 3 (20 vs 20)
5. Balanced 4 (20 vs 20)



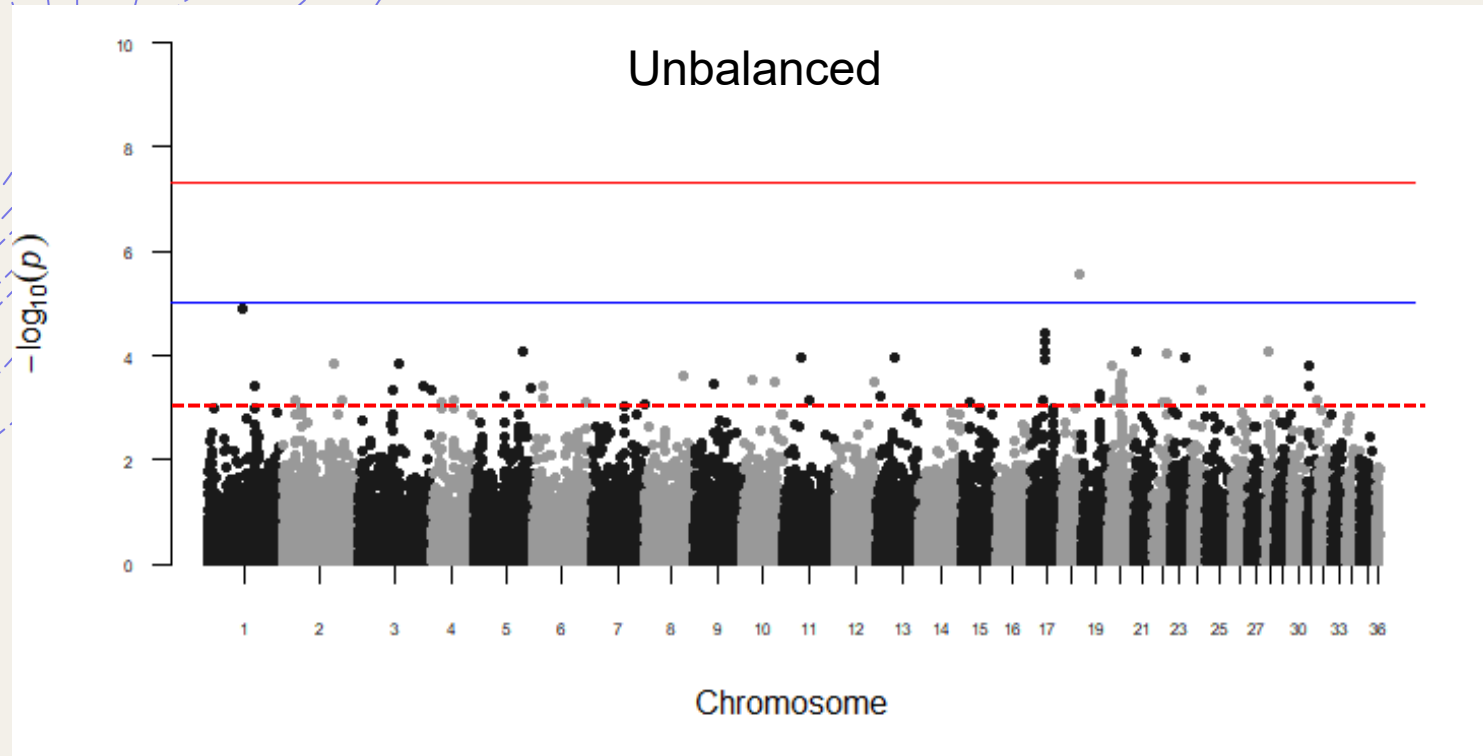
- Cut-off: signals with $-\log_{10}(p) > 3$ in at least **4/5** sub-datasets
- Genes in regions ± 250 kb



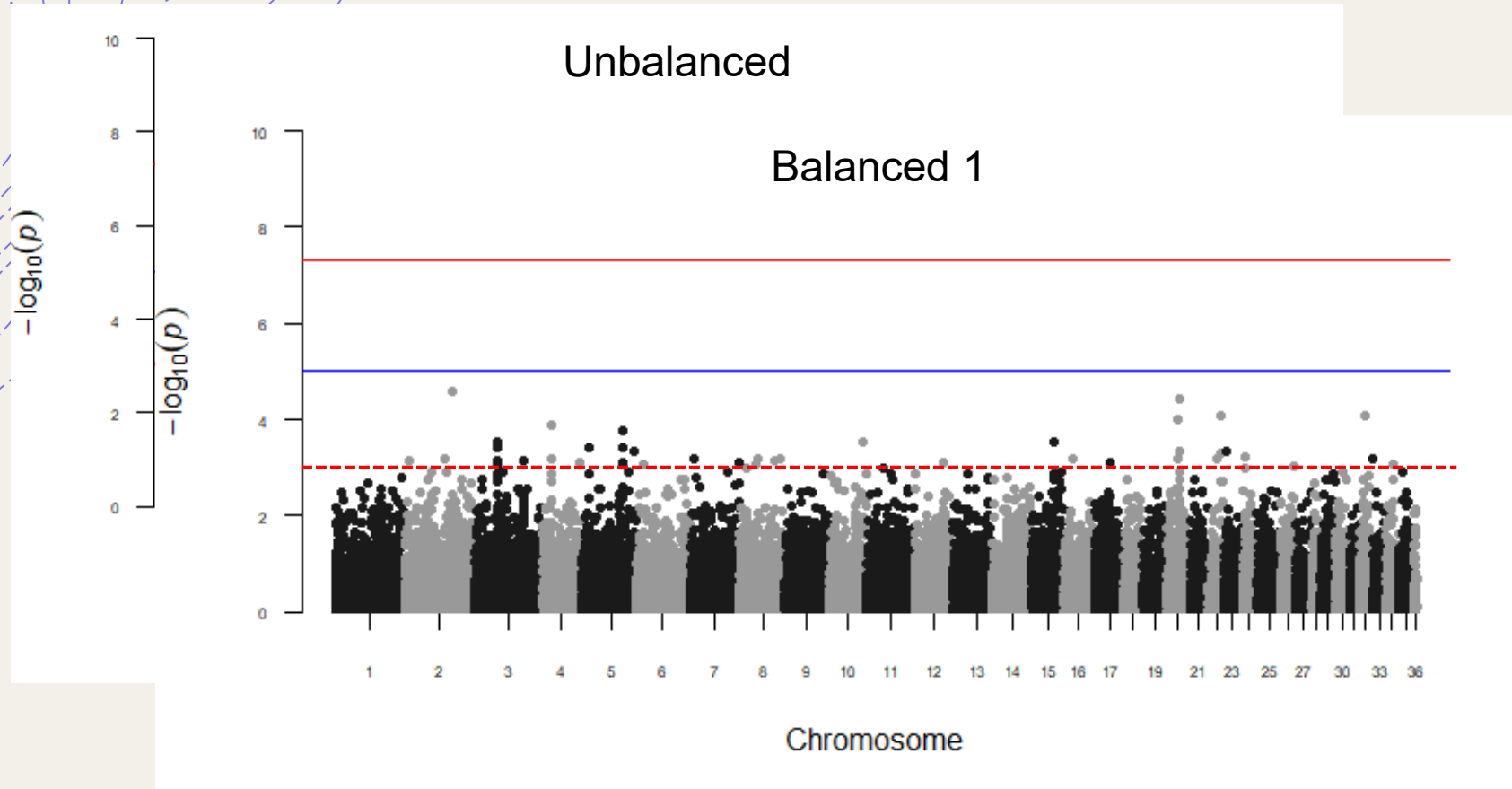
RESULTS



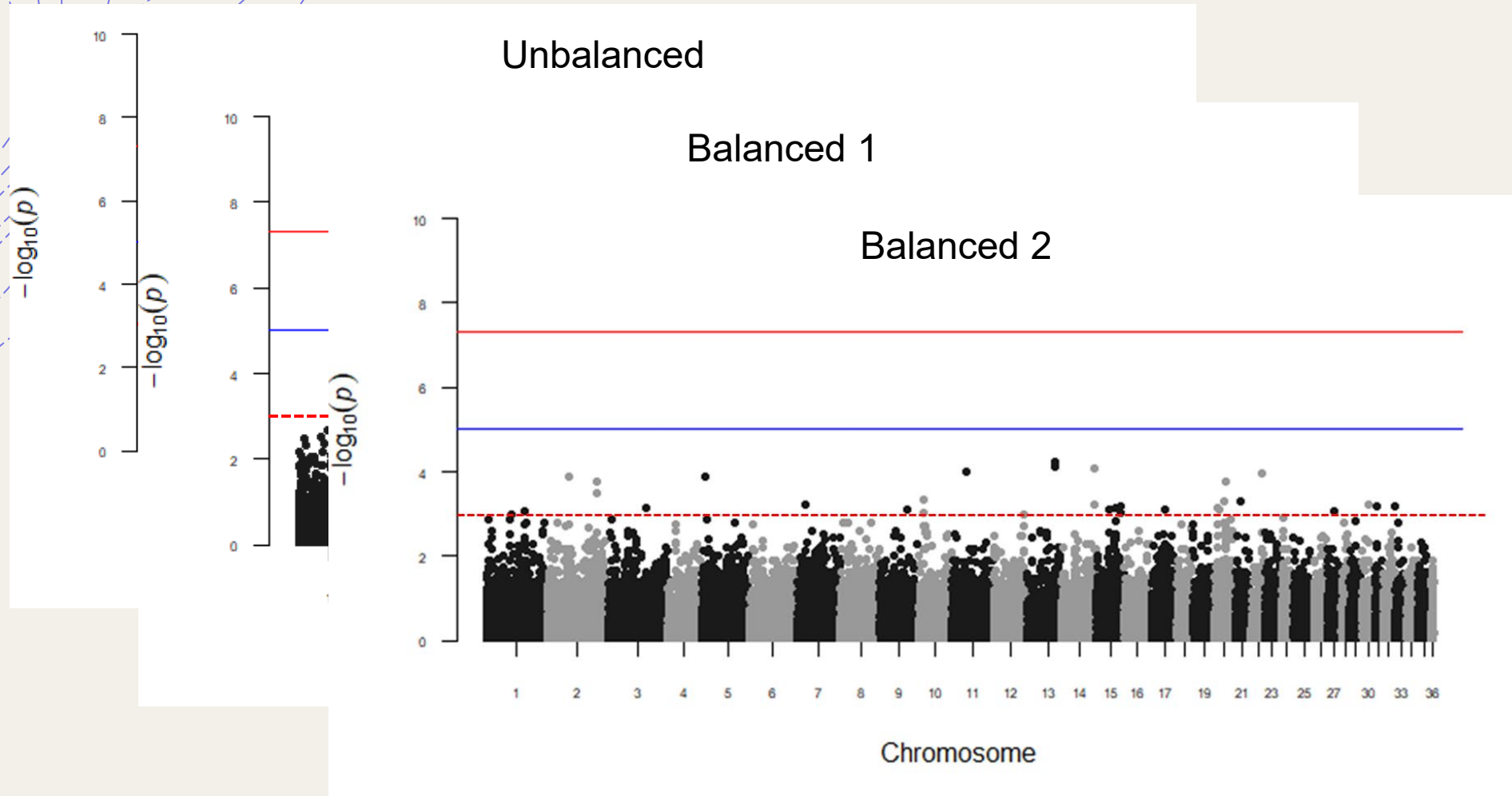
RESULTS



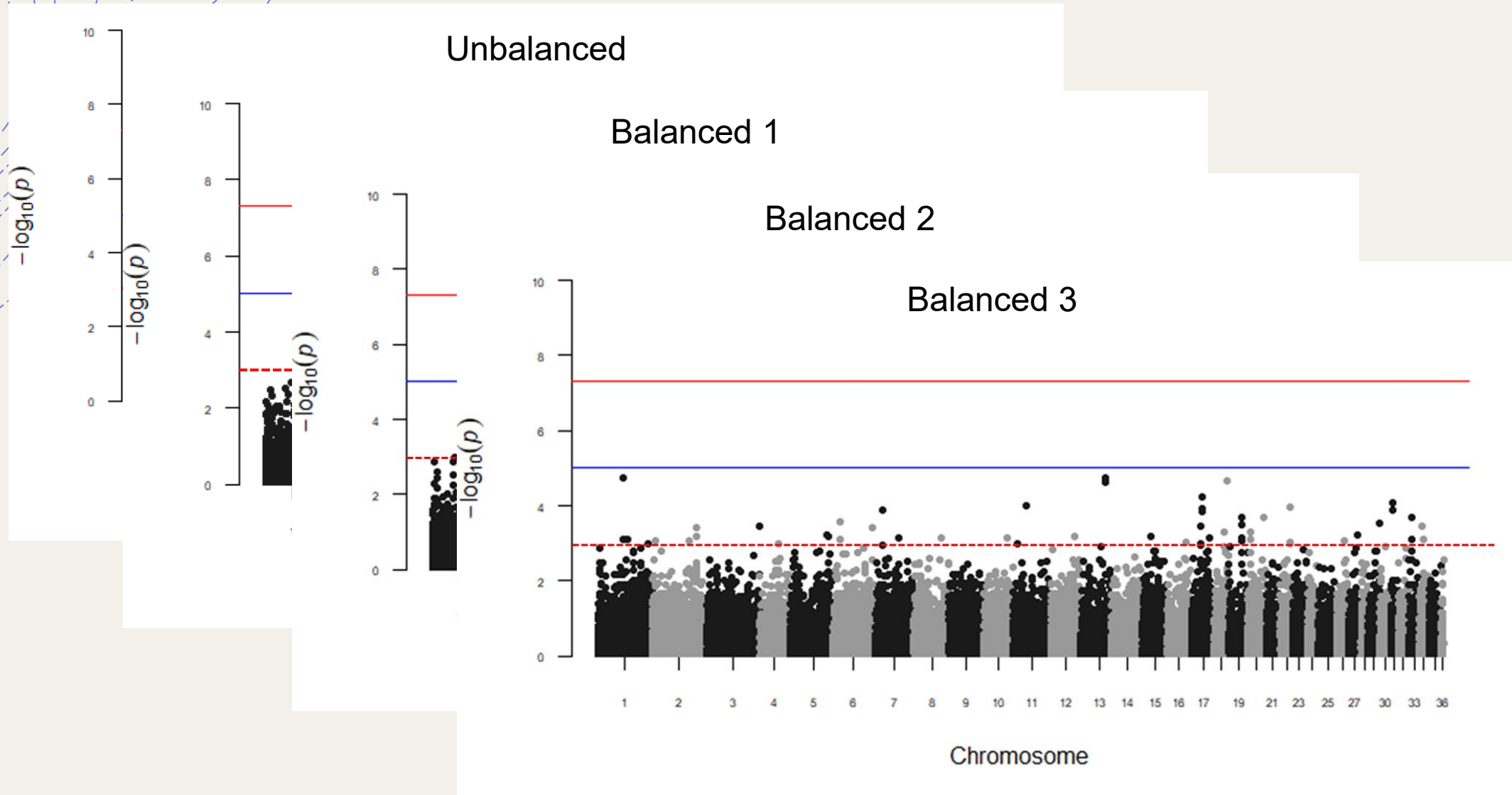
RESULTS



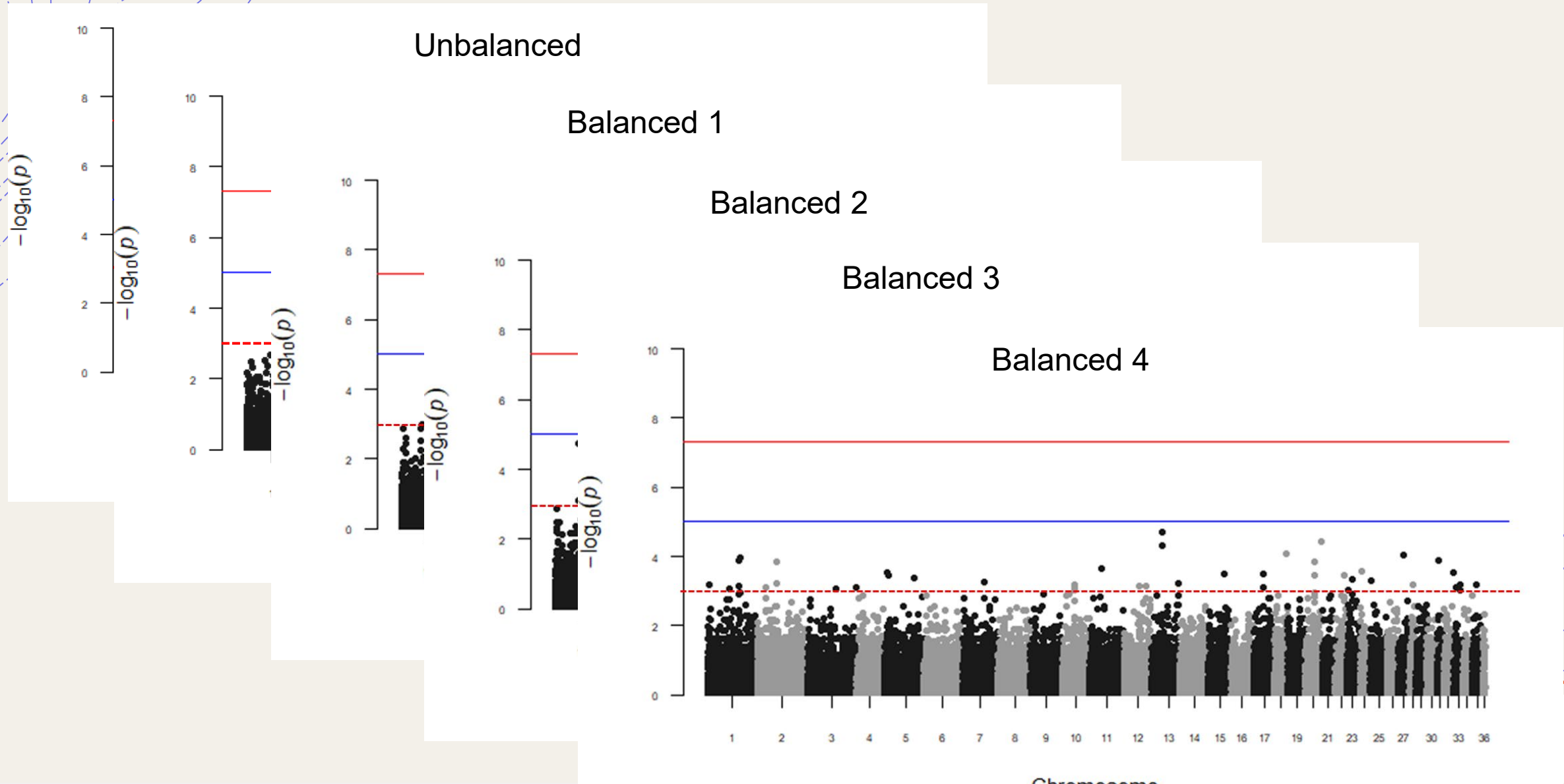
RESULTS



RESULTS



RESULTS



RESULTS

Signals with $-\log_{10}(p) > 3$ in at least **4/5** analyses performed were observed on the following chromosomes:

CHR	POSITION (bp)	$\pm 250\text{kb}$	NUMBER OF SUB-DATASETS	NUMBER OF GENES	GENES
11	28,713,988	$\pm 250\text{kb}$	4	2	KCNMA1, LRMDA
20	22,800,505	$\pm 250\text{kb}$	4	22	TCF19, CCHCR1, PSORS1C2, CDSN, MUC21, SFTA2, VARS2, GTF2H4, DDR1, IER3, FLOT1, TUBB, MDC1, NRM, PPP1R18, DHX16, ATAT1, PPP1R10, ABCF1, PRR3, GNL1, RPP21
22	22,920,408	$\pm 250\text{kb}$	5	7	ERGIC1, RPL26L1, ATP6V0E1, CREBRF, BNIP1, NKX2-5, STC2

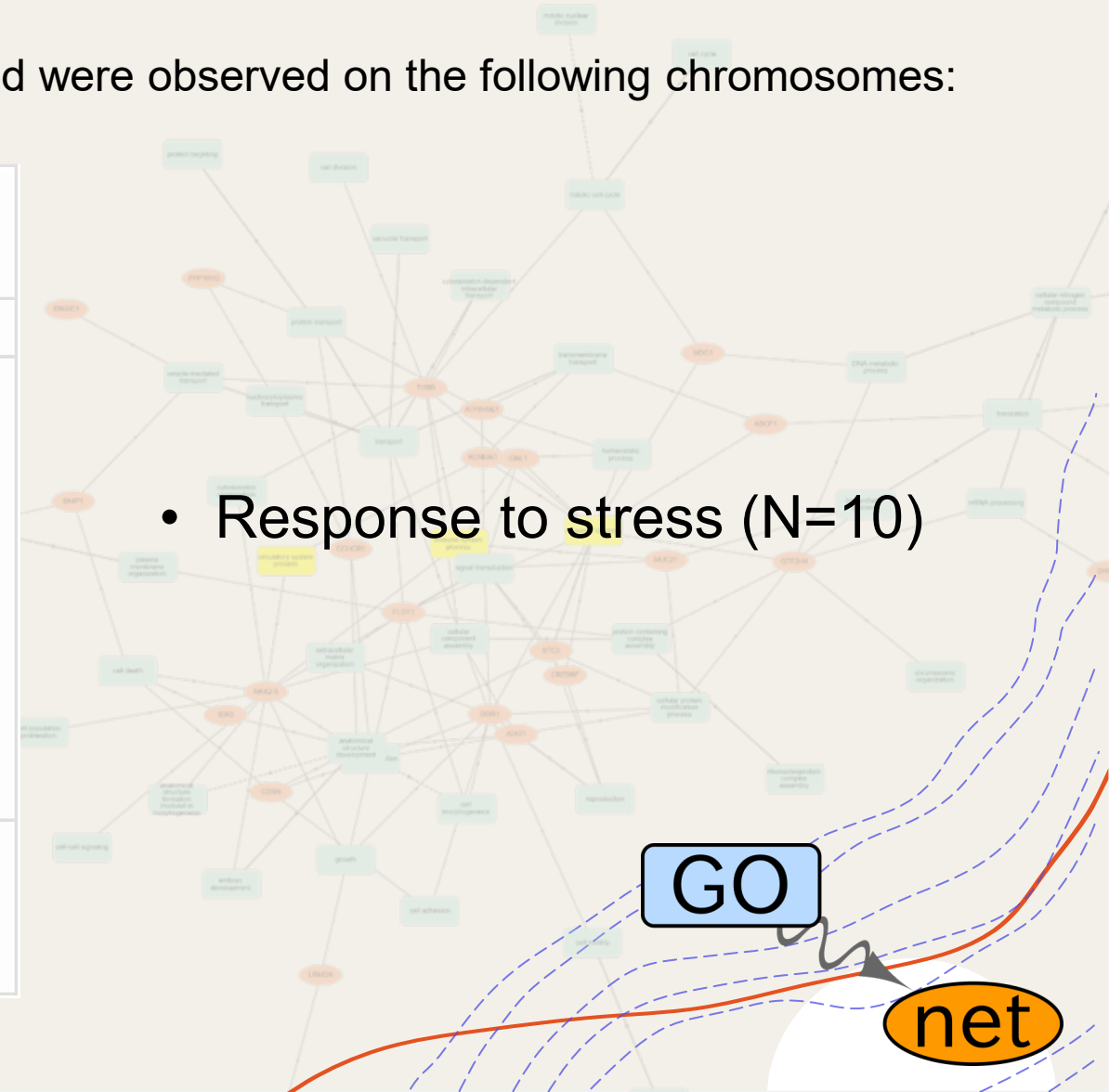
Total = 32

RESULTS

Signals with $-\log_{10}(p) > 3$ in at least **4/5** analyses performed were observed on the following chromosomes:

CHR	NUMBER OF SUB-DATASETS	GENES
11	4	KCNMA1, LRMDA
20	4	TCF19, CCHCR1, PSORS1C2, CDSN, MUC21, SFTA2, VARS2, GTF2H4, DDR1, IER3, FLOT1, <u>TUBB</u> , MDC1, NRM, PPP1R18, DHX16, ATAT1, PPP1R10, ABCF1, PRR3, GNL1, RPP21
22	5	ERGIC1, RPL26L1, ATP6V0E1, CREBRF, BNIP1, NKX2-5, STC2

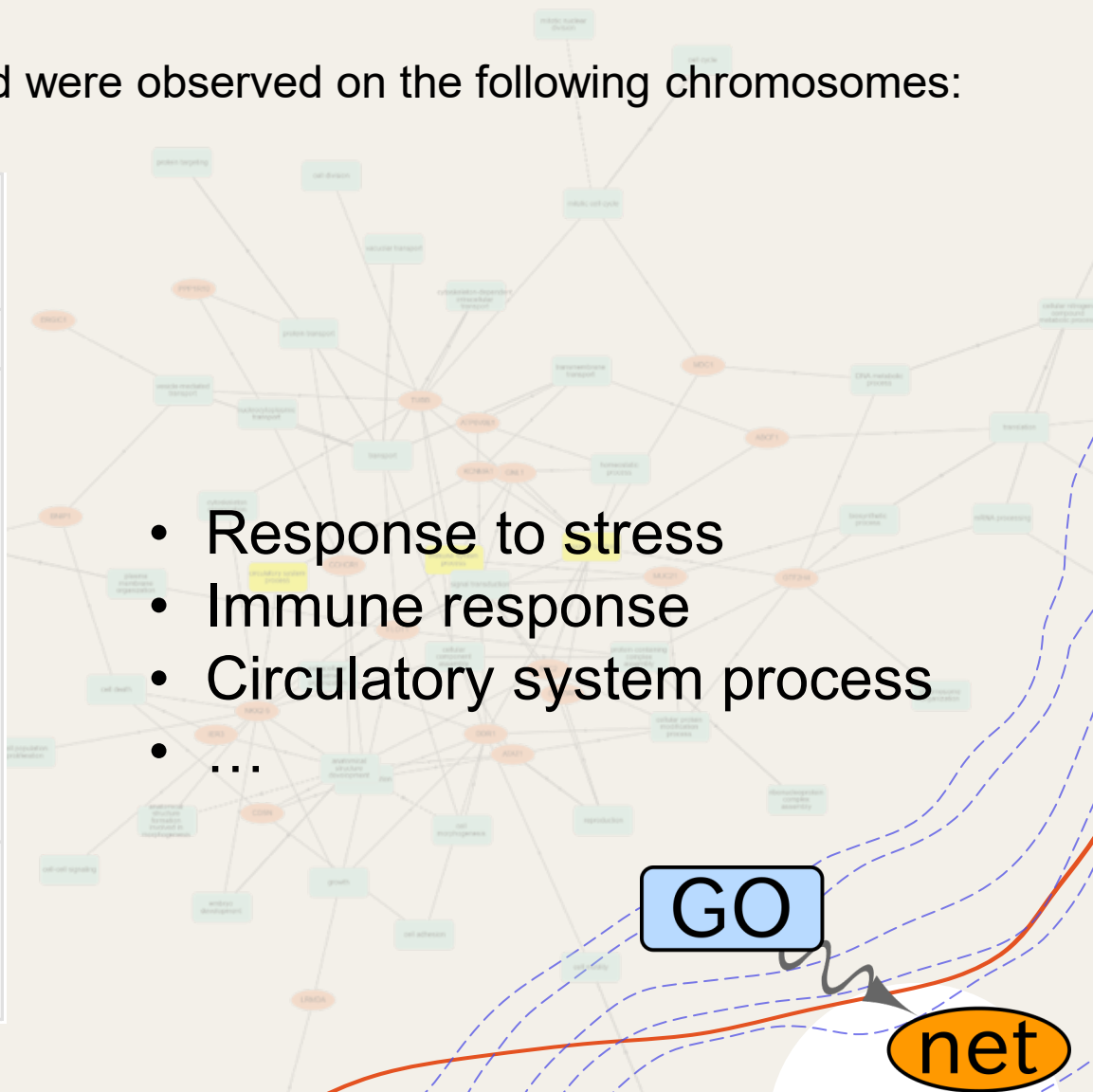
- Response to stress (N=10)



RESULTS

Signals with $-\log_{10}(p) > 3$ in at least **4/5** analyses performed were observed on the following chromosomes:

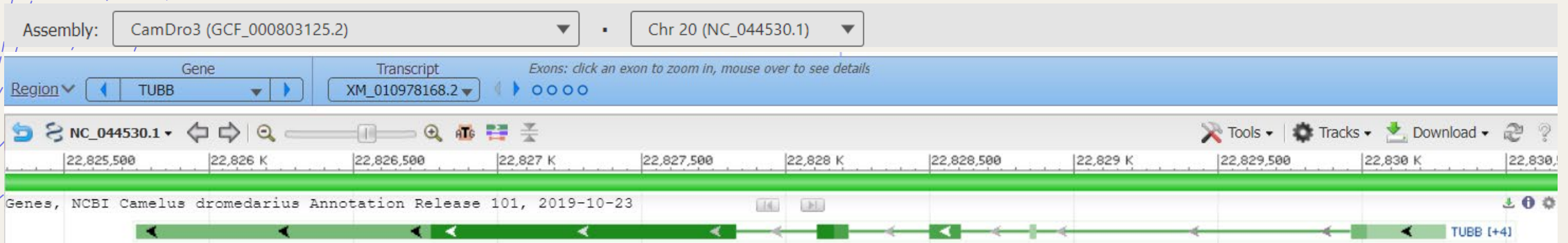
CHR	NUMBER OF SUB-DATASETS	GENES
11	4	KCNMA1, LRMDA
20	4	TCF19, CCHCR1, PSORS1C2, CDSN, MUC21, SFTA2, VARS2, GTF2H4, DDR1, IER3, FLOT1, TUBB , MDC1, NRM, PPP1R18, DHX16, ATAT1, PPP1R10, ABCF1, PRR3, GNL1, RPP21
22	5	ERGIC1, RPL26L1, ATP6V0E1, CREBRF, BNIP1, NKX2-5, STC2

- 
- Response to stress
 - Immune response
 - Circulatory system process
 - ...

GO

net

TUBB GENE (CHR20)



- Encodes a **beta tubulin** protein, a structural component of microtubules.
- Involved in **cytoskeleton** and its regulation.
- **Hub proteins** are exploited by pathogens to gain entry to the host and survive inside it.
- Hub proteins are **well conserved** and represent **good pathogen targets**.
- Target of *Trypanosoma brucei* in humans.

Gupta et al., 2021
Brown et al., 2007
Fraser et al., 2002
Durmus Tekir et al., 2012



CONCLUSIONS



Preliminary study with a small number of samples.



Identification of genes involved in the phenotype under investigation.



Next step: validation of the signal with independent and larger datasets.



Selection signatures analysis is currently ongoing...

ACKNOWLEDGEMENTS



Prof. Semir B.S. Gaouar



PhD student Imane Meghelli



Prof. Elena Ciani

OPEN **Biochemical and genotyping analyses of camels (*Camelus dromedaries*) trypanosomiasis in North Africa**

Ahmed M. Darwish^{1,9}✉, Abdoallah Sharaf^{2,3,9}, Semir Bechir Suheil Gaouar⁴, Neama I. Ali¹, Tamer H. Abd El-Aziz⁵, Asmaa M. Abushady^{3,6}, Zoubeyda Kaouadji⁴, Othman E. Othman¹ & Miroslav Obornik^{7,8}

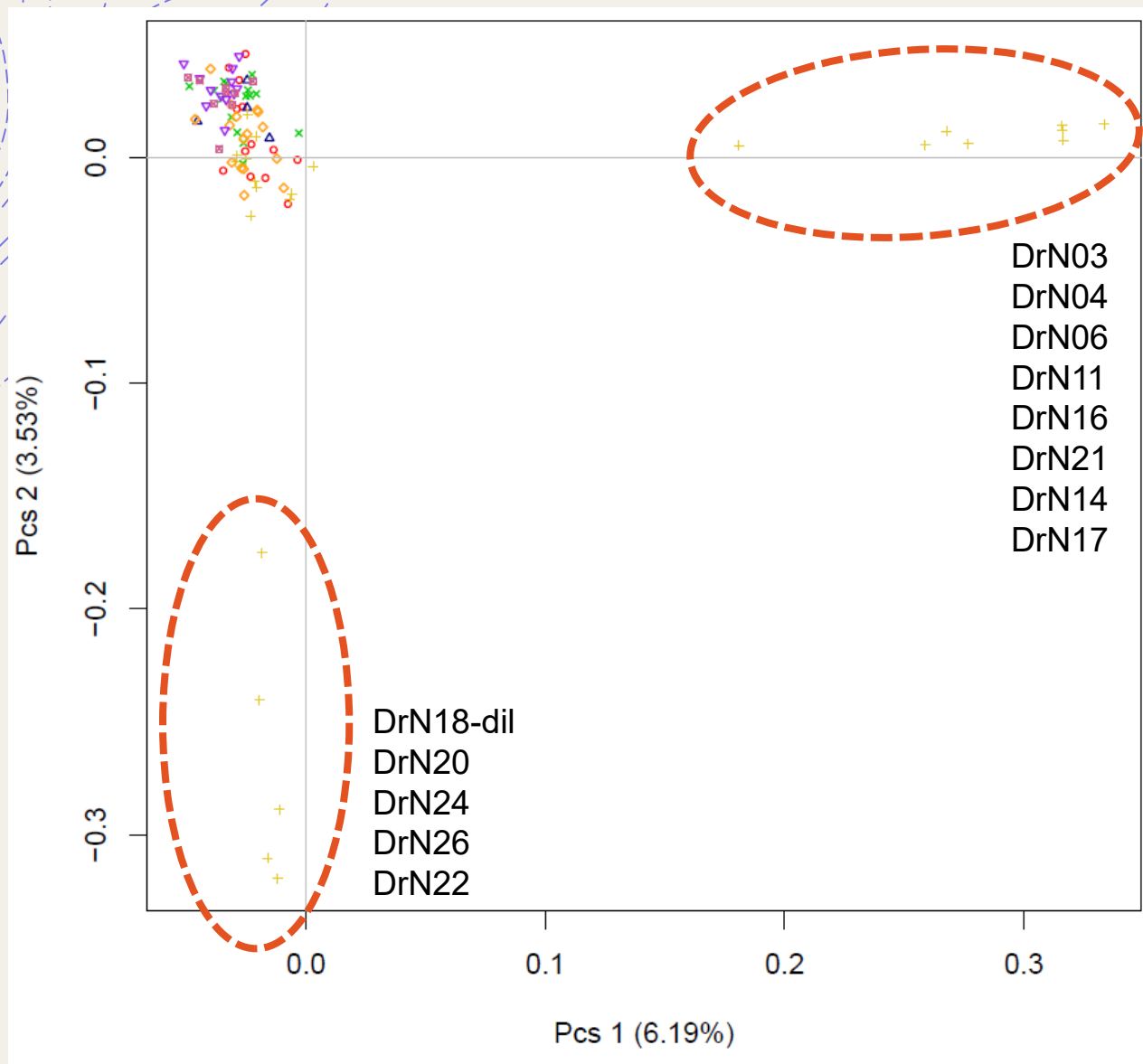
THANK YOU FOR YOUR
ATTENTION!



THANK YOU FOR YOUR
ATTENTION!



MATERIALS AND METHODS

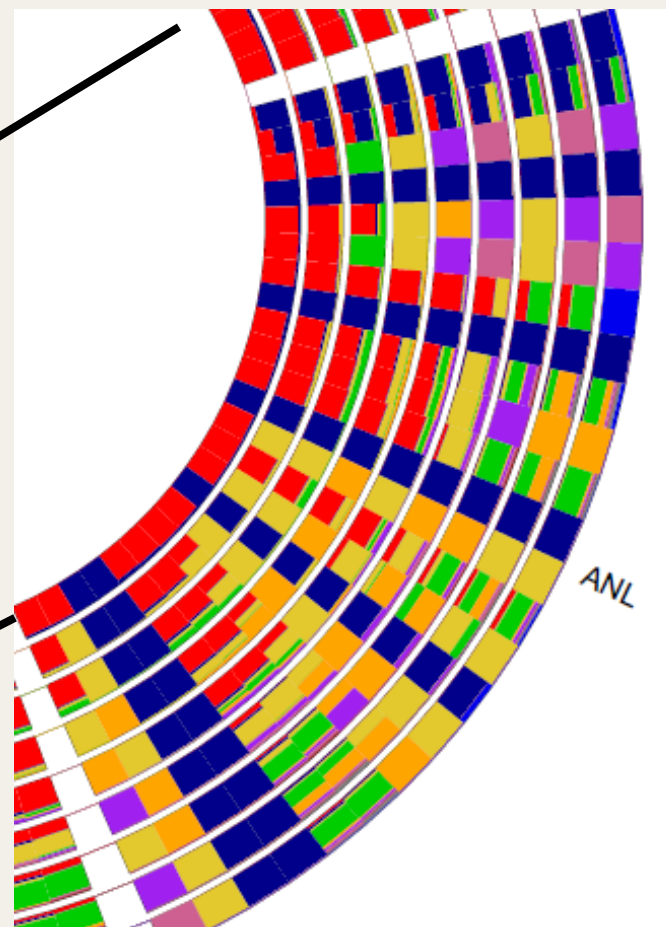
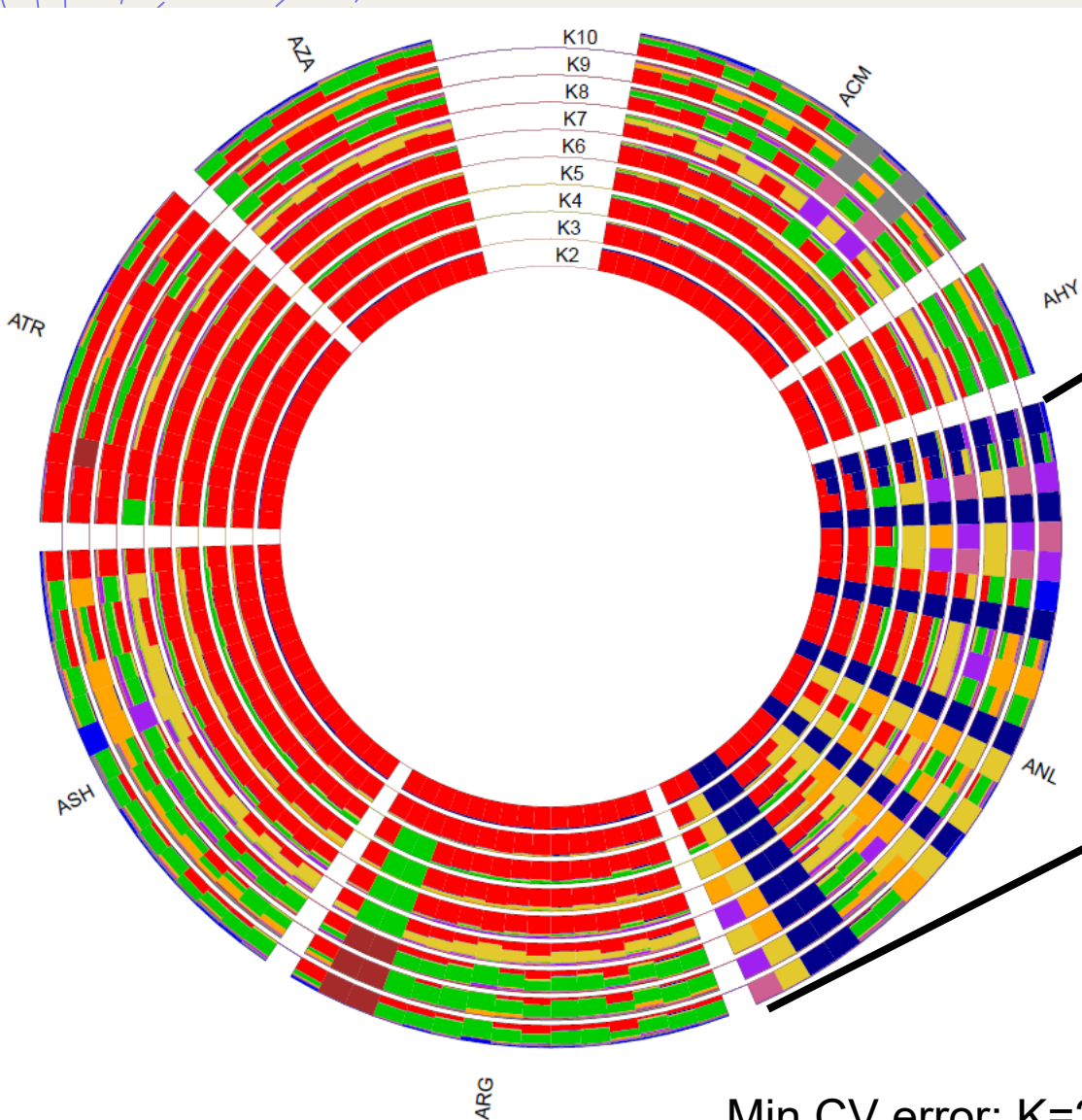


Detection of 13 Naili (ANL) outlier samples
(MDS and *--neighbour* in PLINK)

MATERIALS AND METHODS

ANL (Naili)

These samples are those identified as outliers.



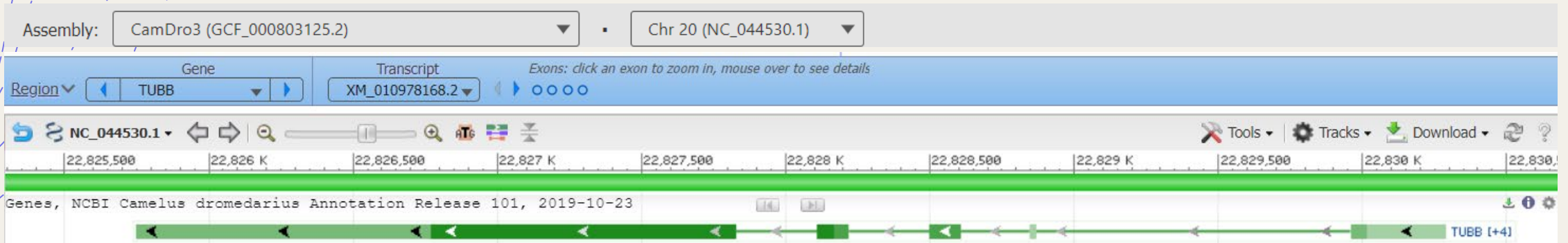
**K2 blue = 8
samples**

**K3 yellow = 5
samples**

DrN03
DrN04
DrN06
DrN11
DrN16
DrN21
DrN14
DrN17

DrN18-dil
DrN20
DrN24
DrN26
DrN22

TUBB GENE (CHR20)



- Encodes a beta tubulin protein,
- Forms a dimer with alpha tubulin and acts as a structural component of microtubules.
- Involved in **cytoskeleton** and its regulation.
- Important component of the cytoskeleton.
- Idea that many pathogens profit from targeting central host processes via the cytoskeleton and host entry by targeting these four proteins.
- hub proteins are exploited by pathogens to gain entry to the host and survive inside it.
- Normally, hub proteins are well conserved [19], [57] and hence represent good pathogen targets [29].
- **Target of T. brucei in humans.**

