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Epigenetic signatures of social status in free-ranging spotted hyenas (*Crocuta crocuta*)

Wildlife Epigenetics

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Epigenetic signatures of social status in female free-ranging spotted hyenas (*Crocuta crocuta*)

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Epigenetics

- Regulation of gene activity without a change in the DNA sequence.
- Epigenetic modifications are dynamic and reversible,

  which is in contrast to modifications in the genetic code.
- Epigenetic patterns in germ cells can be inherited to next generation(s).

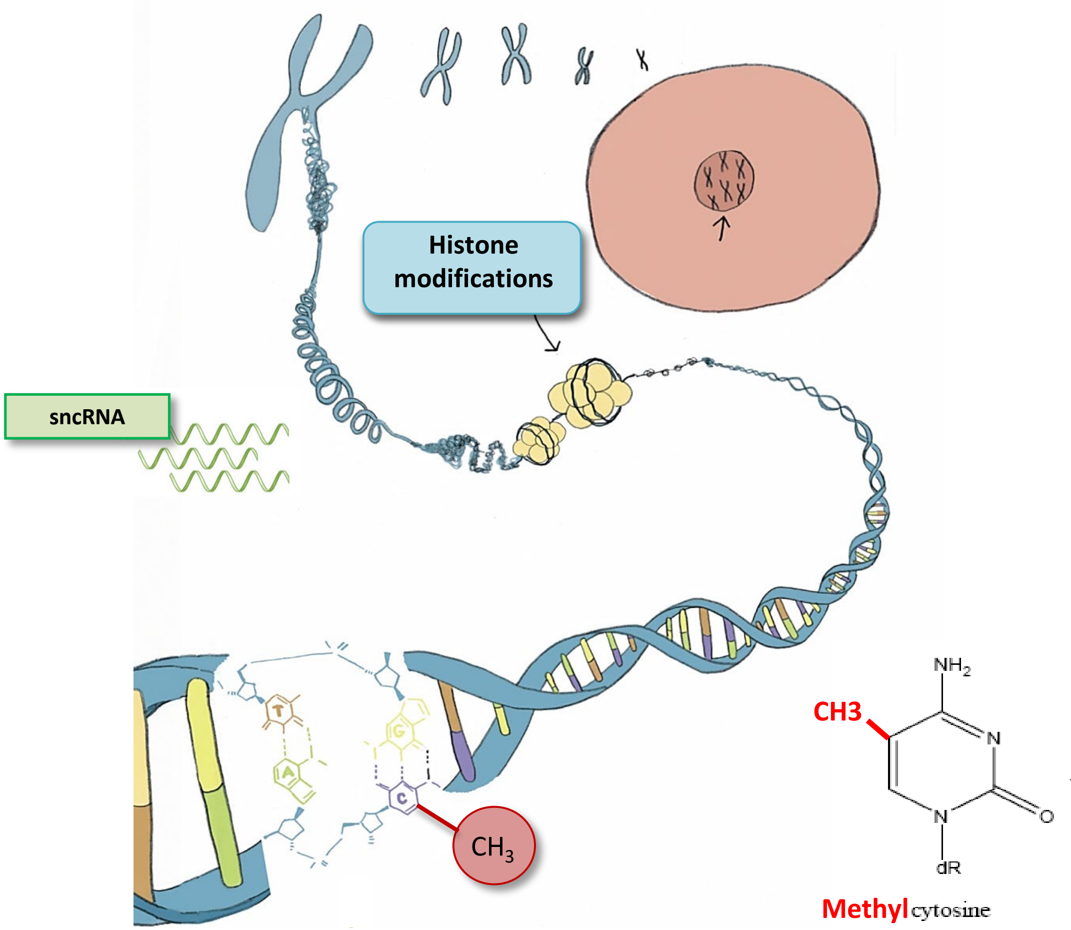
(Bird A. 2007 Nature Reviews)

Epigenetic mechanisms

- DNA methylation
- Histone modifications
- Small non-coding RNAs

Function:

➢ **Regulation of gene activity**



(Weyrich et al. 2016, Comic, JaJa-Verlag)

Epigenetic modifications

1) **Early development** incl. imprinting, cell differentiation (Monk et al. 1987)

2) **Genome stability**, e.g. heterochromatin, silencing of transposable elements (Egger et al. 2004)

3) **Response to environmental alteration** (Lea et al. 2016, Tung et al. 2012; Weyrich et al.)

Captivity

Weyrich et al. 2022

Temperature

Weyrich et al. 2016 a,b, 2020

Territory behaviour

Somerville et al. 2019; Weyrich et al. in prep.

Epigenetic modifications

Weyrich et al. 2018a

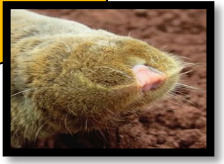
Nutrition

Weyrich et al. 2018b

Social environment

Guerrero et al. 2020, Vullioud et al. 2024

Soil & Speciation



Li, Weyrich et al. 2021

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Question:

Does the social environment

-“social status”-

translate into status-specific epigenetic profiles

across age classes?

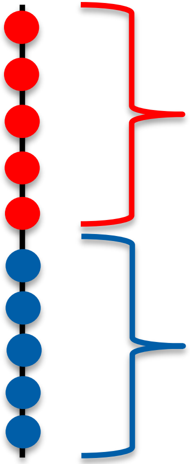
Model species & Social organization

Spotted hyenas (*Crocuta crocuta*)

Picture by S. Ferreira, M.L. East

IZW long-term project:
Continuous monitoring since **1987**
in the Serengeti National Park, Tanzania

Linear dominance hierarchy



HR
10 – 20 adult females

LR
10 – 20 adult females

Large social groups "**clans**",
similar to many primates,
stable female-dominated (philopatry)

(Hofer & East 1993)

Behavioural transmission of social status

HR

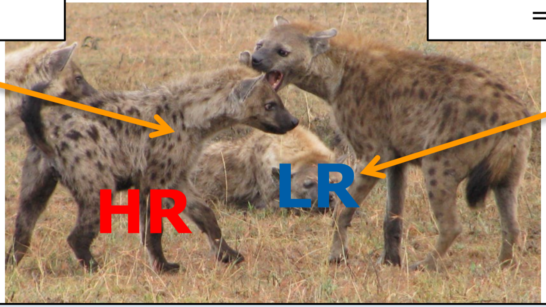
Offspring of **HR** mother
receives **MORE** care,
MORE social support

Learns to behave in a
socially dominant way
= becomes **HR**

LR

Offspring of **LR** mother
receives **LESS** care,
LESS social support

Learns to behave in a
socially subordinate way
= becomes **LR**



Reduction of costly aggression within the clan during encounters

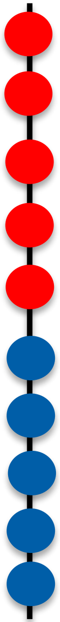
East et al. 2009

Social status

Emergent property determined my dyadic interactions

East et al. 2009

Linear hierarchy



High social rank (**HR**)

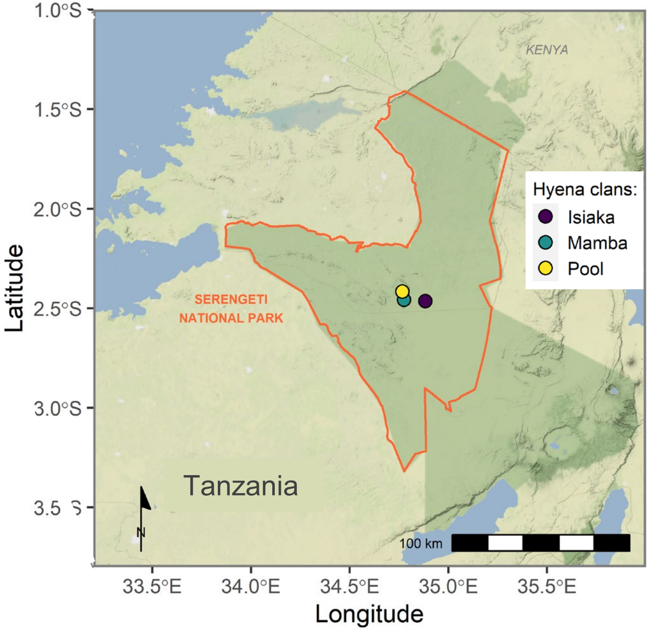
dominant behavior
+ access to resources
+ foraging close proximity to den
+ lactation frequency
- commuting distances
+ health
+ earlier onset of reproduction (Darwinian fitness)

Low social rank (**LR**)

subordinate behaviour
- access to resources
- foraging
- lactation frequency
+ commuting distances
- health
- Darwinian fitness

Sampling and methodical approach

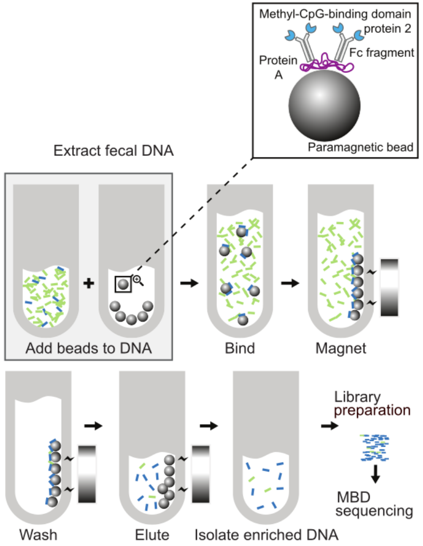
a)



b)

Gut epithelium cells
from faeces mucus layer

c) **DNA methylation &**
capture of mammalian DNA

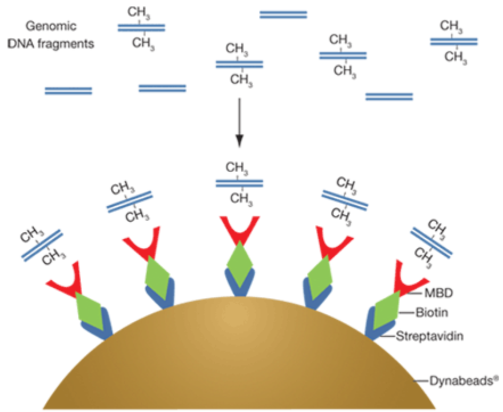


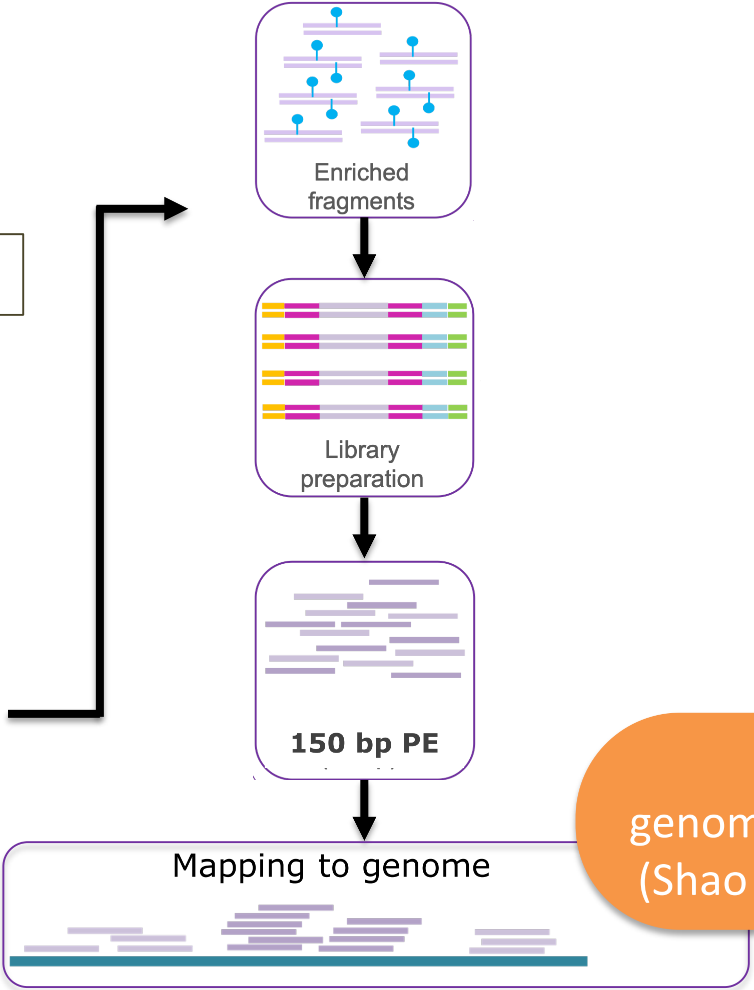
Credits: A) Map by M. Gicquel, B) Pictures M.L.East, C) Workflow adapted from Chiou & Bergey 2018

NEW
sample material

Methylome sequencing

mDNA-enrichment





Enriched fragments

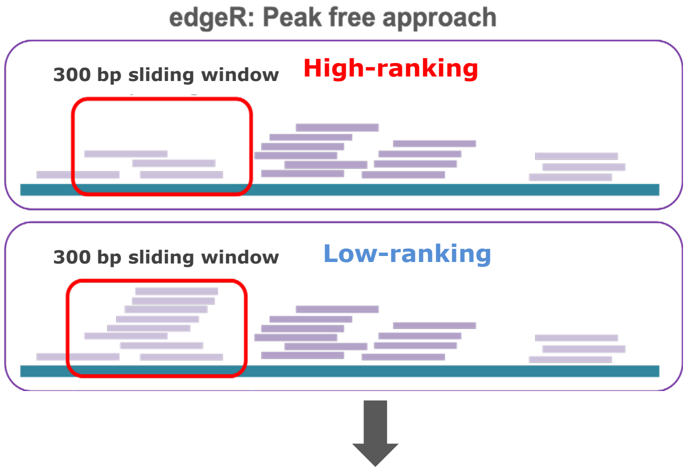
Library preparation

150 bp PE

Mapping to genome

NEW
genome sequence
(Shao et al. 2022)

Differentially methylated regions `DMRs`



edgeR: Peak free approach

300 bp sliding window **High-ranking**

300 bp sliding window **Low-ranking**

n= 18
(9 cubs,
9 adults)

n= 24
(15 cubs,
9 adults)

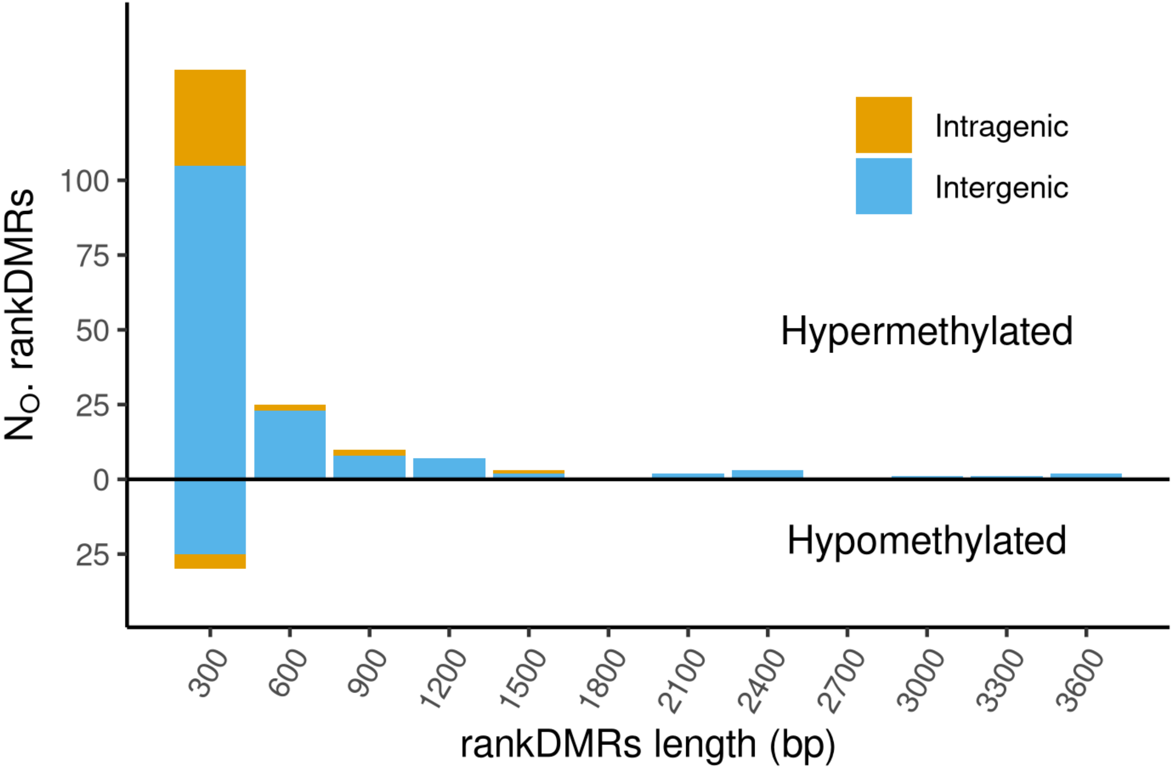
179 rankDMRs
26 hypo and **153 hypermethylated** in low-ranking females

→ **42** rankDMRs overlapped with **genes**

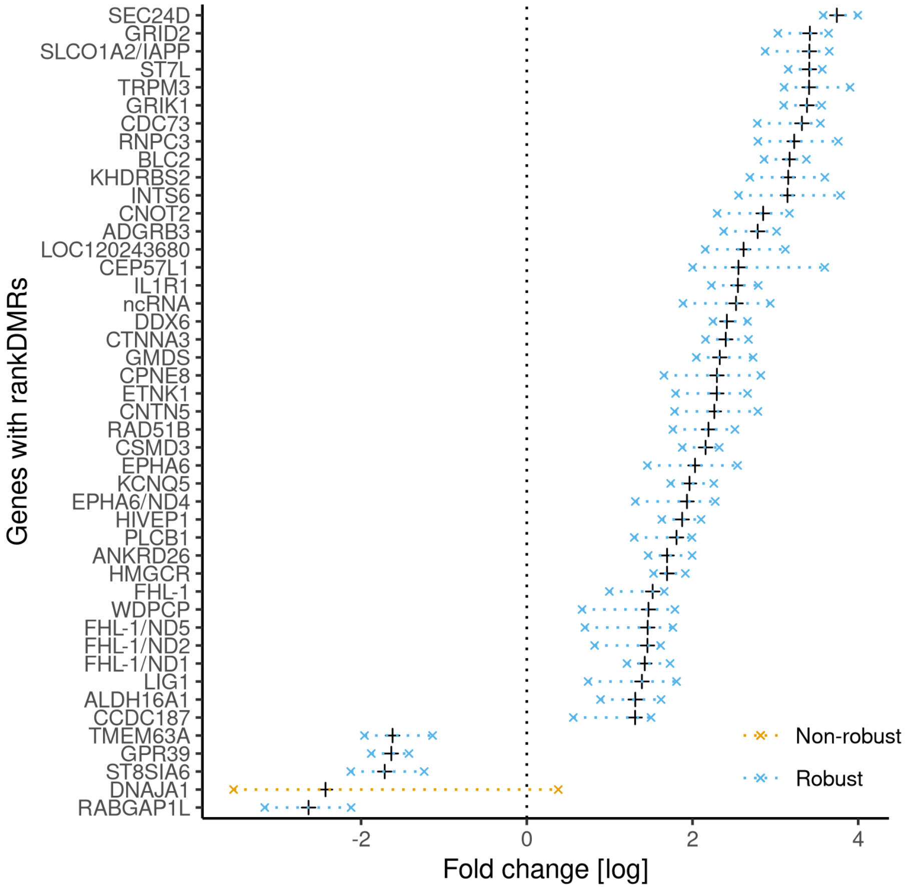
Promoter	**TSS**	**Start-codon**	**Exon**	**Intron**	**Stop-codon**	**Intergenic region**
2	1	1	6	39	2	137

NEW
Custom-made
annotation

Hypermethylated and hypomethylated regions in high-ranking vs low-ranking spotted hyenas



Validation of hyper and hypomethylated genes



Validation of rankDMRs

- Subsampling the 42 samples into 6 subsets, each containing 35 individuals
- We randomly split the individuals into 6 groups and removed 1 group at a time
- Run 6 times, only for the DMR positions in the full dataset
- Redo methylation analysis
- DMR robust when all subsets showed an hypermethylation or hypomethylation
- Subsets independently (p-value ≤ 0.05).

Results:

→ Of total **179 rankDMRs**, 30 were not consistent and excluded

→ Of the 42 rankDMRs overlapping with **45 genes** only DNAJA1 was excluded

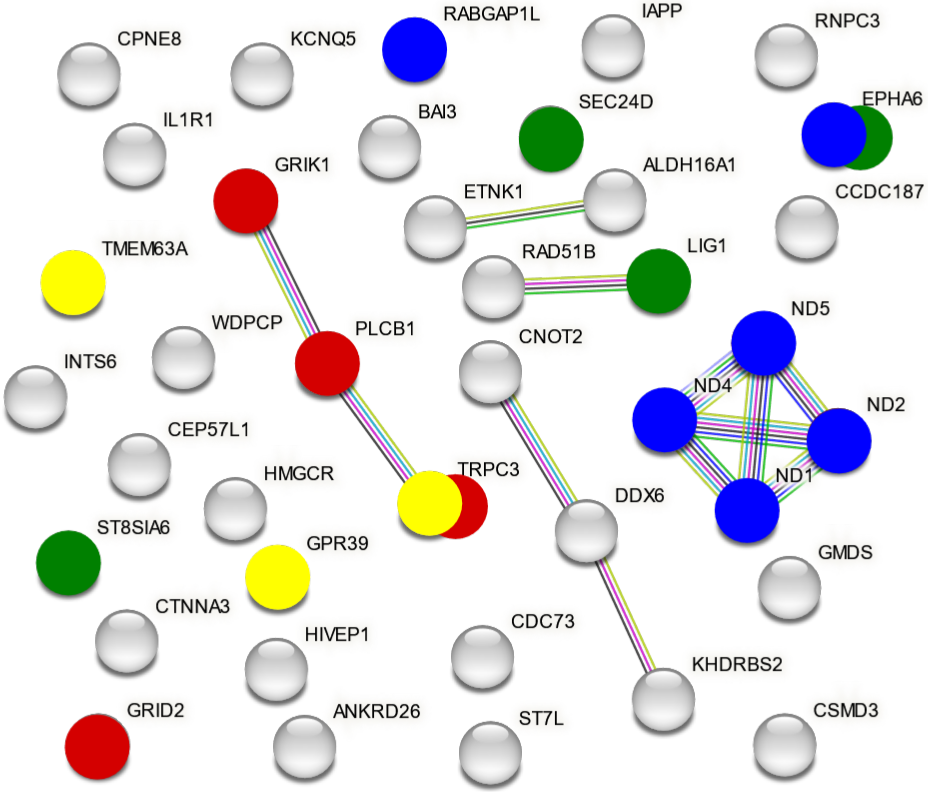
Network analysis of rankDMR genes

Biological function by network analysis

1) energy conversion
2) glutamate receptor signalling
3) immune response
4) ion transportation

Findings:

- May reflect access to resources
- Set of biomarkers for social status in a wild population
- Detectable in a non-invasive sample material, to use in other wildlife studies

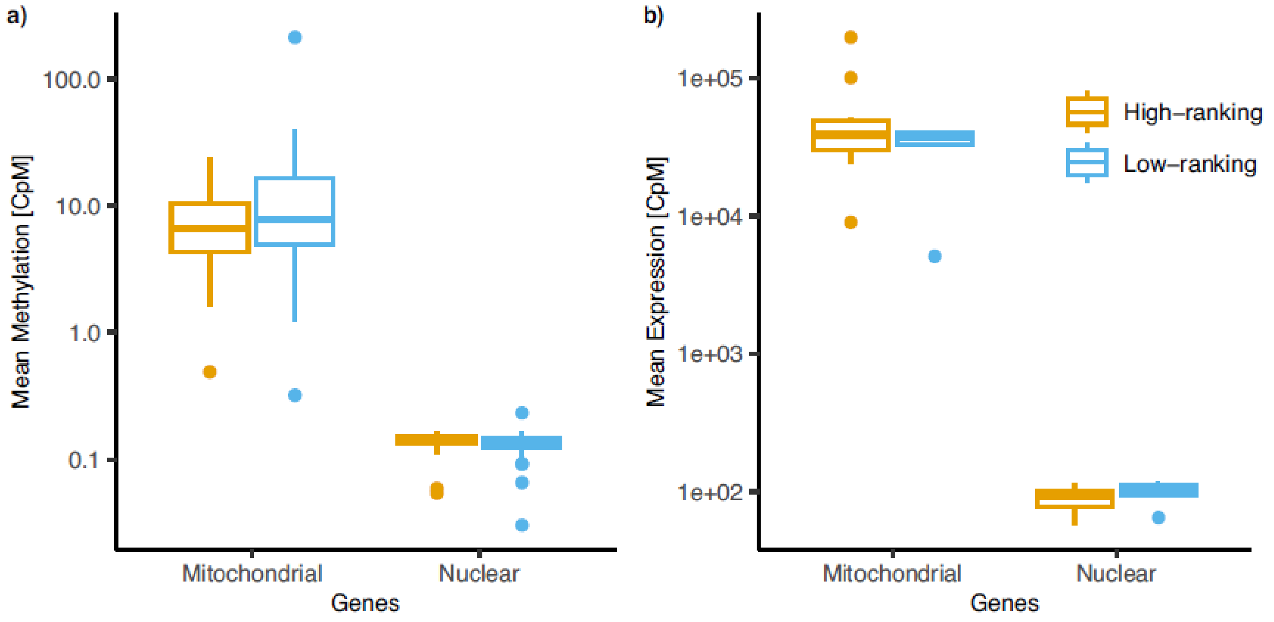


Discriminative power of DMRs between high and low-ranking female spotted hyenas

Differentially methylated regions (DMRs)*	**Out-of-bag error**
rankDMR total	~ 21 %
rankDMR validated	~ 19 %
rankDMR excluded	~ 45 %
mean methylation	~ 50 %

Out-of-bag error with different methylation measures as covariates.

Mitochondria gene activity and methylation in high and low-ranking female spotted hyenas



Mean DNA methylation of mitochondrial and nuclear DNA per window and individual in count per million bases (CPM).

Mean RNA expression per gene and individual in count per million bases.

Greater abundance of methylation and expression in mitochondrial DNA and RNA (n= 16 individuals).

Conclusions

- „Social status goes under your skin across age“
- Indentification of status-specific DMRs
- Energy conversion may reflect access to resources
- Set of biomarkers for social status in a wild population
- Detectable in a non-invasive sample material

and can be used for other wildlife studies.

SAW PAKT 2018 - 2022 – Leibniz Cooperative Excellence

Epigenetic stability and plasticity of social environmental effects

Prof. Michael Hofreiter
Potsdam University

GENOMICS

Prof. Moshe Szyf
McGill University, Canada

SOCIAL EPIGENETICS

Prof. Yoav Soen
Weizmann Institute of Science, Israel

MICROBIOME

IZW

Weyrich

Fickel

EPIGENETICS

Benhaiem

East

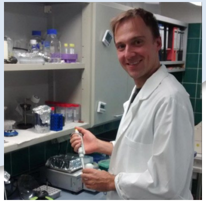
Hofer

SOCIAL BEHAVIOUR, FITNESS, SPOTTED HYENA

Czirják

IMMUNOLOGY

Heitlinger



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Inter-Species Epigenetics - sInSpEc

- **Individual sDiv postdoc project**
- **Dr. Walter Durka** (Helmholtz Center for Environmental Research (UFZ) in Halle and iDiv member)
- **Prof. Christina Richards** (University of South Florida and Eberhard Karls Universität Tübingen)
- **Dr. Marc Schmidt** (MWSchmid GmbH, Switzerland)

Thank you for your attention!

Questions?

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