Landscape genomics of local adaptation in sheep and goats

Badr Benjelloun
Laboratoire d'Ecologie Alpine, CNRS France
CRRA of Tadla, INRA Morocco
badr.benjelloun@gmail.com

On behalf of the NextGen consortium

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Local adaptation... Genetic bases

Context

Scenarios of adaptive convergence: Gene level

- Adaptation → Adaptative trait → Gene(s)
  - Species 1
  - Species 2

E.g., *EPAS1* gene - Altitude in Humans and dogs

(Simonson et al.; Yi et al. 2010. Science; Gou et al. 2014. Genome Res.)
Context

Sheep and goats

- Domestic species with recent divergence time
- Domestication in the same area under similar conditions
- Raised under similar environments

5 - 7 mya
Sheep and goats in Morocco ...

- 20 M of sheep and 6.2 M of goats: 95% of indigenous breeds and populations (FAOSTAT, 2013)
- Adaptation to the highly contrasted environments in the country, i.e. climate, ecology, Husbandry practices,...
- High phenotypic and genetic diversity
### Sheep and goats in Morocco ...

- 20 M of sheep and 6.2 M of goats: 95% of indigenous breeds and populations (FAOSTAT, 2013)
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- High phenotypic and genetic diversity

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**Selection signatures linked to environmental variation in sheep and goats?**

**Congruence of selection signatures in both species?**
Study of the interaction between environmental and genomic variation to understand adaptive diversity (Manel et al. 2003; Manel et Holderegger 2013. *Trends Ecol. Evol.*)

Sheep and goats in Morocco ...

- 20 M of sheep and 6.2 M of goats: 95% of indigenous breeds and populations (FAOSTAT, 2013)
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Selection signatures linked to environmental variation in sheep and goats?
Congruence of selection signatures in both species?

*Landscape genomics*
1412 sheep and 1283 goats sampled in the Northern part of Morocco (≈ 450,000 km²)

164 sheep and 164 goats selected to maximise coverage of environmental gradients
Approach

- 38.6M variants (SNP and small indels) for 160 sheep
- 31.7M variants for 161 goats


Data analysis

Selection signatures

WGS
160 sheep
161 goats

14 Environmental variables
Altitude, Slope, Sunshine duration (2), Temperature (7), Rainfall(3)

Population based approach

Selective sweeps


Selection signatures

WGS
160 sheep
161 goats

14 Environmental variables
Altitude, Slope, Sunshine duration (2), Temperature (7), Rainfall(3)

Data analysis

• Logistic regression using the whole set of individuals. i.e., n=160
Approach

Data analysis

- WGS
  - 160 sheep
  - 161 goats

- 14 Environmental variables
  - Altitude, Slope, Sunshine duration (2), Temperature (7), Rainfall(3)

Selection signatures
- Population-based approach: combination of XP-CLR (Chen et al. 2010. Genome Res.) and 
  $F_{st}$ (Weir et Cockerham. 1984. Evolution)

Effect/function of the identified variants
- Variant effect predictor (VEP; McLaren et al. 2010. Bioinformatics)
- Enrichment of biological pathways using the identified candidate genes

Congruence of selection signatures
- Mapping of the identified goat outliers on the OARv3.1 genome and sheep outliers on 
  the CHIIRv1.0 assembly
## Results

### Genomic regions under selection

<table>
<thead>
<tr>
<th></th>
<th># Variants</th>
<th># Genes</th>
<th># Genomic regions</th>
<th># Genomic regions &gt; 200 kb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sheep</td>
<td>12,966</td>
<td>276</td>
<td>363</td>
<td>24</td>
</tr>
<tr>
<td>Goats</td>
<td>8,055</td>
<td>294</td>
<td>434</td>
<td>28</td>
</tr>
</tbody>
</table>

Genomic regions > 200kb
Results

Categories of candidate variants

<table>
<thead>
<tr>
<th></th>
<th>Sheep (%)</th>
<th>Goats (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Missense</td>
<td>0.2</td>
<td>0.01</td>
</tr>
<tr>
<td>Synonymous</td>
<td>0.4</td>
<td>0</td>
</tr>
<tr>
<td>Intron</td>
<td>27.5</td>
<td>25.5</td>
</tr>
<tr>
<td>5’ UTR</td>
<td>0.1</td>
<td>0.2</td>
</tr>
<tr>
<td>3’ UTR</td>
<td>0.3</td>
<td>0.9</td>
</tr>
<tr>
<td>Downstream</td>
<td>4.6</td>
<td>3.0</td>
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<tr>
<td>Upstream</td>
<td>3.8</td>
<td>3.9</td>
</tr>
<tr>
<td>Inter-genic</td>
<td>60.6</td>
<td>66.3</td>
</tr>
</tbody>
</table>

- Missense candidate variants < 0.2%
- High proportion of non-coding candidate variants
- High regulatory effect in adaptive mechanisms (c.f. Dunham et al. 2012, Nature)?
- hitch-hiking?
Results

Candidate variants and genes

Differentiation across environmental gradients

e.g. Altitude

id1  id2

id1  id2

id1  id2

Fst

Environmental gradient
Results

Candidate variants and genes

Candidate variants

Altitude (m) vs. Fst

Sheep
Results

Candidate variants and genes

Candidate variants

Sheep Rainfall in April

Rainfall (mm)
• 26 outlier variants in goats and 20 variants in sheep at less than 100 kb
• One common genomic region
• One common gene associated to sunshine duration on December 21\textsuperscript{st} (CA2)
Results

Congruence of selection signatures

Candidate genomic regions for sunshine duration

Sheep karyotype
Results

Congruence of selection signatures

Distinguished adaptive mechanisms to local environments between sheep and goats
## Results

### Congruence of selection signatures

**Top candidate genes associated with the higher differentiation scores**

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<tr>
<td>GMDS</td>
<td>Downstream</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>Intron</td>
<td>71</td>
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<tr>
<td>MCM3</td>
<td>Downstream</td>
<td>2</td>
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<tr>
<td></td>
<td>Intron</td>
<td>22</td>
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<tr>
<td></td>
<td>Splice region/intron</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Synonymous</td>
<td>4</td>
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<td>OXR1</td>
<td>Intron</td>
<td>73</td>
</tr>
<tr>
<td>NFIB</td>
<td>Downstream</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Intron</td>
<td>10</td>
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### Results

**Congruence of selection signatures**

#### Top candidate genes associated with the higher differentiation scores

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Genes involved in the same biological pathway?
Divergent adaptation?

Adaptive trait 1
Gene or pool of genes 1
Goats

Adaptive trait 2
Gene or pool of genes 2
Sheep

Adaptive convergence

Highlights ...
Divergent adaptation?

Adaptive trait 1
Gene or pool of genes 1

Adaptive trait 2
Gene or pool of genes 2

MCM3, EPAS1 (hemoglobin?)

Adaptation

Gene 1

Adaptive trait

Gene 2

Sheep

Goats

Sheep

Humans

Regulation
Highlights ...

Adaptive convergence

Divergent adaptation?

- Adaptive trait 1
  - Gene or pool of genes 1
- Adaptive trait 2
  - Gene or pool of genes 2

MCM3, EPAS1 (hemoglobin?)

- Adaptation
- Adaptive trait
  - Gene 1
  - Regulation
  - Gene 2

CA2 (Sunshine)

- Adaptation
- Adaptive trait
  - Gene
  - Sheep
  - Goats
• Landscape genomics applied to whole genome re-sequencing data allows identifying several sets of candidate variants, genes and biological processes that are likely involved in local adaptation to various eco-climatic conditions

• Whole landscape genomics allow illustrating the variation of genetic differentiation over environmental gradients according to several different patterns

• Different adaptive mechanisms to similar environments in sheep and goats … Differences with domestication processes (cf. François Pompanon talk)
Aknowledgements

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Thanks !!!

Sheep and goats in Imilchil region, Morocco (Altitude~2300m)