Accelerating genetic rescue using genomic data

Mike Bruford, Cardiff University
If genetic rescue is such a good thing – why isn’t everybody doing it??
"However, much work is still needed to accurately predict the outcome of translocations, especially those between adaptively and/or genetically divergent populations."
"Two wolves are simply too few to rescue this way, and for that matter, three wolves probably weren’t enough either. For genetic rescue to have had a chance, the park service would have had to act three, four or even five years ago, when the population started its current plunge toward extinction, and maybe try it more than once..."
Draft Environmental Impact Statement to Address the Presence of Wolves

Comments can be made by clicking on the "Comment Now" button on the left side of this page. You may also mail or hand-deliver your written comments to Superintendent Phyllis Green, Isle Royale National Park, ISRO Wolves, 830 East Lakeshore Drive, Houghton, Michigan 49931-1896.

Comment Period: 12/18/2016 - 03/15/2017
Comment period closes in 9 Days, 19 Hours, 11 Min.

Table E81: Summary of Alternative Elements

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<tbody>
<tr>
<td>NPS Wolf Introduction</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Could Occur</td>
<td></td>
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<tr>
<td>Timing of Release</td>
<td>Not applicable</td>
<td>Starting immediately, completed within five years.</td>
<td>Starting immediately, supplemented as needed.</td>
<td>Introduction would not begin immediately, but may take place based on mouse population metrics and other ecological factors.</td>
</tr>
<tr>
<td>Number/Duration of Releases</td>
<td>Not applicable</td>
<td>One release event, lasting up to three to five years.</td>
<td>Multiple release events could take place over the 20-year life of the plan.</td>
<td>Once metrics for introduction are met, same as alternative C.</td>
</tr>
<tr>
<td>Number of Founding Wolves</td>
<td>Not applicable</td>
<td>20-30 wolves selected to maximize genetic diversity and initial predation rates.</td>
<td>6-15 wolves including pairs or packs.</td>
<td>Once metrics for introduction are met, same as alternative C.</td>
</tr>
</tbody>
</table>

Document Content:

- DEIS to Address the Presence of Wolves Isle Royale National Park.pdf (4.7 MB, PDF file)
- ISRO Subject Matter Expert Compiled Questionnaire.pdf (720.6 KB, PDF file)
- Public Review Banner ISRO Wolves.pdf (15.1 MB, PDF file)
- 2017-02-16 Webinar DEIS to Address the Presence of Wolves Isle Royale NP.mp4 (78.9 MB, mp4 file)
- 2017-02-21 Webinar DEIS to Address the Presence of Wolves Isle Royale NP.mp4 (80.2 MB, mp4 file)

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Note: Some of the files may be in PDF format and can be viewed using the Adobe Acrobat Reader software.
You may download a free copy of Acrobat Reader from Adobe Systems.
The recent rise of ‘evolutionary rescue’ – and an increased role for genomics??
57% of loci found in frequencies not consistent with neutral expectation...

Most common: elevated homozygosity, indicating directional selection...
Can AdI accelerate evolutionary rescue? And if so, over what timescales?

(i) maladaptation results in extirpation once populations fall below an extinction threshold (light grey),
(ii) maladaptation followed by evolutionary rescue from standing genetic variation (grey),
(iii) AdI reduces the consequences of maladaptation and enables rapid population growth (black). *indicates the point at which interspecific gene flow is introduced

Sarda Sheep

- 5M domestic sheep in Sardinia
- Raised for milk and lambs
- >15,000t of Pecorino cheese exported 2010

European Mouflon

- Almost 6,000 feral mouflon in Sardinia
- 1,000 animals confined in fenced areas
- Protected species

Adaptive introgression in European sheep: a landscape component?

Mario Barbato
- 92 mouflon from 8 European populations,
- 330 sheep from adjacent locations,
- Illumina 50K SNP array (26 Chr; pruned to avoid ascertainment bias)
- Structure, Admixture, local (genomic) ancestry
- GO analysis of SNPs

Mouflon have lower diversity
Msar3 highest admix
TREEMIX analysis: models the relationship with ancestor using genome-wide allele frequency data accounting for drift. $f$ index quantifies the contribution of each migration vector added to the tree.

Vectors 1-3 denote gene flow from domestic sheep into mouflon on Sardinia, Iran and Cyprus

Vector 4 connects Sardinian mouflon to Sardinian domestic sheep breeds (SAR and SAB), indicating bidirectional gene flow.
But where (in the genome) did the admixture occur?

And how to distinguish from selection?

Recent – large blocks no selection signature

Ancient – localised selection signatures

30% of genome assigned to sheep
Managing introgression in endangered species in a genome-informed way...

~2,000 extant from a founding population of 12 wild indivs and up to four horses.

Complete genomes of 11 individuals, inc all founding lineages, and five museum specimens dated 1878–1929, including the Holotype, and 21 domestic horse. Monitored the impact of 110 years of captivity

Two management groups – ‘pure’ and ‘hybrid’.

Identification of ancestry informative markers and corrections to the Studbook = framework for evaluating genetic variation in future reintroduced populations.
### Genome Diversity

**DIVERSITY**

- **PH**: 0.39–0.59 heterozygous sites/kb
- **DH**: 0.40–0.98
- **Museum PH**: 0.74–2.35

### Runs of Homozygosity (Inbreeding % coverage)

- **PH**: 0.052–0.388
- **DH**: 0.006–0.285

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Figure 3. Heterozygosity and Inbreeding Estimates

(A) Average genome-wide heterozygosity for autosomes, disregarding transitions.

(B) FstH inbreeding coefficient and inbreeding coverage across modern and historical PHs and DHs. X Y-coordinates are not estimated.
**ADMIXTURE – A**
Reddest – DH
Greyest – PH

**ANCESTRY – B**
Reddest: highest levels of horse admixture
Light grey: lowest

Admixture mapping to Chr 5 (LAMP) – C
PH: Grey sections
DH: Red sections

Two groups: 10-19% and 24-31%

Overall, these results confirm the DH introgression depicted in the International Studbook, with individuals tested for the A line (SB159, SB274, SB293, and SB533) considered as the pedigree’s purest line, ..being.. virtually devoid of admixture
Implications

• A new approach?

• Populations can now be managed free of typological concepts of (here ‘A’ or ‘B’), but by using genome data in combination with studbooks and phenotypes..

• Annotated genomes provide the ability to detect and prioritise admixture management for identified GOs, genes and individual SNPs..

• What might a breeding program using such data look like?
Admixture management

• EG if we prioritise ‘purity’:
  • Could aim to maximise *valuable* adaptive introgression while minimising introgression overall
  • ..where perhaps just a few segments contain identified valuable fitness alleles...

• Possibilities and limits to this approach?
1. Let Natural selection take its course
   - Slow, especially on a conservation timescale..
   - Drift might bring maladaptive alleles to high frequency by chance..
   - BUT, unknown beneficial alleles may be maintained..

2. Artificial selection for selected quantitative traits
   - Accelerates the spread of amenable (high heritability) traits
   - Not so good for polygenic, low Heritability traits and does not address genome-wide
     (demographically mediated) introgression

3. Marker-assisted selection
   - Uses functional polymorphism(s) or LD data: breeding individuals with the best allelic combination
     across the genome
   - Efficiency depends on the number of unlinked adaptive genes, and how on recent the introgression
     occurred..

Approach 3 should be the fastest, but would also likely result in a more rapid decline in effective size than Approach 2,
which may not be consistent with other conservation goals.
To optimise the approach we need to be very clear of the intended goals...

Figure 3. Integration of phenotypic and molecular data on polygenic and monogenic traits, including data on direct (D), linkage disequilibrium (LD), and linkage equilibrium (LE) markers, in a selection program that will meet business goals, using analysis tools to estimate breeding values (EBV), molecular scores, and genotypes (or genotype probabilities). Solid and broken arrows indicate the flow of information for polygenic and monogenic traits, respectively.


Mainly considered in an animal and plant breeding context...
Harrisson et al 2014 (Evol Apps)

Approaches and predictions using genome-wide versus candidate variation in model, commercial and conservation species..

Sheep

Panda
Perspective

• Evolutionary rescue and consideration of adaptive introgression are areas that can add value to genetic rescue

• However, more work needs to be done to develop a predictive framework for how it might be implemented

• The balance between locus-specific and genome-wide diversity is dynamic

• ..and selection based on a few ‘key’ traits may result in too great a loss of diversity (low $N_e$)

• ..But may be beneficial under certain circumstances where selection pressures are highly directive and/or predictable..

• And we need much more data on genomic architecture of key conservation traits..!
Thanks

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Pierangela Cabras
Monica Pirastru