# Signatures of historical selection in Moor frog (Rana arvalis)

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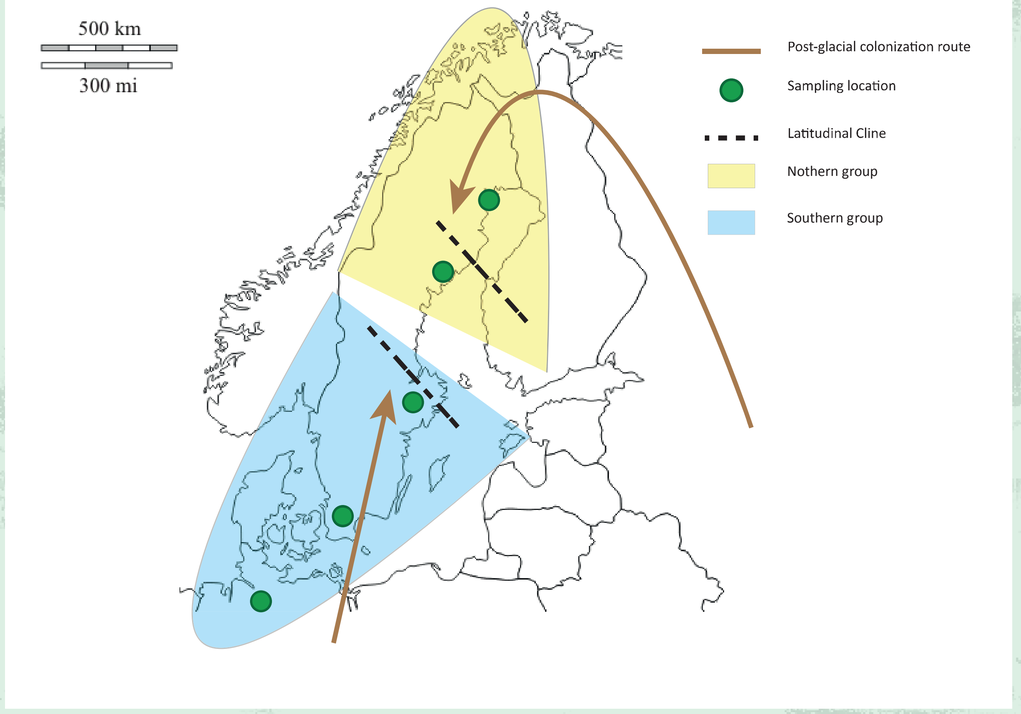
## 1. BACKGROUND

MHC genes are key components in disease resistance and a useful study system for selective pressures acting on genetic variation in natural populations. Patterns of genetic variation observed at MHC genes are likely to be influenced by past and on-going selection as well as demographic fluctuations in population size such as those imposed by post-glacial recolonization processes. In Scandinavian moor frogs, genetic variation at the MHC class II exon 2 is shaped by a complex pattern of past and on-going selection, drift and/or historical demographic events like post-glacial recolonization history since the last glaciation (Cortazar-Chinarro et al. 2017). Here, we investigated signatures of historical selection and demography on a MHC class II gene along a dual post-glacial recolonization route in twelve separated in two subgroups (north group and south group) of moor frog populations along a 1700 km latitudinal gradient




## 2. STUDY AIM

1.Characterize MHC II exon 2 variation in the moor frog Rana arvalis.

2. investigate which mechanisms underlie the historical formation and maintenance of MHC II exon 2 gene variation along this two post-glacial colonization routes.

## 3. METHODS

MHC class II exon 2 sequences were obtained from 204 R. arvalis individuals throught Illumina sequencing (Miseq) and consecutively assigned into two different subgroups (a northern and southern group, respectively) in concordance with findings from a previously described post-glacial colonization route.

## 4. RESULTS

### Sequence variation and phylogenetic reconstruction

| | N | A | Ap | S | AR | $H_o$ | $H_e$ | $F_{IS}$ | k | π | Tajima´s D |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **All Gradient** | 207 | 57 | | 31 | 38 | 0.561* | 0.762 | 0.264 | 10.731 | 0.039 | 1.007 |
| **Northern Cluster** | 77 | 14 | 6 | 19 | 6 | 0.470 | 0.544 | 0.136 | 4.407 | 0.016 | -1.251 |
| **Southern Cluster** | 130 | 47 | 30 | 31 | 12 | 0.613* | 0.806 | 0.239 | 11.739 | 0.043 | 1.289 |

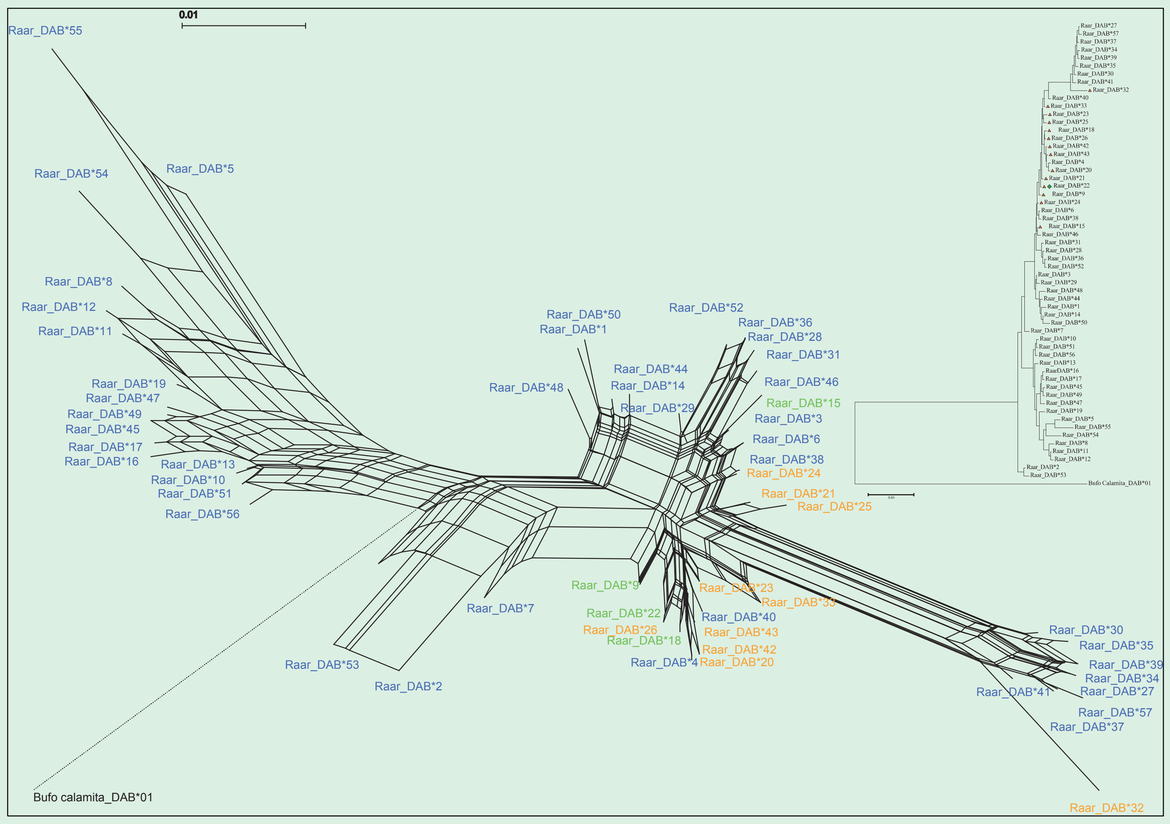
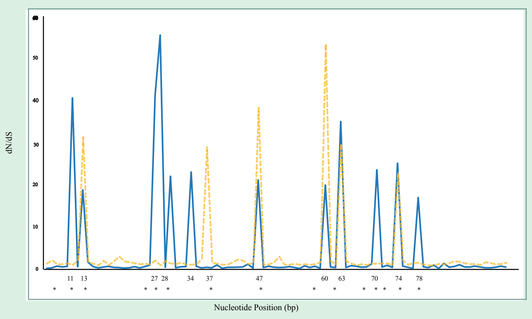



Table above. Genetic diversity measures. Number of individuals (N), number of alleles (A), number of private alleles (Ap), number of segregating sites (s),allelic richness (AR), Observed heterozygosity (Ho), expcted heterozygosity (He), inbreeding coefficient (FIS), average pairwise differences (k), nucleotide diversity ( ), neutrality test summary (Tajima´s D). Significant values (p<0.001) are marked with a *.
Figure below. Neighbour network for MHC II exon 2. 272 moor frog nucleotide sequences of exon 2 are represented in blue (southern cluster), in orange (northern cluster) and in green for the sequences shared between northern and southern cluster. A natterjack toad sequence [Genbank HQ388291.1] from MHC II exon 2 was used as an outgroup

### Selection Analyses

| | dN | dS | dN/dS | (Z) | P | Positively selected codons in Omegamap | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **All Gradient** | | | | | | | | | | | | | | | |
| **PBS** | 0.159 | 0.040 | 3.975 | 3.894 | 0.000 | **11** | **13** | **27** | **28** | **37** | **47** | **60** | **63** | **70** | **74** | **78** |
| **non PBS** | 0.013 | 0.023 | 0.565 | 0.918 | 0.354 | | | | | | | | | | | |
| **all** | 0.043 | 0.027 | 1.592 | 1.33 | 0.183 | | | | | | | | | | | |
| **Nothern Cluster** | | | | | | | | | | | | | | | |
| **PBS** | 0.066 | 0.013 | 5.076 | 2.672 | 0.004 | | | | | | | | | | | |
| **non PBS** | 0.007 | 0.005 | 1.400 | 0.314 | 0.485 | | X | | | X | X | X | X | | X | |
| **all** | 0.019 | 0.006 | 3.166 | 2.144 | 0.017 | | | | | | | | | | | |
| **Southern Cluster** | | | | | | | | | | | | | | | |
| **PBS** | 0.170 | 0.047 | 3.617 | 3.621 | 0.000 | | | | | | | | | | | |
| **non PBS** | 0.014 | 0.028 | 0.5 | 0. 105 | 0.296 | X | X | X | X | | X | X | X | X | X | X |
| **all** | 0.047 | 0.032 | 1.468 | 1.075 | 0.285 | | | | | | | | | | | |
| Distance to Bondinas PBRs | | | | | | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 2 | 0 | 0 | 0 |

Relative rates of non-synonymous (dN) and synonymous (dS) substitutions, the peptide binding region (PBR) and non-PBR according to Bondinas et al. 2007. Significant Positively selective codons have been calculated using Omegmap (Wilson and McVean 2006) and are marked with an X, the numbers represent the amino acid position in the MHC class II molecule.




Sliding window dN/dS, for the 272 bp exon 2 fragments of the MHC II exon 2 (window size 5b, step size 15) in orange for the northern group and in blue for the southern group. PBR position from Bondinas et al. 2007 are represented with a star below the x axes

## 5. DISCUSSION

The results of the current study suggest that selection patterns differ from northern and southern subgroups in R. arvalis. The MHC class II exon 2 have fewer sites subject to positive selection in northern populations compared to southern populations. We believe that the differential selection patterns observed in our study could be explained by the historical post-glacial recolonization processes and by the different selective pressures from parasites in the different populations along the present gradient, which should be investigated in more detail in future studies.