Genetics of Leporidae: Phylogeny, diversity, and evolutionary dynamics

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Abstract. The family Leporidae (Lagomorpha) encompasses rabbits and hares with a worldwide distribution and a complex evolutionary history that is not fully captured by morphology alone. Recent advances in molecular systematics, population genomics, and chromosome-scale genome assemblies have substantially improved the resolution of leporid phylogeny, revealing deep divergences shaped by Miocene and later climatic and geological events. Nuclear genomic data consistently outperform mitochondrial markers in resolving higher-level relationships, while also exposing widespread discordance caused by introgressive hybridization. Genetic diversity within Leporidae is strongly influenced by reticulate evolution, with multiple species exhibiting historical and contemporary gene flow that contributes both neutral and adaptive variation. Domestication in rabbits has further reshaped genomic architecture, producing distinct population structure and strong selection signals, including large-effect structural variants with pronounced phenotypic consequences. Immune gene families display exceptional diversity and cases of trans-species polymorphism, indicating long-term maintenance of adaptive alleles under balancing selection. Collectively, these findings underscore that leporid evolution is driven by an interplay of divergence, hybridization, and selection. Integrating phylogenomics, functional genomics, and disease ecology provides a more realistic framework for understanding leporid biodiversity, with direct implications for taxonomy, health, and conservation management.

Key Words: conservation genetics, domestication, genetic diversity, hybridization, immune genes, introgression, phylogenomics, trans-species polymorphism.

Introduction. The family Leporidae (Order Lagomorpha) comprises rabbits, hares, and related species, distributed globally across varied environments (Petrescu-Mag et al 2019). Although they share a superficial similarity, leporids exhibit substantial genetic diversity and evolutionary complexity, with implications for taxonomy, adaptation, health, and conservation (Proorocu et al 2022; Petrescu-Mag 2023ab; Petrescu-Mag & Oroian 2024). Integrating molecular markers, genome assemblies, and population genetics has reshaped our understanding of how genetic variation organizes within and among leporid species. The aim of this study is to synthesize current phylogenetic, genomic, and population-level evidence to clarify the evolutionary relationships, genetic diversity patterns, and underlying evolutionary processes shaping the Leporidae family, with particular emphasis on hybridization, domestication, and adaptive genetic variation.

Phylogeny and Evolutionary History. Reconstructing robust phylogenies in Leporidae has historically been challenging due to rapid radiations and limited resolution from single genetic loci. Comprehensive molecular supermatrix analyses combining nuclear and mitochondrial genes have significantly improved phylogenetic inference across all eleven genera of Leporidae. Combined nuclear DNA topologies yield far greater resolution than mtDNA alone and clarify relationships among deep nodes in the leporid tree, highlighting evolutionary divergence events likely tied to geological and climatic changes in the Miocene and later periods (Matthee et al 2004).

Recent chromosome-scale assemblies, such as that of *Lepus oiostolus*, provide foundational resources for genome-wide studies of leporid evolution and adaptation. High-quality assemblies allow for identification of structural variants, syntenic relationships, and comparative genomic analyses across leporid species, improving evolutionary frameworks (Feng et al 2024).

Genetic Diversity, Hybridization, and Reticulate Evolution. Leporid speciation is not entirely tree-like: reticulate evolution via introgressive hybridization substantially shapes genetic diversity in several species groups. In Chinese hares (genus *Lepus*), mitochondrial and nuclear loci analyses have shown frequent historical and recent hybridization, resulting in extensive mtDNA introgression and shared nuclear haplotypes across nominal species. This reticulate genetic framework contributes to taxonomic ambiguity and suggests that gene flow has been a recurring evolutionary force (Liu et al 2011).

Functional genetic introgression also occurs beyond neutral variation: for example, brown hares (*Lepus europaeus*) hybridizing with mountain hares (*L. timidus*) can acquire alleles linked to thermoregulation and immune function (Figure 1). Certain introgressed alleles appear to confer adaptive benefits, such as enhanced cold tolerance or immune variation, demonstrating that hybridization can contribute actionable functional diversity in natural populations (Pohjoismäki et al 2021).

Genetic Architecture of Domestication and Breed Traits. Domestication has had marked effects on rabbit genomes. Comparative whole-genome sequencing of wild and domestic rabbit breeds reveals population substructure, selective sweep signatures, and genetic differentiation associated with domestication and breed formation. These studies highlight both breed-specific alleles and broader patterns of selection on loci linked to growth, reproduction, and morphology (Fekete et al 2025).

A well-characterized example from classical genetics concerns a mutation in HMGA2, a gene associated with body size regulation. A ~12.1 kb deletion that disrupts the HMGA2 gene causes dwarfism in domestic rabbits, with homozygotes showing lethal underdevelopment and heterozygotes manifesting reduced size, illustrating the dramatic phenotypic effects of a single structural variant in mammals (Carneiro et al 2017).

Immune Gene Diversity and Trans-Species Polymorphism. Genetic diversity in immune system genes provides insights into both species history and pathogen co-evolution. Investigations into immunoglobulin (Ig) genes across leporids show complex diversity patterns in IgM and IgE, with distinct lineage-specific residues and varying levels of nucleotide diversity across genera and subspecies. These patterns reflect long-standing evolutionary divergence as well as adaptive responses to diverse pathogen pressures (Pinheiro et al 2019).

Moreover, studies of IgA repertoires across hares and rabbits reveal cases of trans-species polymorphism, where allelic lineages pre-date species divergence. This phenomenon indicates that some immune gene variants have been maintained across speciation events, presumably under balancing selection due to their adaptive value in host–pathogen interactions (Pinheiro et al 2023).

Implications for Health, Disease, and Conservation. Genetic research in Leporidae extends into pathogen susceptibility and disease ecology. For example, herpesvirus diversity in leporids is emerging as a significant area of study, with novel gammaherpesviruses identified across multiple lagomorph species. Although the direct functional impact on host genetics is under investigation, the presence of diverse viral lineages underscores the importance of genomic surveillance in disease management and conservation (Matos et al 2025).

Understanding genetic structure also informs conservation: accurate phylogeny and knowledge of hybrid zones enhance taxonomic clarity, essential when defining conservation units, especially for threatened species with overlapping ranges or hybrid ancestry.

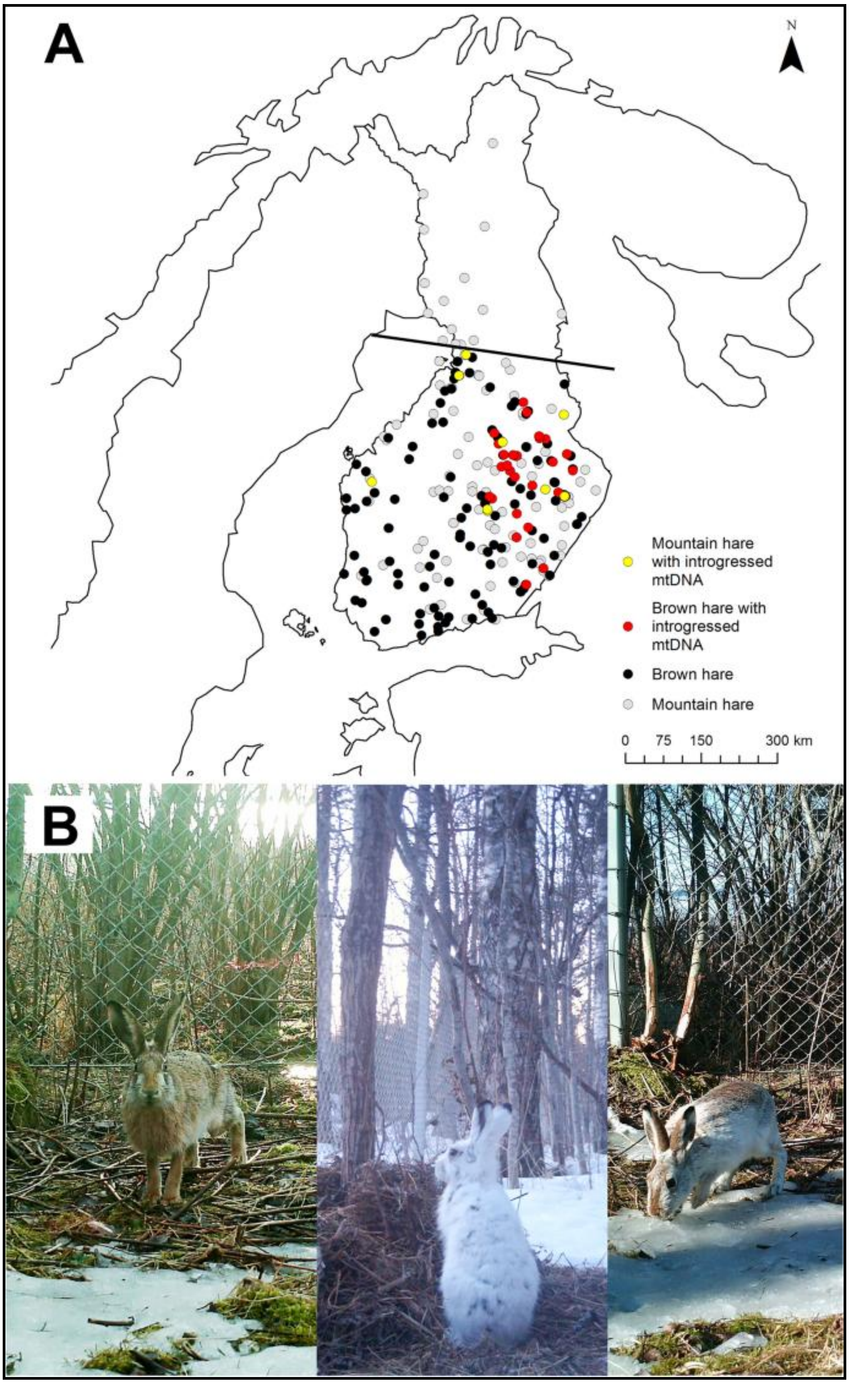

Figure 1. Hybridization among Finnish hares. (A) Distribution of samples used in the study. The level of mtDNA introgression roughly correlates with the expansion front of the brown hare (Levanen et al 2018). The allopatric mountain hare samples north from the line were assumed as "purebred" for the purpose of the TSP analyses (Levanen et al 2018; Pohjoismäki et al 2021). Both species coexist south of the line, although mountain hare abundance decreases notably towards the south-west. (B) Excerpts from game camera images from the same location in Joensuu, Finland in April 2014. Typical brown hare in the left and mountain hare in the middle. Individual on the right was later captured and confirmed as a first-generation hybrid, having brown hare mtDNA, but being heterozygous for the tested nuclear loci. The individual was originally assigned as a brown hare based on morphology and mtDNA genotype (source: Pohjoismäki et al 2021).

Conclusions and Future Directions. Advances in genomic technologies are rapidly refining our understanding of Leporidae genetics, revealing:

- Deep phylogenetic structure anchored by nuclear genomic data;
- Reticulate evolutionary histories with frequent hybridization and adaptive introgression;
- Genetic variants with functional phenotypic impacts, from body size to immunity;
- Trans-species polymorphisms indicating ancient maintenance of adaptive gene lineages.

Future research integrating whole-genome population sampling, functional genomics, and disease ecology promises to further elucidate the roles of selection, drift, and demography in shaping leporid genomes, with direct relevance to evolutionary biology, veterinary health, and species conservation.

Conflict of Interest. The authors declare that there is no conflict of interest.

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