Review

Mini-Review: Convergent Evolutionary Mechanisms of Pulmonary Adaptation to Hypoxia and Fibrosis in High-Altitude and Marine Mammals

Boxiong Guo and Wenhua Ren *

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Mini-Review: Convergent Evolutionary Mechanisms of Pulmonary Adaptation to Hypoxia and Fibrosis in High-Altitude and Marine Mammals

Bo-Xiong Guo [1,2] and Wen-Hua Ren [1,*]

[1] Jiangsu Key Laboratory for Biodiversity and Biotechnology, College of Life Sciences, Nanjing Normal University, Nanjing, Jiangsu, China

[2] Institute of Entomology, College of Life Sciences, Nankai University, Tianjin, 300071 China

* Correspondence: 08162@njnu.edu.cn

Abstract

High-altitude and marine mammals inhabit vastly different ecosystems yet share the selective pressure of chronic hypoxia. Convergent evolutionary adaptations, particularly in pulmonary architecture with increased elastic fibers, facilitate efficient oxygen use under hypoxia. This review synthesizes molecular insights into these adaptations, highlighting gene family dynamics, positive selection, and convergent amino acid substitutions. The findings from comparative genomic studies offer valuable insights for human pulmonary fibrosis research.

Keywords: convergent evolution; pulmonary fibrosis; hypoxia; high-altitude mammals; marine mammals; gene families; positive selection; elastic fibers

Introduction

Hypoxia imposes severe selective pressures, driving convergent evolution among mammals in high-altitude and marine habitats. Despite differing environments, these mammals exhibit parallel adaptations, particularly in lung structure and function, essential for survival in low-oxygen conditions[1–4] (see Figure 1)."

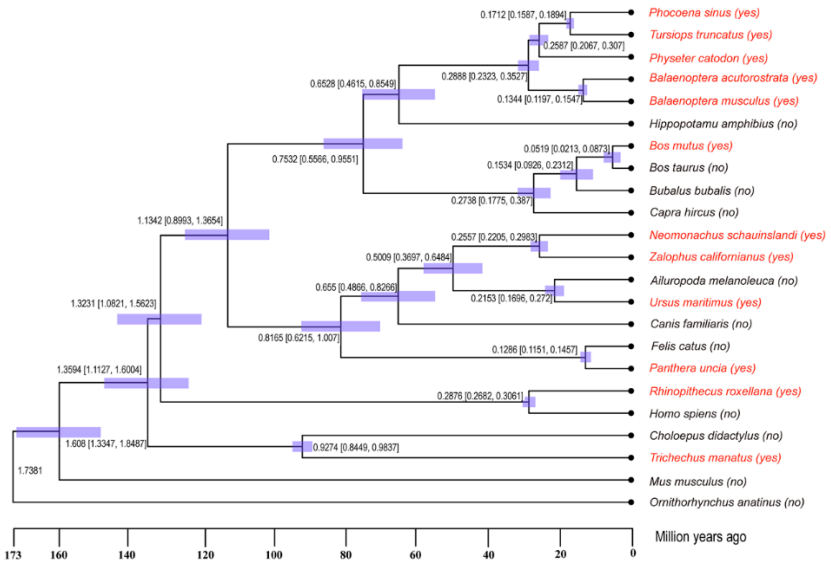

Figure 1. Phylogenetic tree and divergence times based on fourfold degenerate sites of 5,243 one-to-one orthologous genes. Red font and "yes" represent species living in low-oxygen environments; black font and "no" represent closely related species. Adapted from the original article[11].

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Phenotypic Adaptations: Pulmonary Elasticity

Enhanced pulmonary elasticity, characterized by abundant elastic fibers, represents a critical adaptation. High-altitude mammals such as wild yaks and Xizang antelopes exhibit extensive elastic fibers in their alveolar septa, optimizing gas exchange efficiency[5-7]. Marine mammals, including whales and seals, similarly possess elastic-rich alveolar walls enabling lung collapse during deep dives, mitigating decompression sickness risks[8].

Gene Family Expansion and Contraction

Comparative genomic analyses reveal significant expansions and contractions of gene families involved in cell morphogenesis, protein folding, and stress responses (see Figure 2). Notably, contractions in the keratin gene family are consistently observed, correlating with increased pulmonary elasticity and reduced fibrosis susceptibility[9].

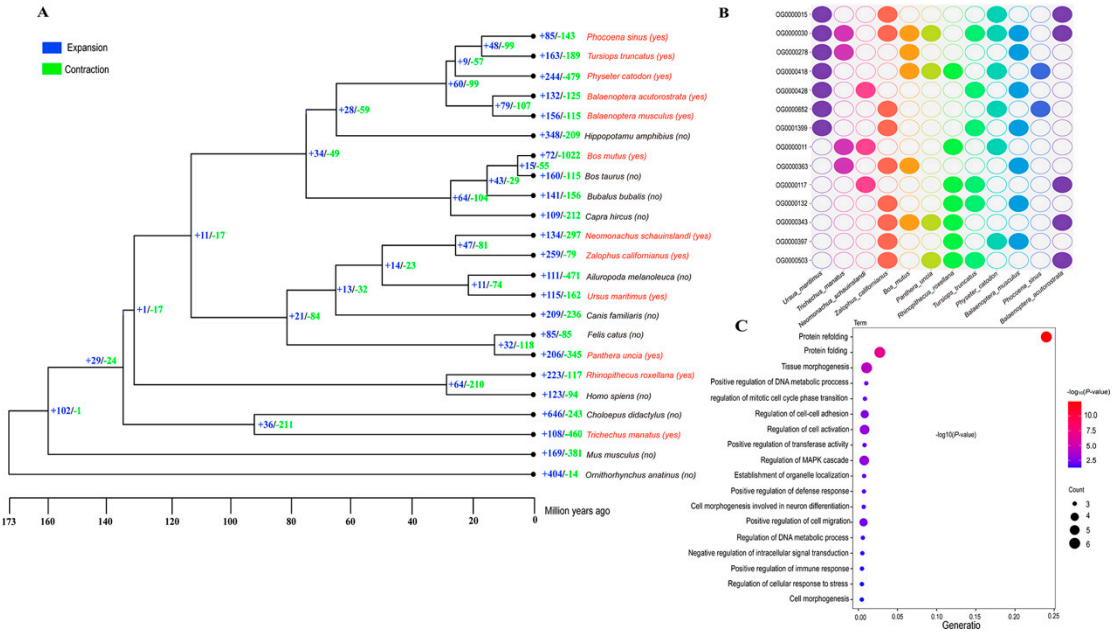

Figure 2. Gene family expansion and contraction in 23 mammalian species. (A) Phylogenetic tree showing expansions (blue) and contractions (green). (B) Significant gene family expansions in hypoxia-tolerant mammals. (C) Functional annotation of significantly expanded gene families. Adapted from original article[11].

Genes Under Positive Selection and Accelerated Evolution

Genes undergoing positive selection and accelerated evolution, such as ZFP36L1, FN1, and NEDD9, are critical to pulmonary fibrosis pathways and lung morphogenesis. These genetic modifications are instrumental in developing enhanced elastic fiber networks crucial for pulmonary adaptation to chronic hypoxia[10].

Convergent Amino Acid Substitutions

Convergent amino acid substitutions, exemplified by the leucine-to-isoleucine mutation in the SLC26A3 gene, influence pulmonary cellular adhesion and vascular development. These changes likely contribute to improved pulmonary functionality under prolonged hypoxic stress[11].

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Convergent Gene Loss

Gene loss analyses reveal convergent pseudogenization of CFAP47, vital in sperm morphology, in hypoxia-tolerant mammals. This relaxation in selective pressure highlights indirect reproductive adaptations potentially related to hypoxia tolerance mechanisms (see Figure 3).

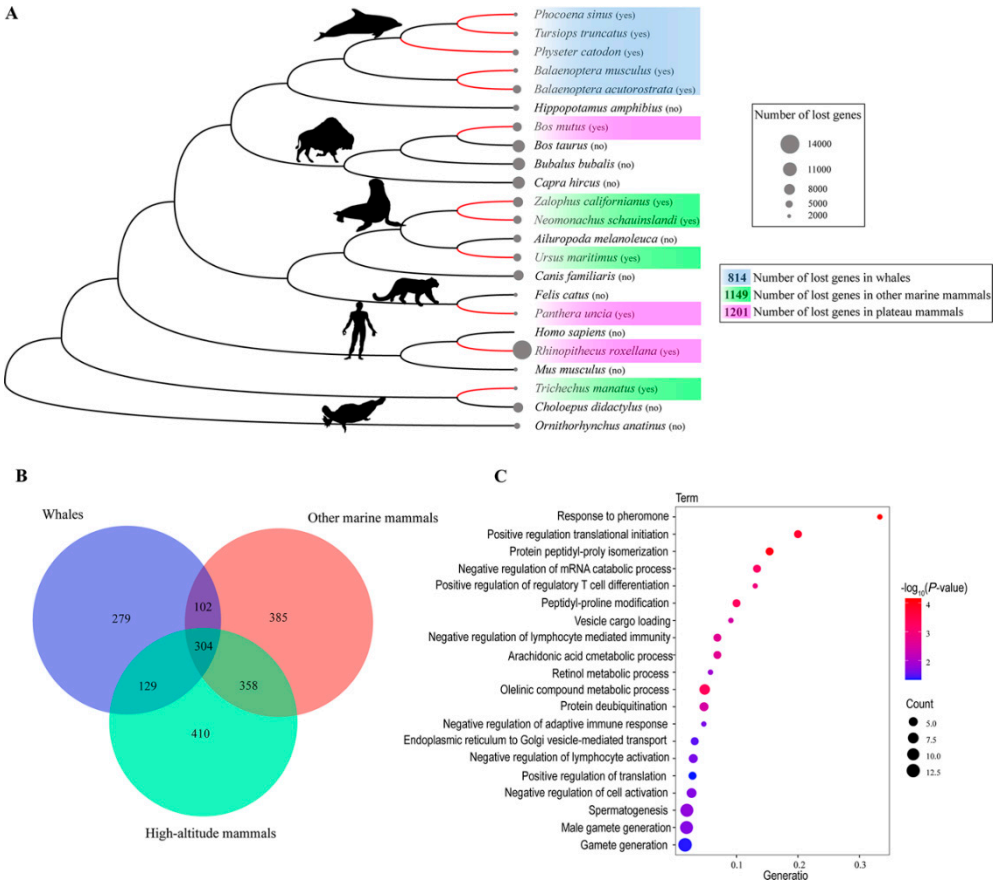

Figure 3. Convergent gene loss and GO term enrichment analysis in whales, marine mammals, and high-altitude mammals. (A) Numbers of gene losses by lineage. (B) Venn diagram of commonly lost genes. (C) GO term enrichment of lost genes. Adapted from original article[11].

Implications for Human Health

These evolutionary insights offer novel perspectives on human pulmonary disorders such as pulmonary fibrosis. In addition to the structural and genomic adaptations discussed above, recent advances in transcriptomic and multi-omics studies have highlighted the importance of regulatory networks—especially those involving non-coding RNAs—in pulmonary fibrosis and hypoxic adaptation. For example, competing endogenous RNA (ceRNA) networks and cross-talks among RNAs play crucial roles in regulating lung tissue remodeling, fibrosis, and cell survival under hypoxic stress, as shown in integrative studies of lung adenocarcinoma and other disease models[12,13]. Identifying these molecular pathways from comparative genomics and network-based research can inform new therapeutic strategies for managing human pulmonary fibrosis and related diseases.

Conclusion and Future Directions

Convergent pulmonary adaptations in hypoxia-adapted mammals involve complex genetic and molecular modifications, notably in lung elasticity and structure. Future studies focusing on functional validations and translational applications could significantly advance treatments for human pulmonary diseases.

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