Porcine Research

Genetic basis of dwarfism in pigs (dwarf and miniature pigs)

[1]Zsolt A. Grabán, [2]Florin D. Bora, [3]Adela M. Dăescu

[1] National Association of Pigeon and Small Animal Breeders of Hungary, Budapest, Hungary; [2] Viticulture and Oenology Department, Advanced Horticultural Research Institute of Transylvania, Faculty of Horticulture and Business for Rural Development, University of Agricultural Sciences and Veterinary Medicine Cluj-Napoca, Cluj-Napoca, Romania; [3] Department of Cell Biology, Histology and Embryology, Faculty of Veterinary Medicine, University of Agricultural Sciences and Veterinary Medicine Cluj-Napoca, Cluj-Napoca, Romania. Corresponding author: A. M. Dăescu, adela.daescu@usamvcluj.ro

Abstract. Dwarf and miniature pigs exhibit a marked reduction in body mass, approximately one order of magnitude compared with commercial breeds, primarily due to artificial selection and, in some cases, pathogenic mutations. Current evidence supports a predominantly polygenic architecture underlying this phenotype, involving both regulatory and coding variation across growth, endocrine, and skeletal pathways. Comparative genomic analyses reveal convergent miniaturization across breeds driven by distinct selection signatures, with recurrent involvement of genes such as PLAG1, CHM, and ESR1. Central to growth regulation is the GH–GHR–IGF1 axis, where both major mutations and subtle regulatory variants contribute to dwarf phenotypes. Functional studies, including CRISPR-mediated knockouts and promoter-specific disruptions, demonstrate that impaired growth hormone receptor (GHR) signaling leads to reduced IGF1 levels and severe postnatal growth restriction. In parallel, structural variation, particularly copy number variation (CNV), adds an additional layer of complexity, with shared and region-specific, copy number variation region (CNVR) influencing growth, metabolism, and physiological adaptation. Integration with broader livestock and developmental biology research highlights conserved pathways, including Insulin/IGF, MAPK, TOR, Hippo, and JNK signaling, as central regulators of body size. Overall, porcine dwarfism and miniaturization emerge as outcomes of multilayered genetic modulation, combining polygenic selection, endocrine regulation, and structural genomic variation.
Keywords: porcine dwarfism, polygenic architecture, GH–IGF axis, copy number variation, convergent evolution, body size genetics.

Introduction. Dwarf and miniature pigs show body mass reductions of roughly one order of magnitude compared with large commercial breeds, arising mainly from artificial selection for small size and, in some cases, clearly pathogenic mutations (Reimer et al., 2018; Petrescu-Mag et al 2020; Kwon et al., 2024). Current work indicates a predominantly polygenic architecture, with both regulatory and coding variants in growth, endocrine and skeletal pathways contributing to reduced stature rather than a single "dwarfism gene" (Gokhale & Shingleton, 2015; Al-Samerria & Radovick, 2021; Pan et al., 2022; Wang et al., 2022; Kwon et al., 2024).

Aim of the Mini-Review. The aim of this mini-review is to synthesize current genomic, endocrine, and functional evidence underlying dwarfism and miniaturization in pigs. Specifically, it seeks to (i) characterize the polygenic basis of reduced body size across miniature and commercial breeds, (ii) evaluate the central role of the GH–GHR–IGF1 signaling axis in both pathological and naturally selected dwarf phenotypes, and (iii) integrate the contribution of structural genomic variation, including copy number variants, to growth regulation. Additionally, the review aims to contextualize porcine findings within

broader vertebrate and livestock models to highlight conserved molecular pathways controlling body size.

Polygenic Architecture and Convergent Miniaturization. Across 41 breeds (8 minipigs), whole-genome sequencing revealed extensive genomic diversity among minipigs, but convergent dwarfism driven by different selection signatures in each breed (Reimer et al., 2018). Selective sweep and F_ST analyses in minipigs and small Chinese breeds identified hundreds of candidate regions and 180–520+ candidate genes linked to reduced body size, supporting a polygenic model (Gokhale & Shingleton, 2015; Cho et al., 2021; Pan et al., 2022; Kwon et al., 2024). PLAG1, CHM and ESR1 emerged as recurrent candidates for body size regulation that diverge in allele frequency and expression between small and large pigs (Reimer et al., 2018). Comparative work in Xiang pigs identified selection on growth and pituitary–hypothalamic genes (IGF1R, PROP1, TBX19, MSTN) consistent with genetic regulation of small stature (Cho et al., 2021) (Table 1).

Table 1

Major body size–associated loci in miniature vs large pigs

Genetic feature / gene	*Main finding related to size*	*Quantitative effect / evidence*	*References*
X-chromosome sweep (52–61 Mb) incl. AR	Long swept haplotype in Goettingen Minipig associated with smaller adult body length	~3% reduction in adult body length in F2 crossbreds; among largest single QTL known in pigs	Kwon et al., 2024
PLAG1, CHM, ESR1	Shared body-size regulators, differently selected across pig populations	Identified in cross-breed WGS of 41 breeds; highlighted as key "convergent dwarfism" genes	Reimer et al., 2018
280 selective regions (187 genes) in 4 small vs 124 large pigs	Body size determination in Diannan, Bama Xiang, Wuzhishan, Jeju black	47,339,509 SNPs scanned; top 1% F_ST and π-ratio windows define 280 regions; enrichment in PI3K–Akt, HIF-1, AMPK pathways	Pan et al., 2022
386 shared CNVRs among 9 miniature breeds	CNVs affecting height and growth phenotypes across regions	33.6 Mb (1.48% of autosomes); enrichment for body height, BMI, cardiovascular traits	Wang et al., 2022
Region-specific CNVRs	Localized adaptations modulating body size/metabolism	132 (America), 47 (Asia/Oceania), 114 (Europe) unique CNVRs; enrichments in lipid metabolism, cardiovascular and circadian traits, etc.	Wang et al., 2022
142 overlapping selective regions (520 genes) in 4 large vs 4 small Chinese breeds	Network highlights bone and size genes	Key genes: NPR3, TNFSF11, TBC1D7, FGF2, IGF1R, plus novel IKBKB, SFRP1, LRP6, SPRY1	Gokhale & Shingleton, 2015

Note: CNV = copy-number variation; CNVR = copy number variation region; WGS = whole genome sequencing; QTL = quantitative trait locus; SNP = single nucleotide polymorphisms; AMPK = AMP-activated protein kinase; BMI = body mass index.

Endocrine Axis: GH–GHR–IGF1 and Monogenic Dwarf Phenotypes. A central axis in pig growth is growth hormone (GH), growth hormone receptor (GHR), and IGF1/IGF1R signaling. Dwarf or "Laron-like" phenotypes can arise from major mutations in this pathway, while subtler regulatory variation modulates miniaturization.

In Banna miniature pigs, serum IGF-1 levels are significantly lower than in Large White pigs ($p < 0.05$), consistent with impaired GH–IGF signaling (Wu et al., 2025). Sequencing identified three amino-acid substitutions in GH (A9V, R22Q in the signal peptide; S104P in the mature protein) and four mutations in the GHR cytoplasmic domain, proposed to affect downstream signaling (Wu et al., 2025). In a CRISPR GHR-knockout model, pigs completely lacking functional GHR had normal birth weight but by 6 months

showed ≈60% lower body weight than controls, markedly reduced IGF1 and IGFBP3 and elevated GH, mirroring human Laron syndrome (Boegheim et al.,T 2017). These animals also had disproportionately small liver, kidneys and heart, increased total body fat, and altered hepatic STAT5, JAK2 and mTOR signaling (Boegheim et al., 2017).

Functional work on GHR regulation shows that promoter 2, rather than promoter 1, is critical for hepatic GHR and IGF1 expression; pigs with bi-allelic P2 knockout have reduced GHR and IGF1 mRNA, low serum IGF1, high GH and impaired postnatal growth, again linking diminished GHR signaling to dwarf stature (Liao et al., 2022). Earlier endocrine studies confirmed that circulating IGF1 correlates strongly with body size across three pig types differing in growth rate and mature weight, and is decreased by hypophysectomy while increased by exogenous GH (Zhang et al., 2025).

At the receptor level, IGF1R variants modulate cell proliferation and muscle development. Synonymous extracellular-domain haplotypes from large Landrace vs small Bama Xiang pigs were cloned and expressed in skeletal muscle cells; the large-breed haplotype increased IGF1R mRNA expression, Cyclin D1, p-AKT, and MyoD, enhancing proliferation and differentiation relative to the dwarf-breed haplotype (Deng et al., 2011). Common variation in IGF1 regulatory regions also influences growth: a length polymorphism in a poly(dA:dT) tract (-264/-255) acts as a positive regulatory element, with alleles 9T–11T showing significant ($p < 0.01$) differences in IGF1 promoter activity and being associated with days to 115 kg and average daily gain in commercial pigs (Denton, 2025). Together, these data place GH, GHR, IGF1, IGF1R and their regulatory elements at the core of both pathological dwarfism and normal size variation.

Structural and Copy-Number Variation in Dwarf and Miniature Pigs. Beyond single single nucleotide polymorphisms (SNPs), structural variants and copy-number variation (CNV) substantially contribute to body size differentiation. In 36 miniature pigs representing 9 breeds, a multi-tool CNV pipeline detected 34 homozygous CNVs overlapping exons in all samples, suggesting shared roles in "uniform growth patterns" and other core phenotypes, and 386 CNVRs common to all breeds plus 293 region-specific CNVRs (Wang et al., 2022). Enrichment analyses showed that genes within common CNVRs are significantly associated with body height and growth-related traits in mammalian phenotype databases (Wang et al., 2022). Region-specific CNVRs further refined this: American minipigs showed enrichment for metabolic regulation, Asian/Oceanian breeds for immune traits, and European breeds for cardiovascular and circadian functions, implying that regional breeding histories layered metabolic and physiological specializations onto a shared dwarf background (Wang et al., 2022).

High-resolution GWAS and resequencing across commercial and local breeds reinforce a structurally complex architecture. In Yorkshire pigs, single-step GWAS using 784,267 SNPs identified 198 significant SNPs for seven linear body size traits and 11 candidate genes affecting bone growth, nutrient absorption and obesity, with LCORL proposed as a major body size gene (Al-Samerria & Radovick, 2021). Whole-genome resequencing of Min pigs (Hebao, Ermin) revealed strong selection on ITGB1 on chromosome 10 with a striking G/A allele-frequency contrast (G = 52.94%, A = 47.06% in larger Ermin vs G = 0%, A = 100% in smaller Hebao pigs), consistent with a role in lipid metabolism and body size differentiation (Buonomo et al., 1987). In Xiang pigs, 876.7 Gb of resequencing data and 900–3,000+ selective regions (depending on comparator) identified growth genes such as IGF1R and MSTN in selected regions, again supporting convergent selection on shared growth pathways in small-bodied breeds (Cho et al., 2021).

Integration with Broader Livestock and Signaling Pathway Evidence. Comparative livestock genetics shows that dwarfism often results from mutations affecting skeletal matrix proteins or growth signaling. In pigs and cattle, mutations in COL10A1 and COL2A1 cause chondrodysplasia-type dwarfism with structural cartilage disruption, while in other species, GH1, GHR, IHH, RNF11, PRKG2, EVC2, ACAN, SHOX, B4GALT7 and SLC13A1 underlie various proportionate and disproportionate dwarf phenotypes (Berghöfer et al., 2025). Many of these genes converge on central size-control pathways, including Insulin/IGF, MAPK, TOR, Hippo, and JNK signaling, which together regulate growth rate,

growth duration and organ scaling (Liu et al., 2020; Xu et al., 2025). Reviews of IGF/IGF1R pathway disorders in humans and developmental size control emphasize that homozygous loss-of-function mutations in IGF1, IGF1R or downstream signaling components typically produce severe pre- and postnatal growth failure, while hypomorphic or regulatory variants modulate stature within the normal to "miniature" range (Liu et al., 2020; Xu et al., 2025). In pigs, the parallel between GHR-knockout dwarfism, low-IGF Banna miniature pigs, and polygenic selection on IGF1/IGF1R axis genes in small breeds underscores the centrality of this axis to porcine dwarfism and miniaturization (Buonomo et al., 1987; Deng et al., 2011; Gokhale & Shingleton, 2015; Boegheim et al., 2017; Cho et al., 2021; Denton, 2025; Wu et al., 2025; Zhang et al., 2025).

Conclusions. Porcine dwarfism and miniaturization are complex traits arising from the interplay of polygenic selection, endocrine regulation, and structural genomic variation. Rather than being driven by a single causative gene, reduced body size reflects coordinated modulation of multiple pathways, with the GH–GHR–IGF1 axis playing a central and recurring role. Both severe mutations and subtle regulatory variants within this pathway can produce a continuum of phenotypes, from pathological dwarfism to adaptive miniaturization. Convergent evolution across miniature pig breeds further demonstrates that similar phenotypic outcomes can arise through distinct genetic routes, often targeting shared biological pathways. Structural variants, particularly CNVs, contribute additional regulatory flexibility and regional adaptation, reinforcing the multilayered architecture of growth control. Integration with comparative livestock and developmental studies underscores the conservation of key signaling networks governing body size. Collectively, these findings position pigs as a valuable model for understanding the genetic and physiological mechanisms of growth regulation in mammals.

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Authors:
Zsolt Attila Grabán (ZAG), National Association of Pigeon and Small Animal Breeders of Hungary, Budapest, Hungary, 1433 Budapest, Pf. 575, Hungary, e-mail: grabanzsolt@gmail.com
Florin Dumitru Bora (FDB), Viticulture and Oenology Department, Advanced Horticultural Research Institute of Transylvania, Faculty of Horticulture and Business in Rural Development, University of Agricultural Sciences and Veterinary Medicine Cluj-Napoca, 3-5 Calea Mănăştur Street, 400372 Cluj-Napoca, Romania, e-mail: florindumitru.bora@usamvcluj.ro
Adela Maria Dăescu (AMD), Department of Cell Biology, Histology and Embryology, Faculty of Veterinary Medicine, University of Agricultural Sciences and Veterinary Medicine Cluj-Napoca, 3-5 Calea Mănăștur Street, 400372 Cluj-Napoca, Romania, e-mail: adela.daescu@usamvcluj.ro

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