Review

Beyond the Classics: The Synergy of AI and Genomics Reveals A New Army of Pigmentation Genes

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Review

Beyond the Classics: The Synergy of AI and Genomics Reveals A New Army of Pigmentation Genes

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Abstract

Pigmentation has long served as a powerful system for exploring gene–trait relationships, yet much of the field has focused on a relatively narrow group of well-established genes involved in melanin production and pigment cell differentiation. Recent advances, however, have allowed pigmentation to be studied through a more comprehensive framework. By combining artificial intelligence (AI)–driven phenotyping with genomic mapping approaches such as genome-wide association studies, QTL mapping, and structural variant analysis, a broader range of pigmentation regulators has been identified across diverse animal taxa. This review highlights studies where AI methods, including deep learning, self-supervised modeling, and pattern recognition, have been used to quantify complex pigmentation traits in animals. These approaches have enabled the discovery of non-classical pigmentation genes involved in membrane trafficking, intracellular signaling, structural organization, and non-coding regulation. Rather than displacing the classical pigmentation paradigm, these findings extend it, revealing a wider set of genetic contributors to coloration and pattern diversity. We introduce the term *AI-pigmentomics* to describe the integration of AI-driven phenotyping with genomic mapping, as part of the broader emergence of AI-omics. Together, AI and genomic mapping are reshaping our understanding of pigmentation by uncovering unexpected biological mechanisms and providing a framework for investigating pigmentation in both model and non-model species.

Keywords: Pigmentation genetics; Artificial intelligence; Genomic mapping; Non-classical pigmentation genes; Deep learning phenotyping

1. Introduction

The study of pigmentation has provided key insights into developmental genetics, cell differentiation, and evolutionary biology (Hoekstra, 2006; Saunders et al., 2019; Parichy, 2021; Kratochwil and Mallarino, 2023). Historically, most research in this field has been shaped by discoveries in model organisms, particularly those that display variation in melanin-based traits (Mills and Patterson, 2009; Caro and Mallarino, 2020; McNamara et al., 2021). Genes such as MC1R, TYR, ASIP, and OCA2 have been repeatedly identified as major regulators of melanin synthesis and pigment type-switching, forming the foundation of what has often been referred to as the "classical" pigmentation gene set (Gerstenblith et al., 2010; Wakamatsu and Ito, 2021). These genes have explained substantial phenotypic variation in mammals and birds and have been central to understanding the genetic control of coloration over the past several decades (Galván and Solano, 2016; Caro and Mallarino, 2020; Eizirik and Trindade, 2021; Elkin et al., 2023). However, pigmentation systems are far more complex than initially understood, even in well-studied organisms such as

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humans (Martin et al., 2017; Quillen et al., 2019). In many taxa, coloration is determined not only by melanin but also by other pigments such as pteridines, carotenoids, and purines, as well as by structural components like iridophores and reflective crystals (Shawkey and D'Alba, 2017; Toews et al., 2017; Andrade and Carneiro, 2021). In teleost fish, for example, at least five distinct pigment cell types have been described, each with specific pigment content and developmental pathways (Parichy, 2021). Regulators of xanthophore and iridophore differentiation, e.g., *csf1r*, *gch2*, *ltk*, *pnp4a*, and *tfec*, have been studied primarily in zebrafish but remain largely uncharacterized in other species (Irion and Nüsslein-Volhard, 2019; Patterson and Parichy, 2019). Although many of these genes are well described within particular lineages (Baxter et al., 2019), their inclusion in broader pigmentation models has often been limited.

As research has expanded into non-model organisms and more diverse pigmentation systems, the limitations of the classical gene framework have become increasingly apparent (Figon et al., 2021a; Kondo et al., 2021; Vöcking et al., 2022). The use of historically well-known regulatory genes fails to explain a large portion of pigmentation diversity outside of model organisms. A growing number of studies have indicated that genes involved in vesicle trafficking (Ullate-Agote et al., 2020; Liu et al., 2022), membrane transport (Ahi et al., 2020b; Podobnik et al., 2020), organelle-associated signaling (Stuckert et al., 2019; Figon et al., 2021b), cytoskeletal organization (Feiner et al., 2022; Lloyd et al., 2024), epigenomic and epitranscriptomic mechanisms (Strowbridge et al., 2025) and non-coding regulatory functions (Feng et al., 2018; Luo et al., 2019) may play substantial roles in determining pigment cell behavior and spatial patterning. These genes frequently fall outside the melanin biosynthetic pathway yet are consistently implicated in pigmentation phenotypes when higher-resolution phenotyping and broader genomic scans are employed (Baxter et al., 2019). This shift in perspective has been facilitated by the growing use of artificial intelligence and machine learning tools for phenotypic characterization, alongside genome-wide mapping techniques that no longer rely solely on prior knowledge of candidate genes (Karagic and Kratochwil, 2025). As a result, pigmentation genetics is being redefined not by discarding the classical framework but by integrating a wider array of biological mechanisms that govern color and pattern formation across animal taxa. This article focuses on how this integration is being achieved through the combined application of AI-based phenotyping and genomic mapping, and how it is expanding the known landscape of pigmentation genes.

2. From Pattern to Phenotype: How AI is Transforming Pigmentation Trait Analysis

Advances in artificial intelligence have introduced new possibilities for quantifying complex traits in animals, such as pigmentation related traits (Fernandes et al., 2020; Lürig et al., 2021). Traditional approaches to phenotype characterization have relied heavily on manual scoring, categorical classification, or measurements of selected regions of interest (Fernandes et al., 2020). While effective in certain contexts, these methods have often lacked the resolution necessary to capture subtle differences in hue, spatial distribution, pattern complexity, or structural coloration (Hemingson et al., 2024). As a result, large portions of pigmentation variation have remained either unquantified or only coarsely approximated (Butler et al., 2011; Siegenthaler et al., 2017). Recent applications of AI-based tools, particularly deep learning methods, have provided more robust and scalable solutions to these limitations (Wu et al., 2019; Niu et al., 2025).

In several systems, convolutional neural networks (CNNs) have been used to extract detailed features from full-body images, such as in the study of ornamental coloration in male guppies (van der Bijl et al., 2025). In that context, network architectures were trained to quantify only coloration on a global spatial scale with high resolution, which would not be feasible to do manually. Once extracted, the quantitative trait values were used for subsequent genomic association analyses to obtain a spatial map for the genetic control or coloration pattern. Similar techniques have been used in studies of feather pigmentation in ducks and chicks, where region-specific melanin content was quantified using pixel-level segmentation algorithms (Heo et al., 2023; Twumasi et al., 2024; Wang et

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al., 2024). In these cases, traits were defined based on measurable output from image data rather than observer-defined categories, thus improving precision and reproducibility.

Beyond standard CNN applications, other AI frameworks such as self-supervised and metric learning have also been employed (Hoyal Cuthill et al., 2019; Xie et al., 2024). In particular, contrastive learning methods have been used to generate latent phenotypic embeddings from human retinal fundus images, providing continuous, data-driven pigmentation scores that are agnostic to predefined labels (Xie et al., 2024). Triplet networks have similarly been used to compare complex wing pattern geometries in butterflies, enabling fine-scale assessment of morphological similarity between individuals or populations (Hoyal Cuthill et al., 2019). These approaches have not only expanded the phenotypic scope of pigmentation research but have also allowed researchers to revisit older datasets with new analytical depth. Archived images or digital specimens can now be reanalyzed with updated models, facilitating retrospective discoveries and longitudinal analyses (Newell et al., 2021; Rosenberg et al., 2021; Hantak et al., 2022). Moreover, as models are trained on increasingly diverse image sets, their generalizability across taxa and environments is expected to improve (Wu et al., 2019). Despite their promise, AI-based phenotyping methods are not without limitations. Models can be biased by training data, may fail to generalize across lighting conditions or image formats, and require significant computational infrastructure (Fernandes et al., 2020). Nonetheless, their ability to detect complex, non-linear, and spatially distributed traits represents a meaningful advancement in the study of pigmentation. When these tools are applied thoughtfully and validated rigorously, they provide a powerful means to expand the trait space available for genomic investigation.

3. Genomic Mapping Methods and Their Integration with AI-Derived Traits

The identification of pigmentation-associated loci has historically depended on either candidate gene studies or classical genetic crosses, which often required prior assumptions about trait architecture. With the advent of genome-wide association studies (GWAS), it became possible to interrogate genotype–phenotype relationships without limiting the analysis to preselected loci (Gerstenblith et al., 2010; Adhikari et al., 2019; Lona-Durazo et al., 2019). However, the resolution and interpretability of GWAS results have always been constrained by the quality of phenotypic data (Bush et al., 2016; Landi et al., 2020; Kim et al., 2024). As AI-derived traits have grown in both resolution and dimensionality, their integration with genomic mapping has resulted in a substantial improvement in the identification of pigmentation genes, particularly those outside classical biosynthetic pathways (see examples in table 1). In recent studies, AI-extracted phenotypes have been used directly as quantitative traits in GWAS pipelines. For example, high resolution color pattern maps extracted from guppy images using CNNs have been employed to identify both autosomal and Y-linked loci influencing complex ornamental patterns (van der Bijl et al., 2025). In the case of human retinal pigmentation, principal components derived from AI-generated pixel embeddings were used to define quantitative pigmentation traits that revealed multiple novel loci through image-GWAS, including genes involved in membrane function and intracellular transport (Rajesh et al., 2025).

Mapping approaches have also been extended beyond GWAS. In scallops and butterflies, where limited reference genomes or recombination maps can present barriers to fine-scale association, quantitative trait locus (QTL) mapping and bulk-segregant analysis have been paired with AI-based pattern scoring to detect non-classic contributors to shell and wing coloration (Woronik et al., 2019; Mao et al., 2020). Similar approaches have been applied in plants, such as peanut, where image-based phenotyping accelerated QTL mapping and QTL × environment interaction analysis of testa color (Zhang et al., 2021). These include genes involved in structural patterning, chromatin regulation, and non-coding RNAs (Woronik et al., 2019; Mao et al., 2020). Integrative approaches such as eQTL mapping and transcriptome-wide association studies (TWAS) are now increasingly used to connect AI-defined traits to regulatory variation (Ferguson et al., 2021; Jackson et al., 2025). This is particularly relevant for genes with subtle or tissue-specific effects on pigmentation, which may not appear as strong GWAS hits but can influence gene expression in pigment cells (Ioannidis et al., 2018; Zhang et

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al., 2018; Lona-Durazo et al., 2021; Song et al., 2024). Functional studies, including CRISPR-mediated validation, can further confirm these novel associations (Crawford et al., 2017; Choi et al., 2020; Bajpai et al., 2023; Xu et al., 2024). Together, these methods are shifting the discovery paradigm away from reliance on known pathways. AI-derived traits, when combined with flexible and comprehensive genomic mapping strategies, are allowing for the identification of previously unrecognized genes involved in coloration. The result is not just a more complete list of pigmentation loci, but a more nuanced understanding of the regulatory, structural, and developmental processes underlying color and pattern formation.

4. AI–Genomics Approaches Reveal Diverse Pigmentation Mechanisms Across Taxa

The integration of AI-driven phenotyping with genomic mapping has led to the discovery of pigmentation-associated genes that had not been previously implicated in classical pigment pathways (see below). These findings span a wide range of animal taxa and reflect a growing recognition that pigmentation traits are regulated by a broader network of cellular and developmental mechanisms than previously appreciated (Table 1). In this section, representative studies are presented to illustrate how this combined approach has enabled the identification of novel genes in fish, birds, mammals and invertebrates.

In humans, AI-derived retinal pigment scores have enabled image-based GWAS that revealed loci associated with pigmentation variation across the fundus (Rajesh et al., 2025). Among the identified genes were involved in ciliary transport and with less known role in cellular signaling. These genes are not part of traditional pigmentation pathways and suggest that pigmentation phenotypes can be influenced by broader cellular physiology.

In guppies, the use of convolutional neural networks to quantify male ornamental color patterns facilitated a high-resolution GWAS that identified both autosomal and Y-linked loci (van der Bijl et al., 2025). Among these were regions containing genes involved in vesicle trafficking and cell polarity, features not typically associated with pigmentation in vertebrates. These genes may affect pigment deposition indirectly through their influence on pigment cell behavior or the spatial organization of pattern elements.

In domestic ducks, melanin content was quantified through automated segmentation of feather images, and GWAS using this trait led to the discovery of *DENND4A* and *PRKG1*. These genes are involved in intracellular transport and signal transduction, respectively, and neither had been linked previously to pigmentation phenotypes (Twumasi et al., 2024). A similar study in Rhode Island Red chicks, using pattern-based classifiers, identified *TMTC3* as a contributor to stripe development (Shen et al., 2022). This gene encodes a transmembrane protein that may influence pattern symmetry through effects on cell adhesion or migration during feather development.

In mollusks, the analysis of shell color in bay scallops using AI-based color classification, followed by GWAS, identified *PKS1*, *GRL101*, and *PLC1*, genes involved in polyketide synthesis and calcium signaling (Zhu et al., 2021). These pathways are not homologous to those involved in melanin or pteridine production and highlight the diversity of pigment chemistries across animal lineages.

In butterflies, AI-driven pattern recognition and QTL mapping have revealed the role of novel genetic regulators and long-range enhancers in the regulation of wing pigmentation (Kronforst and Sheikh, 2023; Fandino et al., 2024; Livraghi et al., 2024). For example, in *Heliconius* species, variation in color pattern elements has been linked to regulatory elements influencing gene expression at loci not previously associated with pigmentation (Kronforst and Sheikh, 2023).

These case studies demonstrate how AI-augmented phenotyping enables the detection of subtle but biologically meaningful trait differences, and how genomic mapping techniques, when freed from candidate gene constraints, are capable of revealing previously unrecognized contributors to pigment variation.

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5. Emerging Functions and Biological Roles of Non-Classical Pigmentation Genes

The expansion of pigmentation genetics into non-classical gene space has revealed a more diverse array of biological functions than was previously considered relevant to color formation (Ahi et al., 2020a; Ganguly et al., 2022; Chong et al., 2024; Marin-Recinos and Pucker, 2024; Qi et al., 2025). Many of the genes identified through AI-assisted genomic mapping are not involved in pigment synthesis per se, but instead influence how pigments are transported, deposited, or spatially organized (Heo et al., 2023; Kim et al., 2024; Lay et al., 2024; Twumasi et al., 2024; Xie et al., 2024; Rajesh et al., 2025; van der Bijl et al., 2025). Others act through indirect mechanisms, such as regulating cell migration, vesicle formation, cytoskeletal dynamics, or intracellular signaling in pigment cells or their precursors (Simcoe et al., 2021; Kirchler et al., 2022; Xie et al., 2024; van der Bijl et al., 2025).

One prominent category includes genes involved in membrane trafficking and vesicle transport. For instance, *DENND4A*, identified in ducks, belongs to a family of guanine nucleotide exchange factors known to regulate endosomal trafficking (Twumasi et al., 2024). Alterations in these pathways may affect the delivery of pigment granules to the cell periphery or influence the stability of pigment-containing organelles. Another example is *COMMD3*, identified through AI-assisted image-based GWAS, which plays a role in endosomal trafficking and melanosome regulation (Xie et al., 2024). In another recent human-based deep learning study of polygenic adaptation, genes such as *MREG*, *USP13*, and *BLOC1S3* were identified as pigmentation-linked candidates, likely influencing phenotypic variation through melanosome transport, intracellular trafficking, and organelle organization (Tripathi et al., 2024). Their functions support a growing view that pigmentation can be shaped by cellular infrastructure beyond pigment biosynthesis itself. In fish, additional genes such as *hps4*, a component of the BLOC-3 complex involved in endosomal cargo delivery, and *dnajc6*, a regulator of clathrin-mediated endocytosis, further represent mechanisms of vesicle formation and intracellular transport contributing to pigment pattern diversification (van der Bijl et al., 2025).

Genes involved in intracellular signaling and second messenger pathways have also been implicated. *PRKG1*, associated with feather pigmentation in ducks, encodes a cGMP-dependent protein kinase and may modulate cellular responses to external patterning signals during development (Twumasi et al., 2024). *PDE3A*, identified in human retinal pigmentation studies, encodes a phosphodiesterase that regulates cyclic nucleotide levels, possibly affecting cell-specific pigment expression patterns or signaling thresholds required for pigment cell differentiation (Rajesh et al., 2025). In guppy fish, several genes with roles in cyclic nucleotide and intracellular signaling pathways have been implicated in pigmentation, including *gsk3aa*, a kinase downstream of cAMP/PKG signaling; *crh*, which activates cAMP through GPCR signaling; *adgra1*, a G protein–coupled receptor influencing second messenger levels; and *prex1*, a Rac-GEF linked to signaling cascades regulating cytoskeletal dynamics and pigment cell behavior (van der Bijl et al., 2025).

In some cases, structural proteins or ciliary transport components such as *IFT122* have been implicated (Rajesh et al., 2025). Although primarily studied in the context of developmental signaling, these genes may influence pigmentation by affecting the spatial organization of pigment cells or by modulating morphogen gradients (e.g., *LRMDA, MEF2C,* and *PROX1*) during pattern formation (Tripathi et al., 2024). In fish, the gene *ush2a*, better known for its role in sensory cilia and photoreceptor maintenance, has also been associated with pigmentation phenotypes, likely through similar effects on cell positioning or organelle trafficking (van der Bijl et al., 2025). The identification of these genes has begun to shift the understanding of pigmentation from a pigment-centric to a systems-level trait. Rather than being governed solely by pathways that synthesize or degrade pigments, pigmentation emerges as a composite phenotype shaped by diverse biological processes. For instance, genes like *BCL2*, *MYLK*, and *DLG1* may contribute to pigmentation in more indirect ways, including by promoting melanocyte survival, regulating cytoskeletal tension, or maintaining epithelial polarity, thus influencing the persistence and geometry of pigment patterns (Tripathi et al.,

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2024). This expanded view invites new hypotheses about how pigment traits evolve, how they are developmentally regulated, and how they might respond to environmental or physiological cues.

Non-coding RNAs have emerged as an additional class of regulators in pigmentation biology. In cashmere goats, a multi-omics and AI-assisted study identified several miRNAs that regulate hair follicle pigmentation-related pathways, including miR-214, miR-29a/b1, and miR-199a-5p (Chunhua et al., 2025). These small RNAs modulate gene expression post-transcriptionally, influencing processes such as melanocyte activity and pigment deposition. By adding a layer of regulatory complexity beyond protein-coding variation, non-coding RNAs may help explain species-specific or sex-specific differences in pigmentation patterns that are not captured by traditional genomic analyses alone.

Although AI tools for RNA modification analysis have not yet been applied directly to pigmentation patterning, their emergence in the field of epitranscriptomics holds significant promise. Recent advances in deep learning models, such as those predicting m^6A methylation from RNA sequence or direct RNA-seq data (Hendra et al., 2022), demonstrate the potential to uncover post-transcriptional regulatory mechanisms that may influence pigment cell fate, differentiation, or gene expression dynamics (Strowbridge et al., 2025). As these methods mature, they are likely to become powerful tools for exploring how RNA modifications contribute to species-specific or environmentally responsive pigmentation phenotypes.

6. Future Perspectives and Challenges in AI-Enabled Pigmentation Genomics

While the integration of AI-based phenotyping and genomic mapping has led to the discovery of numerous non-classical pigmentation genes, several challenges remain that must be addressed to fully realize the potential of this approach. These challenges are both technical and biological in nature and span the processes of data acquisition, model development, trait validation, and cross-species generalization (Nabwire et al., 2021; Dingemans et al., 2023; Athanasopoulou et al., 2025; Wu and Xie, 2025). A major limitation lies in the standardization of phenotypic data (Ying, 2023; Upadhyay et al., 2024). AI models often rely on large datasets of labeled images or segmentation masks, which may be lacking for many non-model organisms (Koblitz et al., 2025). Variation in lighting, resolution, specimen orientation, and background conditions can introduce noise into training data, potentially reducing model performance and interpretability (Zhang et al., 2017; Yang et al., 2018; Billah et al., 2025). Although data augmentation and domain adaptation strategies can partially address these issues (Orouji et al., 2024; Cao et al., 2025), the creation of high-quality, taxonomically diverse training sets remains a significant bottleneck.

Another concern involves the generalizability of AI models across species or even within populations under different ecological conditions (Norman et al., 2023; Okuley et al., 2025). Models trained on one species or developmental stage may perform poorly when applied to others unless explicitly retrained or fine-tuned (Tabak et al., 2019; Mulero-Pázmány et al., 2025). This challenge is particularly relevant for studies aiming to compare pigmentation traits across evolutionary lineages, where color production mechanisms and cell types may differ considerably. On the genomic side, the quality of genome assemblies and annotation strongly affects the resolution of mapping. Many non-model species lack high-contiguity reference genomes or functional annotation for non-coding regions, limiting the ability to link AI-derived phenotypes to specific regulatory elements or structural variants (Schell et al., 2025). Progress in long-read sequencing, chromatin conformation capture, and single-cell transcriptomics may help bridge this gap by enabling more accurate identification of candidate loci and their functional context (Freedman and Sackton, 2024). Validation of newly discovered genes also presents a persistent challenge. Functional assays such as gene editing or transgenics are often unavailable in non-model systems, and pigment traits are frequently polygenic, making it difficult to isolate the effect of a single gene (Gudmunds et al., 2022; Wattad et al., 2024). In this context, the use of comparative genomics, expression profiling, and co-expression networks may serve as useful tools to build evidence for gene function in the absence of direct manipulation (Martin and Fraser, 2018; Ovens et al., 2021; Zogopoulos et al., 2022). Moreover, the

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integration of species-specific interactomes into AI–genomic mapping frameworks could significantly enhance the prioritization of candidate genes (Ahi, 2025). By combining interaction networks with AI-based quantification and GWAS hits, it may become possible to identify pigmentation-relevant gene modules, infer functional pathways, and filter genes based on their network proximity to known pigment regulators (Figure 1). This systems-level context offers a valuable layer of biological interpretation, particularly when applied to taxa where experimental resources are limited.

Looking forward, several opportunities are emerging. The use of AI for real-time, field-based phenotyping may become feasible with the deployment of lightweight mobile imaging systems (Neethirajan and Kemp, 2021; Freitas et al., 2025; Hu et al., 2025). Transfer learning approaches could allow models trained on one species to be adapted to another with minimal retraining (Kutugata et al., 2021), making reproducibility and standardized analysis more reliable. In addition, the integration of multi-omic data, including spatial transcriptomics, chromatin accessibility, and metabolomics, could further enhance the functional interpretation of pigmentation-associated loci. As AI tools become more accessible and genomic resources continue to expand, pigmentation research stands to benefit from a more holistic and data-rich framework. This approach promises not only to identify new genes, but to contextualize them within broader networks of development, physiology, and evolution.

Box 1 | Key concepts in AI-enabled pigmentation genomics

Pigmentation genes (classical): Genes traditionally associated with pigment synthesis or pigment cell development, such as MC1R, TYR, ASIP, and MITF, often focused on melanin pathways.

Pigment cell types: Specialized chromatophores such as melanophores, xanthophores, iridophores, and erythrophores that produce or reflect color through pigments or nanostructures.

Non-classical pigmentation genes: Genes not historically linked to pigmentation but now implicated in color traits, often involved in signaling, membrane trafficking, or regulation.

AI-based phenotyping: The use of machine learning, especially deep learning, to quantify phenotypic traits such as color, pattern, and reflectance from image data.

Convolutional neural networks (CNNs): A deep learning architecture particularly suited to image recognition and feature extraction, widely used in trait analysis.

Self-supervised learning: A machine learning approach that learns structure from unlabeled data, enabling the identification of traits without predefined categories.

Image-based GWAS (iGWAS): A genomic association study that uses AI-extracted phenotypic features from images as input traits instead of manually scored measurements.

Triplet network: A machine learning model that compares trait similarity between images using three-image inputs, useful for pattern-based trait learning.

Retinal pigment score (RPS): A continuous measure of human retinal pigmentation derived from fundus images using AI-based color analysis.

Feather pigmentation quantification: The use of image segmentation or pixel classification to quantify melanin distribution across specific feather regions.

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Phenotypic embedding: A numerical representation of trait variation derived from high-dimensional image data, used as input for downstream analysis.

Pattern recognition: An AI task that identifies and classifies visual patterns, used to analyze complex color and shape variation in natural traits.

Transfer learning: A method where a model trained on one dataset or species is adapted to another with minimal retraining, improving generalizability.

Trait dimensionality: The number and complexity of measurable aspects within a phenotype, which is greatly increased by AI-based feature extraction.

Regulatory variant: A genetic variant that influences gene expression rather than protein structure, often found in pigmentation loci identified by AI-assisted methods.

Systems-level trait: A phenotype governed by multiple layers of biological regulation, including gene networks, cell behavior, and environmental inputs.

Table 1. Summary of representative studies combining AI-based pigmentation phenotyping with genomic mapping.

Taxon/Species	Pigmentation Trait	AI/ML Method	Genomic Mapping Tool	Key Gene(s) Identified	Functional Role	Reference
Guppy fish	Male body coloration pattern	CNN pattern extraction	GWAS + CNV	Y-linked regions, novel autosomal loci	Chromatophore patterning, cell polarity	(van der Bijl et al., 2025)
Tianfu duck	Feather melanin distribution	DL segmentation	GWAS	DENND4A , PRKG1	Vesicle trafficking, signal transduction	(Twumasi et al., 2024; Wang et al., 2024)
RIR chick	Back stripe phenotype	Pattern classifier	GWAS	TMTC3	Transmembrane protein, development	(Shen et al., 2022)
Human (UK Biobank)	Retinal pigmentation	PCA + CNN embeddings	iGWAS	IFT122 , PDE3A , SIK1	Ciliary transport, signaling	(Rajesh et al., 2025)
Bay scallop	Shell color variation	Color quantification	GWAS	PKS1 , GRL101 , PLC1	Polyketide synthesis, calcium signaling	(Zhu et al., 2021)

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Cattle (Sumatran)	Coat color morphs	AI + SNP modeling	GWAS	CYFIP2 , SGSM1	Membrane dynamics, signaling	(Hartati et al., 2024)
Heliconius butterfly	Wing pattern geometry	Triplet network	QTL	Non-coding RNAs, regulatory elements	Pattern regulation	(Kronforst and Sheikh, 2023)
Papilio butterfly	Eye spot and scale color	Clustering analysis	Genomic scans	white , scarlet , lightoid	Pigment transporters	(Liu et al., 2021)

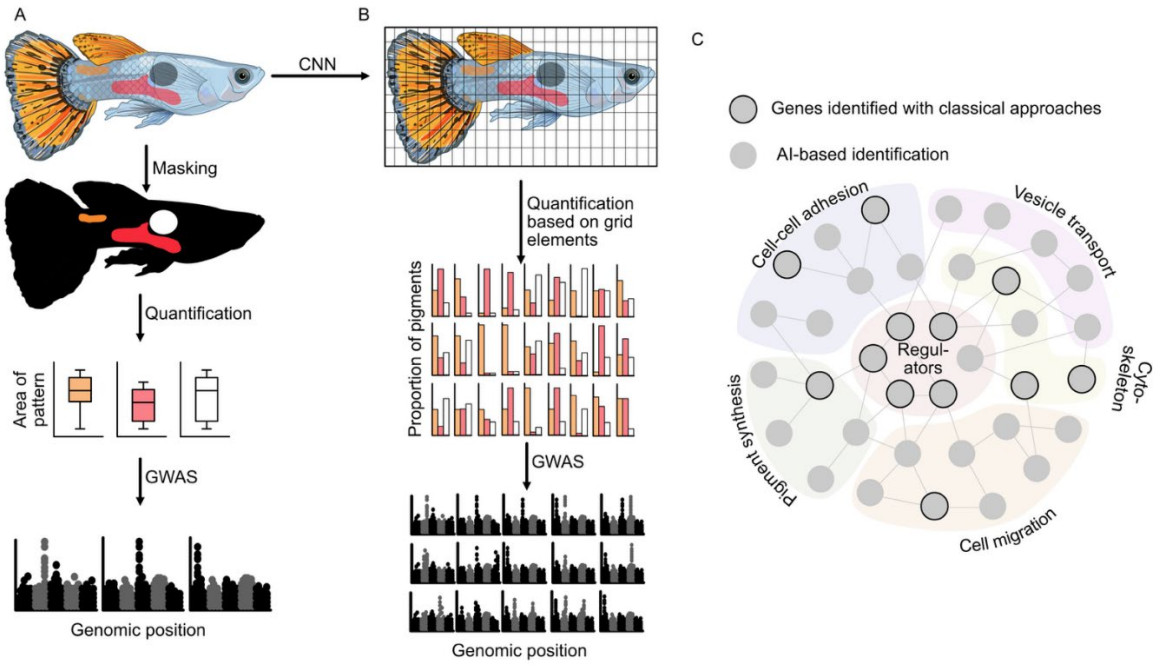

Figure 1. Exemplary comparison of classical approaches and AI-based methods: As exemplified here on a guppy pattern, AI-based methods show far greater throughput and potential to identify diverse gene sets involved in, for example, spatial patterning of color patterns. (A) Classical approach of pattern quantification, where elements of the pattern are masked and individually quantified to be used for GWA analysis. (B) Convoluted neural networks allow for a high-resolution map of a color pattern to identify distinct genetic elements that govern pattern formation and color across the body. (C) AI-based approaches with their high-throughput potential allow for the detection of previously unidentified genes and gene functions/pathways involved in pattern or color formation.

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