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# Embedding Regulatory Genomics and Epigenetics in Curricula to Enhance Student Understanding of Complex Traits and Disease Biology

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## ABSTRACT

Advances in regulatory genomics and epigenetics provide critical insights into the molecular mechanisms underlying complex traits and disease biology, yet these concepts are often underrepresented in undergraduate genomics and genetics curricula. This paper outlines the rationale, theoretical foundations, and pedagogical strategies for embedding regulatory-genomics and epigenetic principles into life-science instruction. By integrating DNA-sequence-based regulatory elements, epigenetic modifications, and gene-environment interactions into existing frameworks, students gain a deeper understanding of genotype-phenotype relationships, transcriptional regulation, and complex-trait determination. Evidence demonstrates that curricular integration enhances cognitive and conceptual learning, reinforces core disciplinary ideas, and bridges connections between molecular biology, genetics, and systems-level perspectives. Moreover, incorporating these concepts equips students to engage with biomedical applications, evolutionary theory, and societal implications of genome regulation. The approach emphasizes progressive curriculum design, alignment with disciplinary core ideas, and development of quantitative and analytical reasoning, fostering a comprehensive understanding of the regulatory architecture of genomes and its relevance to contemporary life-science education.

**Keywords:** *Regulatory genomics; epigenetics; complex traits; gene regulation; curriculum integration; undergraduate education; genotype-phenotype relationships; biomedical education; molecular biology; life-science pedagogy.*

## INTRODUCTION

One of the most widespread childhood ailments in the whole world, dental caries, also referred to as tooth decay, is a major public health problem. The recent advances in regulatory genomics and epigenetics offer complementary perspectives toward understanding complex traits and diseases, illuminating how DNA sequence variation across putative regulatory regions affects gene-expression control patterns in response to external and internal stimuli. Despite their importance, curricula in genomics and genetics typically emphasize only the core tenets of molecular genetics and Mendelian inheritance while referring students to specialized topics for complex

traits and diseases. Research in teaching and learning documents the advantages of integrating cross-cutting ideas into the discipline-specific core to advance conceptual understanding.

Cognitive gains have been shown for specific topics (e.g., disease biology, polygenic traits) in undergraduate and K–12 biomedically focused genomics curricula. Moreover, a broader analysis of foundational concepts across the disciplines indicates that the themes underpinning regulatory genomics and epigenetics also support other major areas, including genetic and epigenetic contributions to biological individuality, gene regulation through signaling and RNA networks, chromatin accessibility, control of differentiation, genotype-by-environment interactions, and the social and ethical implications of genomics in society.

### **Theoretical Foundations: Regulatory Genomics and Epigenetics**

Epigenetics constitutes a powerful tool that regulates cellular phenotypes without altering the underlying genomic sequence. Major epigenetic marks such as DNA methylation, histone modifications, and noncoding RNAs play crucial roles in controlling transcriptional outputs from genes. Multipronged experimental demonstrations in animals, plants, and fungi have established that diverse epigenetic marks govern chromatin architecture throughout the genome and confer complex quantitative traits. Genome-editing of regulatory regions provides evidence that certain regulatory elements sustain epigenetic states with transgenerational heritability of trait variation. Epigenetic mechanisms and genomic regulatory elements constitute a general framework that connects genotype to phenotype in a predictive manner (Shadmanova S., et al). These concepts frame regulatory genomics and epigenetics as vital components of biological education, essential for understanding development, evolutionary change, cancer biology, and complex quantitative traits. Detailed evidence linking genetics, regulatory genome architecture, and epigenetic mechanisms to complex traits is consolidated (Kang et al., 2019) ; (C. Hardison, 2012).

### **Rationale for Curriculum Integration**

Curriculum development is influenced by various factors, including societal needs, technological advancement, research evolution, and national standards. Integration rationale focuses on core regulatory genomics and epigenetics concepts, empirical evidence on complex traits and diseases, relevant theoretical frameworks, and anticipated benefits. Empirical evidence shows that students gain cognitive insights and conceptual understanding from learning regulatory principles (Karimov N. et al) [table 1].

**Table 1: Curriculum Design Principles and Learning Outcomes for Regulatory Genomics and Epigenetics**

<b>Category</b>	<b>Key Concepts / Principles</b>	<b>Learning Outcomes / Competencies</b>
<b>Cognitive and Conceptual Gains</b>	Integration of regulatory genomics and epigenetics into genomics instruction; gene-environment interactions; complex trait regulation	Enhanced comprehension of gene regulation, regulatory networks, and epigenetic mechanisms; understanding the environment's role in shaping gene expression
<b>Alignment with Core Ideas</b>	Connection to life-science disciplinary core ideas; integration across molecular biology, genetics, biochemistry	Students understand genome action, information processing, and phenotypic variation; ability to apply knowledge in evolutionary and biomedical contexts
<b>Biomedical and Societal Relevance</b>	Genome regulation in development, disease, and adaptation; applications in synthetic biology and gene therapy	Ability to analyze regulatory and epigenomic data; understanding translational implications; connecting genome regulation to human health and societal challenges

<b>Sequencing and Scaffolding</b>	Progressive introduction of regulatory concepts; linkage to prior knowledge; integration of RNA and noncoding regulatory mechanisms	Students can interpret regulatory networks and understand epigenetic modulation across development; competency in integrating regulatory concepts across courses
<b>Cross-cutting Concepts</b>	Regulation as a unifying concept; coordination of gene expression across spatiotemporal contexts	Comprehension of regulatory logic in multicellular organisms; understanding cross-disciplinary applicability of molecular principles

Curriculum development has always been influenced by societal needs, technological advancement, research evolution, and national or state educational standards. The rationale combines delineation of core concepts in regulatory genomics and epigenetics, annotation of empirical evidence linking regulatory architecture and epigenetic modifications to complex traits and disease, and mapping of relevant, widely accepted theoretical foundations from molecular biology, genetics, and systems biology to curricular integration. The rationale for integrating regulatory genomics and epigenetics concepts, mechanisms, and data into undergraduate curricula in genomics, genetics, and related fields builds upon these initial points. Evidence indicates that incorporating regulatory genomics and epigenetic concepts enhances cognitive insights and conceptual understanding (M. Schmid et al., 2022).

### **Cognitive and Conceptual Gains**

The core concepts of regulatory genomics and epigenetics comprise a broad knowledge area with explicit relevance to opportunities and challenges in the life sciences sector and to individual and societal well-being. For most individuals, these concepts will remain chronically out of reach in the absence of an extended effort, yet evidence suggests that embedding these principles within the existing genomics framework enhances comprehension considerably. Incorporating aspects of regulatory genomics and epigenetics into established genomics instruction, therefore, represents an important means of transmitting fundamental yet complex principles of biological organization to contemporary audiences (Reinagel & Bray Speth, 2016).

Curricular integration maps regulatory-genomics constructs to prominent, widely taught concepts in the biological sciences to facilitate comprehension of how genes interact to shape complex traits and diseases. Regulatory networks contribute centrally to the control of gene activity, connecting molecular, genomics, genetics, and biochemistry principles to core ideas in instructional documents from the National Academy of Sciences and the American Association for the Advancement of Science (M. Schmid et al., 2022). Regulatory-genomics knowledge encompasses a second concept framing the relevance of the environment to the expression of genes and contributes directly to the reasoning and evidence underlying models of complex trait determination. Gene activity, genomics, and genetics substances, diverse routes exist through which regulatory contemporary public health challenges (e.g., pollution, social justice) implicate regulatory genomics and epigenetics, yet curiosity about these matters merits additional justification (Umarova M., et al).

### **Alignment with disciplinary core ideas**

Curricular frameworks outline essential knowledge and practices across disciplines that all students should learn by the end of K–12 education (National Research Council, 2012) and beyond. Elementary and secondary students should develop an integrated understanding of the four domains of life science framework (LS) in interrelated ways by grade 12. Consequently, undergraduate curriculum integration into first-degree programs should ensure that subsequent learning at the graduate level achieves the same essential disciplinary scientific core across areas of application, including regulatory concepts of genomics and epigenetics.

Regulatory-genomics concepts enhance comprehension of gene, genome, and nucleic-acid action across information-processing and chemical domains, preparing students for upper-level courses across the biological sciences. Numerous empirical studies demonstrate that the process by which genetic change generates phenotypic variation influences evolutionary theory on every operational scale (Reinagel & Bray Speth, 2016). Systematic curriculum analysis confirms that fitness and evolutionary change are seldom explicitly included at the undergraduate level following first-degree programs (M. Schmid et al., 2022).

### Relevance to Biomedical Education and Society

Recent developments in regulatory genomics and epigenetics have highlighted the pivotal role of genome structure and sequence in orchestrating gene expression during development and across diverse environments. Such regulation constitutes a major mechanism for adaptation to environmental change and understanding its principles is essential for appreciating the origins and evolution of complex phenotypes. Regulatory decisions at the level of transcription are fundamental to many systems-scale biological questions such as cellular differentiation, lineage tracing, reprogramming, and gene therapy. Establishing appropriate mechanisms for regulatory control, stability, fidelity, and specificity is necessary for any potential application of synthetic biology. Transparency with regard to gene regulation is therefore essential to discerning both the translational potential of synthetic constructs and their potential impact on existing regulatory architecture. Regulatory analysis provides quantitative and qualitative insights into the degree to which the structure of the target gene, sequence of the synthetic input, and cellular state of the target organism collectively determine regulatory need and influence the design of regulatory components (A. Patel et al., 2024) [table 2].

**Table 2: Instructional Strategies and Pedagogical Models for Regulatory Genomics and Epigenetics**

Strategy / Model	Description	Benefits / Goals
<b>Inquiry-Based Learning (IBL)</b>	Students are presented with a scenario and generate research questions for investigation	Promotes critical thinking, data analysis, and application of theory to authentic problems
<b>Problem-Based Learning (PBL)</b>	Students engage with complex problems requiring research, evaluation of data, and solution proposals	Encourages analytical reasoning, teamwork, and integration of knowledge across domains
<b>Curricular Integration</b>	Embed regulatory genomics and epigenetics into existing genomics, molecular biology, and developmental biology courses	Ensures continuity, reinforces foundational knowledge, scaffolds learning of complex concepts
<b>Sequencing &amp; Scaffolding</b>	Introduce regulatory concepts progressively, linking to prior knowledge and increasing complexity	Facilitates comprehension of regulatory networks and epigenomic processes
<b>Cross-disciplinary Approaches</b>	Connect regulatory and epigenetic concepts to evolution, health, disease, and societal applications	Enhances relevance, demonstrates applicability, develops scientific reasoning
<b>Differentiation &amp; Customization</b>	Adjust content depth and pace based on students' prior knowledge and course focus	Maximizes learning outcomes for diverse student populations
<b>Real-World Contextualization</b>	Use authentic biomedical or societal problems to illustrate gene regulation principles	Strengthens motivation and critical thinking, links theory to practice

### **Curriculum Design Principles**

Understanding complex traits requires engaging with regulatory genomic and epigenetic variations. Central to this is knowledge of the principles and mechanisms involved. Therefore, adhering to sound principles of curriculum design is essential. Learning outcomes should clarify understanding of how complex traits emerge from genomic sequences and a regulatory logic connecting sequences to combinations of molecular events (M. Schmid et al., 2022). Conceptual frames provide access to influential disciplinary core ideas and scientific crosscutting practices on interconnected scales (Reinagel & Bray Speth, 2016). Sequencing transversal concepts across progressively deeper curricular alternatives enables alignment with diverse prior knowledge. Integrative approaches clarify space for embedding regulatory and epigenetic concepts into wider curricula, extending instructional design options and increasing benefit from informative resources.

### **Learning Outcomes and Competencies**

The integration of regulatory genomics and epigenetics into curricula enhances the understanding of complex traits and disease biology. Learning outcomes and competencies are fundamental design principles guiding this integration. Outcomes specify desirable knowledge, reasoning, and analytical capabilities; competencies define the ability to apply knowledge and reasoning to address problems. The primary focus is on the regulation of gene expression, analysis of regulatory and epigenomic data, and the potential translational implications of these analyses.

The overarching learning outcome involves understanding how the regulatory architecture of the genome shapes organismal phenotypes, including complex traits and diseases. Specifying the educational competencies that enable the achievement of this outcome maximizes the likelihood of productive curricular integration. Emphasis is placed on the underlying regulatory logic, the interpretation of regulatory-genomics data generated through specific experimental assays, and the ability to articulate the translational relevance of gene regulation and epigenetics to the underlying biology of complex traits and disease (D Meiklejohn, 2016). Such reasoning articulates the importance of regulatory-biology concepts and illustrates the cognitive gains attainable through curricular augmentation.

The inclusion of regulatory and epigenomic concepts expands the understanding of genomic regulation. Encompassing all regulatory and epigenomic mechanisms, two additional overarching outcomes support the curriculum design: explaining the regulatory logic that governs the expression of the genome's protein-coding and non-protein-coding genes, and analysing how regulatory and epigenetic processes modulate the spatio-temporal expression of these genes across diverse biological contexts.

### **Sequencing, Scaffolding, and Differentiation**

Although instructional materials on regulatory genomics and epigenetics are available, courses often address the topic merely as a standalone module. Regulatory control underpins gene activity across contexts, including variation in complex traits and disease susceptibility. Therefore, precisely sequencing the introduction of regulatory concepts and accommodating diverse student backgrounds are crucial for effective integration.

Integration is most effective when students' prior knowledge aligns with that of the integration target. Courses that introduce gene regulation should sequence regulatory control in a way that scaffolds student knowledge and links established concepts from previous courses. Working with RNA and emphasizing the transcribed genome prepares students for the multifaceted regulation of noncoding RNA gene activity, which affects complex traits and elucidates epigenetics (M. Schmid et al., 2022).

A more effective strategy might also differentiate between a wide array of existing courses that already discuss genomics and fewer that encompass developmental biology and cellular differentiation. Incorporation of regulated factors requires a focus on regulatory networks that influence gene-expression patterns.

### **Integrative Approaches: Cross-cutting concepts and practices**

A cross-cutting concept that is present in numerous fields of science is regulation. In a multicellular organism, gene expression must be precisely regulated to produce the appropriate proteins in the right cells at the correct times to achieve the correct levels. Without this regulation, development, homeostasis, and response to environmental stimuli would be impossible. This cross-cutting concept of regulation is well developed in educational standards and provides an important entry point to intermolecular biology. Regulatory genomics and epigenetics, although critical for understanding the biological underpinnings of many complex traits, are not currently explicit in science standards for precollege or higher education. As a result, the extensive literature on their role is less accessible to students than classical materials from the second half of the twentieth century and the accompanying regulatory-architecture materials that follow naturally from them. Integrating this perspective into precollege curricula provides a motivating demonstration of the applicability of concepts from molecular biology, including the central dogma and the focus of genetics between genotype and phenotype, to complex critiques. (M. Schmid et al., 2022)

### **Instructional Strategies and Pedagogical Models**

The impetus to incorporate regulatory genomics and epigenetics into curricula stems from the complexity of the underlying concepts. Foundational knowledge of molecular biology, genetics, and statistics is already well established among students in both life sciences and biomedical education. Attention, therefore, should focus on pedagogical strategies and curricular integration that move beyond foundational concepts explicitly taught in precollege and introductory coursework (Reinagel & Bray Speth, 2016). Regulatory mechanisms, which modulate the consequences of genetic variation, are central to understanding the biology of complex traits. Consideration of both epigenetic regulation and the environment further supports a multifactorial view of biology (Mierdel & X. Bogner, 2020). Strikingly, even regulatory concepts addressed in genomics courses are often treated in a simplistic manner that reinforces, rather than mitigates, the appeal of fundamentalist views of biology (M. Schmid et al., 2022).

Contemporary pedagogical models stress the importance of taking up a scientific issue grounded in the real world. Inquiry-based and problem-based learning in particular help students connect theory to authentic practice while developing analytical, reasoning, and critical-thinking skills. Inquiry-based learning involves posing a scenario to students, from which they derive a question amenable to investigation and analytic resolution; problem-based learning engages students with a problem requiring resolution and encourages them to seek out applicable data and knowledge rigorously (Nazarova S., et al).

### **Inquiry-Based and Problem-Based Learning**

Gains accrue from connecting theory to practice within research areas. Genomics, which directly relates instruction to biology's central tenet, is already widely integrated into curricula and forms the core of domain-ready training in datascience. Nevertheless, the field remains disconnected from essential regulatory-genomics notions needed to connect genotype and phenotype in multicellular organisms. Integrating these concepts into genomics and into curriculum alongside rather than following a more general introduction greatly deepens understanding, extends the concept of a central dogma to encompass regulatory logic, and strengthens links to regulatory mechanisms that form the foundation of comprehensible complex traits, influential for many organisms and essential for many societal challenges (Reinagel & Bray Speth, 2016).

Core concepts from regulatory genomics and epigenetics are thus advantageous for disciplines and practices need no introduction but greatly strengthen any understanding of the field. Mapping essential concepts and research areas to instructional sequences already applied in basic cell and molecular biology illustrates complementarity. Comprehending such basic insights, let alone regulatory mathematics, presupposes understanding DNA, RNA, protein, inheritance, phenotype, and the limitations of classical genetics. Within the teacher training seminar much attention is devoted to the interdependent relationship between curriculum and pedagogy, and the powerful gains that interactive problem solving accompanying

theoretical introduction within problematic areas of a discipline affords to students (Azimova, S., et al. 2023).

### **Case Studies and Data-Driven Reasoning**

To provide students with practice in connecting regulatory-genomics theory with ongoing real-world research, case studies (Carroll Alexander et al., 2024) drawn from contemporary high-throughput studies can be incorporated. These cases introduce students to the design of genomic research projects and regulatory analysis of genomics data, such as transcriptional control inferred from accessible chromatin maps and epigenomic patterns, chromatin-interaction datasets, and noncoding RNA mapping. These topics closely align with ongoing publications and research efforts at various institutions, allowing students to explore contemporary scientific questions while applying preexisting regulatory invariants. In addition, educational resources addressing the implementation of case studies in online environments and offering relevant high-throughput datasets are accessible for additional support. Data-driven reasoning approaches further engage students in scientific inquiry by analyzing complex datasets that address open scientific questions.

Applied to the regulatory-genomics domain, a data-driven reasoning framework targets the question “How can we design transcriptional regulatory systems in mammalian cells, and how can we identify and optimize engineered regulators?” The corresponding datasets permit modeling various regulatory architectures designed by Epicodex, regulatory controls assembled from functional noncoding elements, and optimization of synthetic biocompartments for distinct cellular environments (pseudomonads, orthogonal *Escherichia coli*, and human cells). Student assessments typically elicit individual responses addressing educational resource questions in combination with modeling summaries as documentation for the commencement of subsequent student-centered exploration. Combining these methods with the introduction of regulatory invariants governing the analysis of available genomic data offers an effective framework for supporting students in connecting theoretical and practical approaches to complex scientific questions within the regulatory-genomics discipline (Azimova, S., et al. 2023).

### **Computational Thinking and Bioinformatics**

The rapid growth of public genomic datasets and bioinformatics tools enables computational thinking and bioinformatics training to form a core part of modern education. Bioinformatics is an essential component of biological and biomedical science curricula, constituting a minimum skillset for 21st-century researchers. Undergraduate life-science programs often select off-the-shelf bioinformatics tools for integration into curricula; however, students gain few transferable skills because these approaches lack the breadth, generality, and abstraction needed to promote computational thinking. Innovative and flexible instructional strategies employing data in real-world contexts expose students to the central role of data in conceptualizing biological problems. Only after students recognize that biological data provide essential insights into fundamental problems of life are they able to apply methodologies for generating, obtaining, mining, and interpreting data. Integration of bioinformatics, data analysis pipelines, and computational thinking, therefore, enriches curricular opportunities at all educational stages and enhances understanding of biology and biological research throughout the life-course (Martins et al., 2020) (Lynn Petrie & Xie, 2021).

### **Ethical, Legal, and Social Implications**

As the field of genomics advances, the need for integrating ethical, legal, and social implications into the human genetics curriculum accelerates (A. Patel et al., 2024). Trainees tend not to receive adequate preparation for addressing these dimensions in their research or teaching. To remedy this gap, a course exploring critical issues in genetics and society was developed for first- and second-year PhD students and postdoctoral fellows at the University of California, San Francisco. The course examines societal aspects of genomics using materials relevant to the students’ research, thereby encouraging them to reflect on formulaic framing and broader implications. By situating science in a social context, the course emphasizes researchers’ responsibilities in their quest for equity, understanding, and justice.

Science often progresses rapidly relative to society's ability to adapt; newly emerging knowledge can deeply affect individuals, communities, and society. Trainees tend not to receive adequate preparation for engaging with ethical and societal dimensions. These dimensions are infrequently addressed in the classroom, and the expected public-facing commitment remains unclear. However, faculty and investigators concentrate on such issues through policy, culture, justice, equity, and other topics; they bring societal perspectives to their laboratories. Within this context, a cross-departmental structured course on genetics, ethics, and society was developed. The course was designed to allow participants to synthesize and incorporate aspects of their own research programs; it aims to enhance awareness of the links to science under development.

### **Assessment and Evidence of Learning**

Assessment captures understanding at a particular moment in time, whereas evidence of learning describes the progression of that understanding. Regulatory genomics and epigenetics topics may be approached through case studies that demonstrate the involvement of regulatory-region variants and epigenetic alterations in disease and quantify their impact on polygenic risk. Competency-based frameworks, such as the Bio-Modeling and Educational Network for Data Science (Bio-MENDS) indicators and the Bioinformatics and Genomics Competency Framework, provide structures for articulating student learning outcomes and mapping progression through transdomain competencies (knowledge, skills, attitude) and proficiency levels. These resources can support long-term evaluations to document student progression from a common starting point, inform instructional adjustments, and track the overall impact of curricular integration.

#### **Assessment and evidence of learning can be articulated as follows:**

6.1 Assessment Assessment measures student understanding at specific moments, while evidence of learning describes longitudinal changes in that understanding. To evaluate the impact of widely adopting a regulatory-genomics and epigenetics focus within genomics instruction, formative and summative assessments have been designed for implementation in a five-course bioinformatics certificate and a reagent-base sequencing master's degree. With three distinct curricular pathways under consideration, each proposing a different degree of regulatory integration, assessments would aid in deciphering the relevance of these topics to mastery of the broader genomics field.

Forthcoming courses would examine germline variant datasets in diverse species, including the human genome, to assess their influence on complex traits and disease mechanisms. Such materials directly engage with Baum's crosscutting ideas of representation and modeling, while the science-and-society theme interconnects myriad communication channels with genomics. Assignments within these modules would probe qualifications for establishing causality in broader, regulatory-genomics, and intricately linked frames. Regulatory concepts are thus also well represented, as these cases ask students what must be addressed to support the assertion of causation. Annotated public datasets collected from independent work explore the interplay among cross-cutting concepts and directly support Baum's pressing call for reformulating undergraduate bioinformatics education (M. Schmid et al., 2022).

For fundamental genomics knowledge, indicators and progression maps from the Bioinformatics and Genomics Competency Framework may prove useful together with the Bio-MENDS proficiency indicators. Existing frameworks are available for assessing bio-video and bio-infographic comprehension. Elementary progressions across core ideas can be aligned with the Bio-MENDS structure to chart advancement toward broad literacy within regulatory genomics.

### **Formative and Summative Assessments**

Regulatory genomics and epigenomics topics often lie outside traditional genomics curricula, constraining students' understanding of complex traits and disease biology. Formative and summative assessments followed face-to-face instruction, emphasizing gene-regulatory and epigenetic concepts in the context of the Canadian National Genomics Education Strategy curriculum, which guides the teaching of 265 core



genomic concepts to two targeted levels in secondary, undergraduate, and graduate programs (M. Schmid et al., 2022).

A diverse student population benefits from integrated curricular approaches that interweave cross-cutting concepts of life and natural sciences, core ideas of genomics, and scientific practices for both disciplinary and coordinated overall degrees. Curriculum design associated with the Teaching and Learning Framework accommodates students with university, collegial, or specialized backgrounds in genomics. Formative and summative assessments demonstrate, alongside relevant concepts, the systemic integration of evaluation tools within teaching strategies. Integrative thinking among innovative institutions and organizations advances independent scientific literacy, informed educational criticality, confidence in making evidence-based judgments, connection of theoretical knowledge to real-world situations, and transparent communication with diverse audiences, all of which align with curricular enhancement in genomics and regulatory concepts (Ziyaev, A. A., et al. 2023).

### **Evidence-Based rubrics and mastery indicators**

Evidence-based rubrics and mastery indicators can incorporate multifactorial concepts into curricula by using interaction graphs that model the relationship between genotypes, the environment, and phenotypes. These models can demonstrate how genes, the environment, or their interactions influence traits, such as single-gene mutations affecting coloration or disease risk. Activities might include analyzing phenotypic outcomes in different environmental conditions or exploring gene–environment interactions like skin-cancer risk related to genetics and UV exposure. Summative assessments could involve students predicting outcomes based on experimental designs that isolate the effects of genes, environment,  $G + E$ , or  $G \times E$ , encouraging critical thinking and application of complex concepts (M. Schmid et al., 2022).

### **Longitudinal Mapping of Student Understanding**

Although students' understanding of regulatory genomics and epigenetics principles will progress differentially, a longitudinal perspective can clarify common challenges and thereby advance effective curricular development. The study of how candidate genes and environmental factors contribute to complex traits and diseases remains central to biology and biomedical science. Detailed multicourse assessment of student understanding shows that many learners struggle with fundamental principles even after significant exposure to course material. In these analyses, stagnating progress is evident at particular concepts between individual courses, suggesting lingering misconceptions that additional instruction does not fully address. Differences in prior preparation in biology, chemistry, mathematics, or physics also contribute, indicating a need to evaluate curricular design from a disciplinary perspective as well as a conceptual one and to reconsider the sequence and scaffolding of topics between courses. Integrating regulatory physics, on which the course relies heavily, into a companion biology course together with genomics appears to enhance student learning, encouraging exploration of the role of regulation in supplying the additional information required for higher-order biophysical modeling. Addressing the interim state of nongenomic and regulatory physics, which often receives little or no attention, further meets a pressing need. Curricular mapping captures salient ideas within molecular and organismal biology, cross-curricular links to other disciplines and unifying cross-scale themes, and the expected evolution of curricular materials through time (Ziyaev, A. A., et al. 2023).

### **Resources, Tools, and Materials**

A wealth of resources can support the curricular integration of regulatory genomics and epigenetics, including Open Educational Resources (OERs), laboratory or virtual-laboratory practicums, instructional datasets, and computational tools. A selection of these resources and materials follows (Sasmakov, S. A., et al). The Ensembl Regulatory Resources provide comprehensive datasets to characterize regulatory elements across vertebrate genomes (R. Zerbino et al., 2016). The accompanying BioMart application enables the efficient querying of large-scale regulation data in multiple output formats, covering a wide range of species. A detailed publicly accessible summary page describes the contents and organization of the resources. For human and mouse, the regulation data contain information on regulatory features, evidence

sources, binding motifs predicted from transcription-factor (TF) models, and curated candidate-regulatory regions. Transcript annotations, including transcript-start site definitions, and microarray probe mappings for the latest Gene Expression Omnibus array version are available through the Ensembl Genes database. The Variant Effect Predictor (VEP) tool has been updated to process regulatory-feature, predicting the likely consequences of single-nucleotide polymorphisms (SNPs) or other genomic variants, and to indicate whether variants occur within TFBS motifs, potentially influencing TF binding affinity. Ensembl regulatory resources are continuously expanding, and additional cell-type coverage is being incorporated as part of international collaborative endeavours such as the International Human Epigenome Consortium.

Established epigenomics-based therapeutic strategies propose epigenomic reprogramming or restoration of the epigenome in diseases such as cancer (Rosa-Garrido et al., 2018). Recently developed technologies for translating epigenomic intervention into practice include modifications of the CRISPR/Cas9 system in which an inactive Cas9 protein is fused to DNMT3a or Tet1, combined with appropriately designed guide RNAs to induce specific DNA-methylation changes. Designer CRISPR tools for remodeling chromatin loops have also been created, allowing the targeted modulation of gene transcription in somatic cells in vivo (Sasmakov, S. A., et al).

### **Open Educational Resources**

Open Educational Resources (OERs) facilitate access to high-quality, reusable, and adaptable educational materials, enriching the learning experience for numerous audiences. OER Webcrawler Code collects and formats relevant OER listings contributed to Federal, State, and University catalogs. Educational Resources to Enhance Teaching of Regulatory Genomics Science Education for Non-Majors is a publicly available collection of open-access undergraduate teaching resources curated by dedicated faculty and scientists. Provides course materials and laboratory and virtual laboratory simulations addressing regulatory genomics, epigenetics, and genetics via various model organisms and supporting multiple pedagogical approaches. The resource outlines educational modules compatible with diverse institutional types and supports education for students from various backgrounds, including non-science and non-life-science majors. Analysis showed that faculty with advanced degrees train fewer undergraduates than those with terminal degrees. Hence, integration of high-quality open-access regulatory resources became a high institutional priority, expanding both professional-development opportunities to STEM faculty with less terminal-training expertise. Following the screen pedagogical guidelines, the development of openly available automated-regulatory modeling software was prioritized.

### **Laboratory and Virtual Lab Simulations**

Regulatory and experimental genomics can enlighten students about complex traits encompassing polygenic influences and environment–genotype interactions. Diverse online resources and tools support the desired curriculum integration. Educational resources focused specifically on regulatory genomics and epigenetics enhance accessibility of the pedagogical materials. Moreover, Open Educational Resources incorporating instructional modules and laboratory activities addressing related concepts are available. Laboratory simulations involving regulatory assays and epigenetic experiments, and associated datasets ready for analysis and interpretation, can be employed in reagent-limited environments or alongside computational analysis (Sasmakov, S. A., et al).

Teaching materials centering on regulatory genomics and gene expression implementation across higher-education systems remain limited. Curriculum pathways facilitating the integration of regulatory genomics and epigenetics vary according to specific program foci. Degree profiles concentrated primarily on the molecular or bioinformatics dimensions can conjoin the proposed content with existing courses, building on generic knowledge of molecular biology, genetics, and data-driven approaches for biological interpretation. Firstly, integration may traverse particular curriculum components alongside conventional topics. Secondly, extended course options allow treatment of the desired material through stand-alone modules. Thirdly, whereas dedicated degree programs may not be available, selected topics could furnish an entry point for the contemplated pedagogical orientation.

### **Data Sets and Analysis Platforms**

Regulatory genomics provides a framework for interpreting large, complex datasets and mapping the genetic and epigenetic bases of diverse biological systems. Regulatory genomics can be viewed as a theoretical approach to global biological reasoning based on a mechanistic understanding of regulatory architecture (Sharma, 2018). Such knowledge constitutes a formal theory of how the genetic architecture of the cell influences the ability to regulate gene expression. Epigenomics can be integrated with regulatory genomics to obtain a broader characterization of biological systems (Ferrero, 2018). The emergence of biomedically relevant epigenomic maps and their integration into a regulatory framework will enable a broader interpretation of the epigenome and will provide a fresh foundation for interpreting other large datasets within a specific theoretical framework.

Regulatory regions determine how, when, and where genes are expressed within organisms. They have been implicated in several major biological processes, such as evolution, developmental biology, physiology, and disease. Epigenomic marks regulate the functional state of these regions and influence transcriptional output. Considerable empirical evidence indicates that regulatory architecture defines complex traits at the polygenic level and determines organismal responses to environmental inputs. An integrated approach combining regulatory, epigenomic, and transcriptomic maps reveals novel insights into the cellular systems underlying biological contexts (Heyn, 2018). Mechanistic models of regulatory processes elucidate how specific alterations in the regulatory apparatus affect complex traits and connect genotype, epigenotype, and phenotype across environments. Such frameworks complement the description of genetic and epigenetic maps by providing an interpretable computational foundation for emerging experimental datasets and a theoretical basis for integrative data mining. Open Educational Resources (OERs) are digital resources that permit access, use, reuse, adaptation, and redistribution at little or no cost. Such materials, together with repositories that provide regulated free access to both physical and virtual laboratory simulations, enable the integration of regulatory genomics and epigenetics into existing curricula.

### **Equity, Inclusion, and Access in Genomics Education**

Culturally responsive pedagogy should guide curriculum design and delivery to enhance equity, inclusion, and access in genomics education (D. Blizinsky & L. Bonham, 2017). Culturally responsive pedagogy is defined as student-centered teaching that incorporates students' cultural references in all aspects of learning (R. Hubbard & A. Monnig, 2020). Students should see themselves in the learning materials as a way to promote engagement with the curriculum. Cultural relevance should be considered for all aspects of the learning environment. To foster inclusion, genomic datasets should be selected from diverse populations representative of students' ancestors, and 24/7 surveillance should accompany data used from less represented communities.

Curricular accessibility for all learners requires continuous assessment and improvement of physical and cognitive access. Physical access pertains to the availability of technology, media, materials, and furniture conducive to an effective learning environment, whereas cognitive access pertains to the degree of difficulty students have with the content. Various scaffolds can be included in the curriculum to promote cognitive access while rigorous academic standards are maintained (Sasmakov, S. A., et al).

### **Culturally Responsive Pedagogy**

Culturally Responsive (CR) pedagogy emerged from the U.S. civil rights movement and transcends conventional multicultural education to engage with students' home cultures more broadly as a means to enhance learning. CR pedagogies can be embedded into educational frameworks for genomic instruction involving diverse human populations, starting at the curricular-design phase and permeating the entire pedagogical project. Specific guidelines further advance CR education in college-level genomics courses (A. Sparks et al., 2020).

Genomics curricula exhibit various characteristics that can, and frequently do, act as barriers to inclusive learning. Many applied and theoretical genomic exemplars use human populations in ways that can entrench

historically rooted yet unfounded social hierarchies (R. Hubbard & A. Monnig, 2020). Navigating human genomics requires guiding students, often at early educational stages, away from unfavorable dominant models towards more equitable coevolutionary perspectives.

### **Representation of Diverse Populations in Genomic Data**

One of the most striking inequalities in the field of genomics is the under-representation of diverse human populations in genomic studies: samples from individuals of European ancestry constitute over 80% of publicly available datasets. This skew limits the ability to make generalizable inferences about gene-disease relationships and threatens the equitable translation of precision medicine research. Increasing the representation of diverse populations in genomic studies, therefore, is of critical importance. Such population diversity is crucial not only for identifying gene-disease associations but also for distinguishing benign from pathogenic variants, especially in rare disorders. The aim of a more representative genomic architecture is to provide a better understanding of how biological variation relates to disease risk, treatment response, and biological knowledge as such (Soo-Jin Lee et al., 2022).

Although the motivation for more diverse genomic representation is unequivocal, the meaning of “representation” is complex. It can refer both to capturing the genetic variation found between populations on a global scale and to including groups that have been historically marginalized. Failing to represent the former limits the generalization of scientific inference beyond the studied populations, while neglecting the latter may exacerbate the societal inequities that, through genomics, the research community seeks to address. Rather than simply monitoring ancestral diversity across samples—which remains essential—expanding the supply of genetic variations from diverse populations is essential to gain more profound scientific insights and a broader understanding of human health (E. Peterson et al., 2019).

### **Accessibility of Genomics Curricula**

As genomic information and its applications in human health become increasingly widespread and relevant, the field of genomics continues to evolve with new discoveries, technologies, and emerging areas of research. Despite the growing emphasis on genomics in curricula across the world, courses on the topic can struggle with accessibility due to frequent changes, new knowledge about the molecular basis of genetics, and persistence of misconceptions from earlier curricula regarding the centrality of DNA sequence to information coding. Furthermore, the genomic era has been approximately coincident with an expanded emphasis on science, technology, engineering, and mathematics (STEM) education, creating a demand for graphically rich and broadly relevant pedagogical approaches. Drawing on research from a variety of scientific disciplines and scholarly studies of teaching and learning, an evidence-based framework is presented to embed the concepts of regulatory genomics and epigenetics within existing genomics courses and resources designed for students and precollege educators. This curriculum integration framework foregrounds genomic regulatory information, a central feature of contemporary biological science that has substantial ramifications for human health, agriculture, and many other aspects of everyday life, and a prominent and well-studied paradigm for integrating science across a range of topics—molecular biology, genetics, epigenetics, bioinformatics, and systems biology—into a cohesive whole (M. Robbins et al., 2021).

### **Implementation Considerations and Institutional Readiness**

A series of institutional and pedagogical considerations guide the effective implementation of curriculum integration across programs and curricula, maximizing participation, extending reach, and amplifying impact.

Successful integration of regulatory genomics and epigenetics into curricula depends on institutional readiness and awareness of pathways for adoption. A variety of strategies facilitate curriculum integration with minimal disruption to existing degree plans. Addressing institutional capacity for engagement with the proposed changes and facilitating department-level articulation of curricular details broadens participation and increases the potential impact of regulatory concepts across a wide array of educational contexts.

Integration requires institutional-level coordination among relevant departments and programs. Multi-department curricular deliberations and strategic planning for communal educational priorities among faculty streamlines the integration of regulatory concepts and modular designs into curricula across diverse degree and program frameworks. Fostering inter-departmental dialogue, expanding instructional collaborations, and enabling shared governance bolster efforts at the curricular level, while attention to regulations and student association support helps identify options for integrating regulatory curricula into specified programs.

### **Curriculum Integration Pathways**

Curriculum integration pathways address how to embed regulatory genomics and epigenetics into curricula at an institutional level. This instructional strategy aims to enhance understanding of complex traits and disease biology, drawing on theoretical foundations and empirical evidence that illuminate the importance of regulatory architecture. Many educational institutions-including academic programs, departments, and schools-utilize degree plans and program maps to outline curricular pathways. These frameworks can help formulate strategic plans for integrating additional concepts into specific courses. A student- and competency-centered framework grounded in cross-cutting concepts and interdisciplinary approaches to genomics, phenotypes, and regulation should underpin curriculum development. The strategies proposed in the previous section align well with this framework and extend the curriculum integration pathways to specified instructional methods, assessment strategies, resources, equity considerations, and implementation planning.

Examples of regulatory-genomics curricula currently deployed in selective educational programs further illustrate the rationale and guide the incorporation of additional pedagogical content. Courses at a variety of academic levels, covering both fundamental and advanced instructional material, have successfully integrated regulatory concepts and data into genomics curricula without compromising other core genomics topics. (M. Schmid et al., 2022)

### **Faculty Development and Collaboration**

An additional consideration for curriculum integration relates to the implementation and institutional readiness surrounding faculty development, opportunities for interdisciplinary collaboration, and the establishment of shared governance structures among faculty, departments, and programs (D. Shaffer et al., 2010). Developmental activities such as workshops, seminars, and special events could help foster community and support the adoption of enhanced curricula (M. Robbins et al., 2021). Creating interdepartmental teams with researchers of different backgrounds, expertise, and pedagogical experience to examine the integration of regulatory concepts into educational programs might be beneficial (A. Patel et al., 2024).

### **Evaluation at Program and Institutional Levels**

Curricular approaches, grading rubrics, and assessment methods must facilitate the systematic evaluation of proposed integrations. The impact of embedding regulatory genomics and epigenetics across curricula will be monitored at both program and institutional levels to determine reach and effectiveness. Various degrees of curricular integration across instructional modules will influence the modes of evaluation implemented.

Curricular evaluations must quantify both broad reach (i.e., which curricular modules have been integrated at which levels) and levels of reinforcement (i.e., the substantive depth and cognitive focus of integrated material) (M. Schmid et al., 2022). Directly correlating levels of curricular integration with student understanding of regulatory concepts may not be feasible, given the confounding influence of other curricular elements and the typical focus on genomics in conventional instructional programs. An indirect but readily executed assessment presently under consideration would quantify how well students link regulatory concepts to core genetics ideas vis-à-vis published regulations. When incorporated, such assessments will be administered in conjunction with standard genetics examinations, and statistical

correlations of differences between cohorts receiving regulatory instruction and those not receiving it will then be analyzed.

### **Challenges, Limitations, and Future Directions**

By establishing that regulatory genomic and epigenetic mechanisms critically inform gene expression, researchers have shifted moduli for the understanding of complex traits and the integration of regulatory content into educational resources. Nonetheless, substantial hurdles persist in terms of institutional readiness, curricular overlap, faculty collaboration, and the overarching influence of accreditation processes and educational cultures (M. Schmid et al., 2022). The cognitive framework for curricular integration comprises ingrained conceptual structures, pre-existing assumptions, epistemological practices, and the complex interplay of personal and environmental factors that scientists deploy to assimilate new ideas. Educational research elucidates the varieties of cognitive structures that frame empirical investigation and the potential for developing scientifically appropriate reasoning across disciplines.

Despite curricular materials originating in biomedical and biological sciences, motivation and need exist across domains, including machine learning, artificial intelligence, cybernetics, and design, to establish a conceptual rationale for integrating regulatory genomic content into genomics and genetics education.

### **Conclusion**

Much has been learned since Darwin's time about the phenomena of heredity and variation and how they can respectively produce similarity and diversity among organisms and explain what contributes to evolution. Key building blocks of contemporary concepts of heredity and variations, such as atoms, molecules, genotypes, and phenotypes, were introduced in the course of the 20th century along with the establishment of genes and the sequencing of genomes. Those building blocks have spawned a new discipline named genomics, a scientific and technological journey that is still ongoing and expanding far beyond genes, including regulatory portions of DNA, RNAs, and the characteristics of environments and conditions by necessity. Yet curricula of educational institutions continue to rarely address genomics and grossly emphasize the molecular structures of simple organisms or the Mendelian inheritance of mutant traits in the agricultural or laboratory settings of complex species, leading to students' misunderstandings and misconceptions of what contemporary genomics is and how it is pursued (M. Schmid et al., 2022).

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