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Paralympic Science in the Genomic and Post-Genomic Era: A Historical and Critical Literature Review

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A B S T R A C T

Exercise physiology has evolved from exercise biochemistry to sports and exercise genetics and, more recently, to network physiology and complex systems science of exercise: if the former was mostly reductionist, by incorporating cellular and molecular aspects, the latter leverages an integrative approach. Even though exercise physiology has been able to provide impressive insights into the genomic and post-genomic landscape that shapes the human response and adaptation to exercise and training, it has studied mostly able-bodied subjects, failing to include diverse, heterogeneous athletic populations. Only by diversifying athlete cohorts and testing them is it possible to better understand the profound interrelations and interconnections of health status, susceptibility towards injuries and diseases, underlying diseases/impairments, exercise physiology, response and adaptation to exercise, performance traits, and performance-related outcomes. Only by fully embracing pluralism and combining precision with equity, diversity, and inclusion, the "challenge of genomics" for people living with disabilities can be properly addressed and the "historic trauma" between (post-)genomic science and disability can be effectively solved and reconciled, providing the outlook necessary to decipher the molecular foundation of physical performance. In the present review, we will explore the historical evolution of sports genetics/genomics and post-genomics, utilizing a critical approach. More specifically, we will adopt a "critical disability perspective", according to which disability is conceived as a series of lived, meaningful experiences of people with disabilities, and as social and political constructs and interpretations.

Keywords: *paralympic sports; genomics and post-genomics; sportomics; equity, diversity, and inclusion*

1. Introduction

"Molecular and cellular exercise physiology", an emerging sub-discipline within the broader field of exercise physiology, has marked a significant shift in the scientific understanding of how the human body responds and adapts to physical activity at the biological level. This field was notably pioneered by Frank W. Booth, whose seminal work helped establish the foundational link between cellular mechanisms and exercise-induced physiological adaptations. Preceded by traditional exercise biochemistry, which primarily focused on metabolic pathways and energy systems during exercise, molecular and cellular exercise

physiology expanded the scope of inquiry by integrating the tools and concepts of molecular biology, genetics, and cell signaling into sports science (1-3). This biologically driven progression coincided with advances in molecular sciences, including the mapping of the human genome, and naturally evolved into what is now known as "sports and exercise genetics". This subfield, which was initially introduced under terms such as "kinesiogenetics" or "genetics of fitness and physical performance", gained momentum through the work of pioneers like Claude W. Bouchard, who was instrumental in framing the genetic basis of physical activity traits while working between Canada and the United States, and Vassilis Klissouras, who laid critical groundwork for understanding hereditary influences on endurance and muscular strength in Greece (4).

These foundational efforts underscored the heritability of various exercise-related phenotypes and established the importance of identifying genetic variants associated with performance traits, injury susceptibility, and adaptation to training stimuli. In the present review, we expand upon this historical trajectory by exploring the evolution of sports genetics and genomics (5) while incorporating a critical interpretive lens that challenges the prevailing assumptions of neutrality and universality within biomedical science. Specifically, we adopt a "critical disability perspective" (6), a framework that interrogates how the biological sciences, genomics included, have historically marginalized people with disabilities by treating disability primarily as a medicalized deviation from a presumed norm. Within this perspective, disability is conceived not only as a biological or functional condition but as a lived, contextualized experience, shaped by social, cultural, and political forces. This theoretical approach reframes scientific inquiry by emphasizing that the epistemologies of science, the ways we construct knowledge, are not detached from power relations and dynamics. Instead, they are embedded within societal norms that define who is included or excluded in the production of scientific knowledge. Therefore, applying a critical disability lens allows for a re-examination of how genomic and post-genomic sciences might inadvertently reinforce ableist assumptions or exclude populations with disabilities from participation, data representation, or benefit.

The present review invites an intersectional, equity-driven reflection on how research in sports genomics and post-genomics can evolve to be more inclusive, representative, and socially responsive, aligning with the broader values of equity, diversity, and inclusion (EDI) in science.

2. Materials and methods

In this critical narrative review, we explored the intersection of exercise physiology, sports genomics, and disability studies through a historical and sociopolitical lens. Our approach was rooted in critical disability theory and guided by principles of EDI. We applied a critical interpretive framework, drawing on: i) critical disability perspectives, which view disability as a lived and socially constructed experience; ii) intersectional bioethics, to examine how genomic and post-genomic science impacts diverse athletes, including those with disabilities; and, iii) pluralistic systems thinking, inspired by network science, to move beyond reductionist views of human performance.

We conducted a comprehensive literature search across scholarly databases including PubMed, Scopus, Web of Science, and Google Scholar, as well as relevant gray literature such as policy documents from international sports organizations and disability advocacy reports. Search terms included sports genomics, Paralympic, inclusive cohorts, and bioethics in sport. We focused on English-language sources that addressed both the molecular and sociocultural dimensions of genomics in sport, particularly regarding athletes with disabilities. Our thematic synthesis was organized around three main axes: namely, i) the historical evolution from exercise biochemistry to sport genomics and network physiology; ii) the critical gaps and biases in genomic and post-genomic research related to the exclusion of athletes with disabilities; and, iii) transformative opportunities for inclusive and equitable approaches to future research.

Throughout the process, we engaged in ongoing reflexivity regarding our disciplinary positions and the structural limitations of the field, particularly the scarcity of empirical genomic and post-genomic studies involving athletes with disabilities, which this paper seeks to foreground and address.

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3. Sports genomics and post-genomics

In the last decades, after the successful completion of the "Human Genome Project" (7), which has enabled the deciphering of the complete human DNA sequence and has provided impressive insights into the genomic landscape, research in the sports arena has entered the genomic and post-genomic era (8-11). Sports-genomics and post-genomics can be defined as the scientific disciplines that focus on the structural organization and function of the genome and its products (transcripts, proteins, and metabolites, among others) in athletes and, in particular, elite athletes (8). By positing that phenotypic traits are the complex result of the non-linear, multifaceted interplay between the (post-)genetic components and environmental variables, advancements in molecular technologies (including whole-genome sequencing) and related methodologies (genome-wide linkage and association studies) (8) would enable the design and implementation of personalized training and conditioning strategies to identify talents, enhance and optimize sports performance, target nutritional needs, prevent, and counteract the insurgence of sports injuries and exercise-related diseases (8-11).

Several genetic markers known as single-nucleotide polymorphisms (SNPs) have been found to be associated with athlete status (elite/world-class), performance (endurance-, power-, and strength-related phenotypes), and risk of developing injuries, despite only a few having been consistently replicated by collaborative projects and meta-analytical studies (8).

Initially relying on small, highly heterogeneous cohort studies, that genotyped a limited number of SNPs or insertion/deletion (indel) variants in athletes from different sports specialties, utilizing candidate gene approaches, sports genomics has been recently harnessing larger and more ambitious projects, such as ELITE, GAMES, Gene SMART, GENESIS, and POWERGENE (12, 13), under the umbrella of the "Athlome Project Consortium" (12) and of the "Molecular Transducers of Physical Activity Consortium" (MoTrPAC)(14)

Some of the reasons underlying the low replicability and reproducibility of sports genomics-based studies, besides their sample sizes and methodological issues, could be that i) gene regulation and expression are complex, ii) physical performance is a complex phenotypical trait, and iii) genotype-phenotype interactions are complex as well (9, 15, 16). Significant portions of the mechanisms and driving events of gene modulation, including DNA methylation and RNA and histone modifications (known as epigenetic patterns or epi-markers), that impact DNA availability for transcription, are integrated into the field of epigenetics/epigenomics (17).

A key role in epigenetic regulation is played by microRNAs (also known as miRNAs), which are small noncoding RNAs, about 18-25 nucleotides in length (18). miRNAs affect the protein levels of the target mRNAs and, in turn, can be affected by epigenetic modifications, the interplay of which can result in complex miRNA-epigenetic feedback loops. The field of sports miRNAomics (19, 20) is an emerging molecular specialty, which is expected to broaden our understanding of regulatory mechanisms and physiological processes of systemic changes in response to exercise and training (20).

Besides sports genomics, transcriptomics, epigenomics, and miRNAomics (21, 22), the last years have also seen an increasing trend of sports proteomics- and metabolomics-based studies, of increasingly higher quality, better design and implementation, more clinically oriented, and mass spectrometry-based [23-25]. These studies have involved larger numbers of participants and have contributed to the identification of larger numbers of metabolites (23-25).

An emerging sports discipline is represented by sports microbiomics (26, 27), which is the sports discipline devoted to the study of the complex and dynamic populations of microorganisms harbored by the human gastrointestinal tract, the gut microbiota (28), in athletes. The gut microbiome is able to exert a marked impact on the host during both homeostatic conditions and diseases. Multiple factors, including exercise, have been found to influence the human gut and its microbiota in terms of intestinal permeability and microbial composition, respectively. The relationship between exercise and microbiome is bidirectional, with the former impacting the gut microbiota, favoring a higher microbial diversity, causing shifts toward bacterial species involved in the biosynthesis of amino acids, and in the metabolism of carbohydrates and fibers(26-29). The gut microbiome, in turn, impacts performance-related outcomes. This mutual interconnection is mediated/moderated by several variables, including athlete

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status, intensity, and duration of exercise and training, among others (26-29).

Big Data- and omics biomarkers-based (30) initiatives, as well as investigations relying on increasingly complex frameworks, such as system and network physiology (31), and converging into what has been termed "sportomics" (32, 33), a holistic, comprehensive molecular approach, are anticipated to elucidate the cellular and molecular basis of exercise and physical activity (6, 34) and advance the sports and exercise sciences.

4. Disability and genomics/post-genomics: rethinking disability (and genomics/post-genomics)

However, paradoxically, sports genomics and post-genomics have generally excluded athletes with disabilities from research, despite the profound inter-relation between disability and genetics/genomics. As posited by Scully(35, 36), genetics/genomics and disability are connected by a "pragmatic and clear" logic (35), in that genetics/genomics deals with uncovering and dissecting the molecular paths from genotype to phenotype. In contemporary society, disability constructs, social representations, and structural ableism are interwoven with genetic essentialism and meliorism, according to which a person with a disability is "a phenotype that deviates from the norm" (35). Also, disability and genetics/genomics are closely, methodologically linked, since genetics/genomics insights on mutations that affect or even the pathways of gene expression and its regulation can "illuminate the normal routes of genotype-to-phenotype causation. Therefore, geneticists have always been interested in illness and disability as the clinical manifestations of allelic variation, independent of any practical aim of alleviating genetic conditions" (35). However, precision (sports) medicine initiatives and *consortia* rarely recruit subjects with disabilities and, from an intersectional standpoint, marginalized gender, racial, and ethnic communities, whilst including disability-specific cohorts may advance our current understanding of disability (37, 38).

Some disability activists, advocates, and members of the community have attempted to stress the importance of disentangling the biological contributions (i.e., phenotype-related features) from those social and/or environmental (in terms of disadvantages deriving from societal arrangements and expectations of how a "perfect" body should appear and be functioning), differentiating, as such, between "impairment" and "disability" (39), in the effort to shift from a "medicalized"/"geneticized" view of disability (40) to a bio-psycho-social model of disability (41).

5. How people with disabilities could benefit from genomics/post-genomics

Genetics and genomics hold significant potential to improve the lives of people with disabilities by addressing both the biological and therapeutic aspects of their conditions. They can, first, contribute to a deeper understanding of the natural history of various disabling conditions by elucidating their etiopathogenesis, inheritance patterns, and prognostic markers. This knowledge allows for the identification of underlying genetic variants that influence disease progression and response to interventions, thereby enabling the development of condition-specific management strategies (35). Second, genomics offers the ability to capture the heterogeneity of these conditions, recognizing that disabilities often arise from diverse genetic and environmental interactions. By mapping these variations, researchers can better categorize phenotypes and identify subgroups of patients who may benefit from tailored interventions or specific rehabilitation protocols. Third, genomics can improve differential diagnosis, particularly in cases where clinical symptoms overlap between multiple disorders, by pinpointing causative genetic mutations or expression patterns that distinguish one condition from another. This precision is critical not only for clinical decision-making but also for reducing misdiagnosis and unnecessary treatments (35). Fourth, genomic technologies allow for the presymptomatic identification of late-onset or progressive disorders, providing a window for early lifestyle interventions, targeted therapies, or preventive measures. Early detection of such conditions, particularly through predictive genetic testing, can significantly alter health trajectories and enhance long-term quality of life. Fifth, genomics enables the provision of personalized treatment and management plans, leveraging data on gene-drug interactions and individual metabolic pathways to select the most effective medications or training regimens. This is particularly relevant in precision rehabilitation and sports medicine, where genomic insights can guide adaptations in

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training loads, nutritional strategies, or assistive technology design for athletes with disabilities (35). Lastly, advances in molecular biology and computational genomics are accelerating the discovery of druggable gene targets and the development of innovative theranostics approaches, such as individualized gene therapy, CRISPR-based genome editing, pharmacogenomics, and antisense oligonucleotide treatments. These disruptive technologies promise to not only alleviate symptoms but also potentially modify or reverse the course of certain disabling conditions (35). When combined with multi-omics approaches, such as epigenomics, proteomics, and metabolomics, genomic research can generate a holistic view of how molecular networks interact with training, environmental factors, and assistive technologies. This integrative perspective is essential for designing interventions that are not only biologically precise but also socially and ethically aligned with the principles of equity, diversity, and inclusion.

6. Paralympic science meets genomics/post-genomics sciences

Illuminating as a case study is the clinical story of the UK paracyclist Tom Staniford, who lives with a rare genetic metabolic condition, known as the MDP syndrome, characterized by a constellation of diseases, including mandibular dysplasia, deafness, and progeroid features (42). The identification of the genetic component of this disabling condition has been made possible by technological and scientific advancements in the arena of genomic and post-genomic research (42). In this case, as well as in other similar cases, omics sciences can enable a better understanding not only of the role of genetic variation and its impact on cardiorespiratory fitness and performance-related outcomes, but also of gene-exercise interactions in the complex biology of adaptation to exercise and physical activity (43, 44).

Exercise should be considered as an effective drug (45), with generally beneficial impacts and rare side effects, but it can also be, sometimes, a risk factor for some disabling conditions, such as amyotrophic lateral sclerosis, as shown by convergent evidence from Mendelian randomization, transcriptomics, and risk genotypes (46).

Moreover, incorporating disability in precision medicine projects would not only foster and enhance population health, but also, and especially, promote an equitable, person-centered approach and enable the achievement of social justice for one of the groups most disproportionately impacted by health disparities (47). According to a survey conducted to explore the points of view of people with disabilities about precision medicine research, the community is highly willing to support studies by providing and sharing (socio-demographic, lifestyle, biological, and medical) data. On the other hand, according to 76% of the interviewees, there exist various obstacles and barriers that should be removed. Several primary precision medicine research sites (including those based in medical schools, research centers, and universities) are, indeed, often difficult to access, have limited knowledge of accommodations, rarely implement accommodation policies and procedures, and are tremendously underrepresented by colleagues with disabilities. Researchers may lack cultural competencies, which are particularly required when dealing with diverse populations and people from largely marginalized groups, such as those living with disabilities (47).

Efforts should be made to have a diverse, representative, cross-disciplinary team of precision sports medicine researchers, including sports scientists, coaches, geneticists, genetic counselors, and genome scientists, molecular biologists, laboratory technicians, practitioners in the field of physical medicine and rehabilitation, as well as clinical and sports psychologists, sociologists, and experts in disability studies, among others (37).

Inclusive and “equitable diversification of genomics” (and post-genomics) research, in particular in the field of precision sports medicine research, should be urgently prioritized (14, 48). It is highly recommended to proactively pursue community engagement and outreach by developing disability-sensitive strategies that empower and benefit people with disabilities.

7. Conclusions and future research directions

Since the inception of exercise biochemistry and the subsequent emergence of sports genomics and post-genomics, the field of exercise science has undergone significant scientific transformation. From focusing on biochemical pathways to decoding the genome and integrating complex systems approaches such as network physiology and complex systems science of exercise (31,

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49), the discipline has continuously expanded its methodological and conceptual scope.

Yet, this evolution has not been accompanied by a proportional diversification of research subjects. Most notably, athletes with disabilities, despite representing a vital and growing segment of the athletic population, have remained largely invisible in omics-based research and precision sports medicine initiatives. This systematic exclusion reflects a broader issue within biomedical research: the tendency to standardize and homogenize study populations, often in ways that marginalize those who do not fit normative bodily ideals. The failure to include athletes with disabilities in genomic and post-genomic studies not only limits the scope of scientific discovery but also perpetuates structural ableism within sports science (35, 36). Genomic and post-genomic technologies offer powerful tools to uncover the biological mechanisms underlying performance, adaptation, recovery, and injury susceptibility (8-11). However, without inclusive sampling and cohort design, the results risk being incomplete, biased, or even misleading. To redress this imbalance, researchers must reframe the foundations of sports genomics and post-genomics to incorporate diversity and intersectionality as essential scientific principles, rather than optional ethical considerations (37, 38).

This involves designing studies that actively include athletes with disabilities, not only as subjects but as co-creators of knowledge. It also necessitates cultural competence within research teams, interdisciplinary collaborations with scholars with disabilities, and structural accommodations that make participation in research accessible for people with varying physical, sensory, or cognitive conditions (47).

Inclusion of athletes with disabilities in omics and precision sports medicine research is not merely a matter of representation: it is a scientific imperative. Only through the study of complex, heterogeneous populations can we fully understand the multifactorial nature of physical performance and health. Variables such as baseline impairments, assistive technologies, training adaptations, and social environments interact in unique ways within disabled athletic populations. These interactions may offer novel insights into exercise physiology, resilience, metabolic plasticity, and the genomic and post-genomic regulation of adaptation.

Furthermore, pluralism in research, embracing both molecular precision and social context, can help bridge the longstanding epistemological divide between genomics and disability studies (35, 36). Addressing the so-called "genomic challenge" (36) for people with disabilities requires reconciliation of the historical tensions between medicalized views of impairment and the lived realities of disability as shaped by social and political structures. Genomic and post-genomic science must evolve beyond reductionist frameworks toward integrative, equity-centered paradigms.

In conclusion, the future of sports and exercise science lies in its capacity to be inclusive, critical, and interdisciplinary. By embracing pluralism, fostering community engagement, and ensuring accessibility at every stage of the research process, we can develop a truly representative science of human performance. Only then can we resolve the "historic trauma" between genome science and disability (35) and generate the comprehensive understanding needed to decode the molecular foundation of physical activity, not just for some, but for all (17).

Authors' Contributions

Authors equally contributed to this study.

Declaration

In order to correct and improve the academic writing of our paper, we have used the language model ChatGPT.

Transparency Statement

Data are available for research purposes upon reasonable request to the corresponding author.

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Declaration of Interest

The authors report no conflict of interest.

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