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Genetic Testing for Sports Performance, Responses to Training and Injury Risk: Practical and Ethical Considerations

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Abstract

This paper addresses practical and ethical considerations regarding genetic tests to predict performance and/or risk of exercise-related injury or illness. Various people might wish to conduct sport-related genetic tests for a variety of reasons. For example, an individual might seek personal genetic information to help guide their own sport participation. A sports coach might wish to test young athletes to aid team selection or individualize training. A physician might want to predict the risk of injury or illness in athletes and advise regarding selection or preventative measures. An insurance company might seek to estimate the risk of career-threatening injury for athletes based partly on genetic information. Whilst this information is, in part, encoded in our DNA sequence, the available tests allow generally only a poor prediction of the aforementioned variables. In other words, the current genetic tests and analysis methods are not powerful enough to inform important decisions in sport to a substantial degree. It is particularly disappointing that more than half of the commercially available genetic tests related to exercise and sport do not appear to identify publicly the genetic variants they assess, making scrutiny by academic scholars and consumers (or their representatives) impossible. There are also challenging ethical issues to consider. For example, the imposition of genetic tests on individuals (especially young people) by third parties is potentially susceptible to abuse. Scientists and practitioners should understand the limitations of the tests currently available, the ethical concerns and the importance of counselling before and after testing so that they are only used in a responsible manner.

The focus of this paper is on the potential use of genetic tests to predict performance and/or the risk of exercise-related injury or illness. Several earlier papers of this book, including those of Venezia and Roth (regarding genes and training adaptations), Ahmetov et al. (regarding genes and sport performance), Rahim et al. (regarding genes

and musculoskeletal injuries) and Collins et al. (genes and musculoskeletal phenotypes) [this vol., pp. 29–40, 41–54, 68–91, 92–104], contain information and ideas relevant to the notion of testing athletes or other individuals for sport- and exercise-related traits. However, this review will deliberately focus on both the scientific and ethical issues regarding the validity, utility and practicality of genetic testing of athletes at the current time.

Commercially Available Tests

There are already several commercial operations that offer 'mail order' or 'direct-to-consumer' (DTC) genetic testing of polymorphisms apparently associated with physical performance capacity or exercise-related health. We believe the first commercial operation began in Australia in 2004 and was marketed as the ACTN3 Sports Performance Test™ by the company Genetic Technologies. Most recently, surveys [1, 2] of available tests identified 39 companies providing DTC genetic tests marketed in relation to human sport or exercise performance or injury (table 1).

In that recent analysis mentioned [1], the most commonly tested variant remained the R577X variant in the *ACTN3* gene, tested by 89% of the 18 companies that appeared to present information about their genetic tests on their websites. That observation corresponds with assessments that *ACTN3* R577X is currently the polymorphism with the strongest scientific evidence in support of an association with athlete phenotypes [3–5]. However, there is limited information that can be gleaned from discrete, single-marker genetic tests at common polymorphisms, beyond an 'interest' at an individual level. Therefore, the companies that test only a single variant should clearly not claim to provide information on which personal exercise training or sport decisions can reasonably be made. The level of qualification and explanation given alongside the raw genetic information to individuals also varied considerably, as pointed out previously [6]. Some companies appear to treat the genetic data in a cautious manner and are suitably careful not to extend preliminary scientific findings into claims that extend beyond the published scientific literature base. However, that sensible approach is not universally adopted, and thus some of the claims (overt or implied) for the extent of the usefulness of the single genetic marker information are not supported by sufficiently strong scientific evidence. Thus, some individuals might make decisions about their personal exercise and sport participation on the basis of DTC genetic test information that are not warranted. It is therefore understandable to some extent why the majority of the companies identified [1] as offering defined DTC genetic tests assessed a panel of multiple genetic variants. The next most tested variant was in the *ACE* gene (61% of the 18 companies), while the median number of variants tested was 6, ranging from 1 to 27. However, as one considers genetic variants beyond those in the *ACTN3* and *ACE* genes that are reasonably well studied, the level of scientific evidence to support the choice of any particular polymorphism reduces

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Table 1. Companies found to be providing DTC genetic tests marketed as being related to sport and exercise performance or sports injury

Company	Website name	Variants tested, n	Genes of variants tested (according to websites/client reports)
23andMe	23andme.com	1	*ACTN3*
Advanced Business Services	abservices.eu	n.f.	n.f.
Agoga	agoga.com.au	n.f.	n.f.
Asper Biotech	asperbio.com	2	*ACE, ACTN3*
Athletigen	athletigen.com	18	*ACTN3, ADRB2, AGT, AMPD1, CILP, COL1A1, COL5A1, CREB1, IL1B, HIF1A, MMP3, NAT2, PPARD, PPARG, PPARGC1A, RAD23A*
Atlas Sports Genetics	atlasgene.com	1	*ACTN3*
C2DNA	c2dna.com	n.f.	n.f.
Cosmetics DNA	cosmetics-dna.com	n.f.	n.f.
CyGene Direct	cygene.infinityarts.com	6	*ACE, APOE, BDKRB2, ENOS, VDR*
DNA Fit	dnafit.com	21	*ACE, ACTN3, ADRB2, AGT, BDRKB2, COL1A1, COL5A1, CRP, GDF5, GSTM1, GSTT1, IL6, IL-6R, NRF-2, PPARA, PPARGC1A, SOD2, TNF, TRHR, VDR, VEGF*
DNA Spectrum	dnaspectrum.com	7	*ACE, ACTN3, ADRB2, ADR3B, ENOS, FTO*
DNAeX	dnaex.net	14	*ACE, ACTN3, ADRB2, AGT, BDKRB2, COL5A1, CRP, IL6, NRF, PPARA, PPARGC1A, TRHR, VDR, VEGF*
DNAlysis	dnalysis.co.za	19	*ACE, ACTN3, ADRB2, AGT, BDRKB, COL1A1, COL5A1, CRP, GDF5, IL6, IL-6R, NRF-2, PPARA, PPARGC1A, SOD2, TNF, TRHR, VDR, VEGF*
GenePlanet	geneplanet.com	2	*ACTN3, PPARA*
Genetic Center	genetic-center.com	n.f.	n.f.
Genetic Performance	geneticperformance.com	n.f.	n.f.
Genetrainer	genetrainer.com	n.f.	n.f.
Gknowmix	gknowmix.com	n.f.	n.f.
Gonidio	gonidio.com	27	*ACE, ACTN3, ADRA2A, ADRB1, ADRB2, AMPD1, BDKRB2, CHRM2, CK-MM, COL1A1, COL5A1, DIO1, EPOR, HBB, HIF-1, MCT-1, MMP3, NOS3, PPARD, PPARGC1, VDR, VEGF*
IgnitePlay	igniteplay.com	n.f.	n.f.
Institute for Optimum Nutrition	ion.ac.uk	n.f.	n.f.
Lyfgene DNA	lyfgene.com	n.f.	n.f.

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Table 1. Continued

Company	Website name	Variants tested, n	Genes of variants tested (according to websites/client reports)
Molecular Testing Labs Fitness	mtlfitness.com	9	*ACTN3, EDN1, INSIG2, LIPC, LPL, MMP3, PPARD, PPARGC1A, SLC30A9*
Musclegenes	musclegenes.com	n.f.	n.f.
MyInnerGo	myinnergo.com	n.f.	n.f.
MyRISQ	myrisq.com	n.f.	n.f.
Nordic Laboratories	nordiclabs.com	20	*ACE, ACTN3, ADRB2, AGT, BDRKB, COL1A1, COL5A1, CRP, GDF5, IL6, IL6R, NRF, PPARA, PPARGC1A, SOD2, TNF, TRHR, VDR, VEGF*
Nutragene	nutragene.com	n.f.	n.f.
Pathway Genomics	pathway.com	n.f.	n.f.
Phenom Biosciences	iamaphenom.com	n.f.	n.f.
PlayDNA	playdna.co.uk	n.f.	n.f.
Simplified Genetics	simplifiedgenetics.com	5	*ADRB2, ADRB3, APOE, PPARG*
Sports Gene	sportsgene.ee	6	*ACE, ACTN3, AMPD1, GDF8, NOS3, PPARGC1A*
The Wellness Gene	wellnessgene.com	23	*ACE, ACTN3, AMPD1, BDKRB2, CHRM2, CKMM, COL1A1, COL5A1, DIO1, EPOR, HBB, HIF1A, MCT1, MMP3, NOS3, PPARD, PPARGC1A, VDR, VEGF*
TheMakingsofMe	themakingsofme.com	3	*ACTN3, HIF1A, NOS3*
ThinnerGene	thinnergene.com	n.f.	n.f.
ThriveLondon	thrivelondon.com	n.f.	n.f.
Woblab	woblab.com	6	*ACE, ACTN3, AMPD1, GDF8, NOS3, PPARGC1A*
XRGenomics	xrgenomics.com	n.f.	n.f.

Data may not be 100% accurate because it is dependent on the ability to navigate the websites appropriately, and updating of the information provided on the websites. Gene names are in most instances listed verbatim as presented on the company websites, even though some gene names given did not conform to the standard nomenclature. n.f. = Information not found. From the supplementary file in Webborn et al. [1], with permission.

considerably in volume, and the scientific evidence is considered weak by the majority of sport and exercise genetics researchers [1, 4, 7, 8], including ourselves. While commercial pressures undoubtedly exist, it would be wise, and more responsible, to wait for a greater scientific consensus before offering tests that currently have only weak supporting evidence. Counselling that puts the genetic information – including the limitations of its usefulness – into the proper context is recommended as a minimum, although not even a sophisticated counselling service can resolve scientific controversy.

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It is particularly disappointing that 54% of the companies offering DTC genetic tests related to exercise and sport did apparently not publicly state which genetic variants they assessed [1]. Again, while commercial pressures undoubtedly exist, it is impossible for anyone – academic scholar or otherwise – to scrutinize the service provided by the companies if the detail is not presented to consumers. The detail is absolutely crucial, because quite literally millions of genetic tests could theoretically be conducted, and the choice of variants to be tested – and how those results are interpreted – is fundamental to the usefulness of the test. Such apparent secrecy is presumably due to commercial sensitivity in part, although failing to publicize the tests conducted is arguably a tacit admission that the scientific evidence supporting the genetic variants chosen is weak. Perhaps the specific genetic variants tested by a particular company will change over time as scientific knowledge in this field progresses, but if that happens, then it severely questions the validity of the original test.

In broad terms, based on scientific evidence, the information provided by these tests may be of interest to many people and may help individuals (or sports coaches, etc.) attempt to 'better understand' their observed physical limitations to performance or training adaptations. However, there is currently little evidence (there is lack of replication, in particular [9]) that these kinds of tests provide information regarding either predisposition for a particular sport or prediction of the training response likely to occur to a particular training programme that are useful in a practical sense. For example, a thorough multidisciplinary analysis of the efficacy of these tests in talent identification would need to be conducted to determine whether genetic data provide information not already captured within other, traditional non-genetic tests of physiological, anthropometric and performance characteristics that are already routinely used in talent identification.

Nevertheless, the availability of such tests for virtually anyone to access is certainly an interesting development and probably heralds a new era of genetic testing for all manners of individual characteristics. It is likely that such tests will become more widely requested, at least in part, because recent legislation in the USA ensures that consumers need not fear insurance or employment discrimination on the basis of genetic test results [10]. However, a significant debate exists regarding the science that is purported to underpin such tests. In addition, there are wider ethical concerns regarding issues such as the confidentiality of data, the need for counselling when interpreting personal genetic data, the use of genetic data in assessing insurance risk, etc. We will now address such issues in this paper.

Is There a Fundamental Difference between Genetic Tests and Non-Genetic Tests?

Discrimination on the basis of partially inherited factors is already common in sport today – for example, when strength is measured to identify children that have a talent for weightlifting or to select a national weightlifting team. So does it matter whether

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talent is identified by genetic or by non-genetic tests? Is there a fundamental difference?

To give an example, one could rightly ask: 'What is the difference between a performance test that measures a variable which predicts ~2% of an individual's muscle power as opposed to the commercially available *ACTN3* R577X genetic test which perhaps measures something very similar?' The term 'genetic exceptionalism' is sometimes used in this debate meaning that genetic tests are special and thus require specific legislation that is different from that for other biological tests [11]. In their analysis, Green and Botkin [11] focus on medical tests and conclude that 'no clear, significant distinctions between genetic and non-genetic tests justify a different approach [...]' although they state that genetic tests may lead to stigmatization, family discord and psychological stress – but much of this also applies to some non-genetic tests such as HIV tests.

The working party that developed the BASES position stand in *Genetic Research and Testing in Sport and Exercise Science* [12] identified 2 fundamental differences between genetic and non-genetic (performance) tests, and we include a third in this paper as we did previously [13]:

(1) The information gained from a genetic test does not change with age, whereas the information derived from a traditional performance test, and consequently the predictive quality of that test, does change with age

(2) Not all the predictions that can be made with a genetic test may be known at the time when the genetic test is conducted

(3) Genetic tests have more implications for relatives and partners than other tests

These three points are now discussed in more detail:

(1) The genome of an individual and the variations therein are constant throughout life (there are exceptions not relevant for this argument). Consequently, genetic tests can be performed as soon as the DNA of an individual can be obtained – even before birth. This is fundamentally different from other tests such as a lactate test where the information derived from the test, and consequently its predictive quality (for example, the ability to predict marathon running ability) depends very much on the age when this test is performed. This difference is important because it opens up possibilities for the misuse of genetic tests, especially when used before birth or in minors. One scenario could be that these tests are used to select embryos on the basis of sporting, intellectual or other abilities (a 'new eugenics'?). Also, with young children such tests could be used to make decisions for or against a sporting career.

(2) Both genetic and non-genetic performance tests may later be linked to other variables such as disease. We think that this risk is higher for genetic tests than for other performance tests. However, common performance-related variables have also been linked to disease. For example, muscle strength has been inversely associated with mortality [14], which means a hitherto unanticipated higher risk of death for individuals who had previously performed poorly in a strength test. However, our opinion is that the risk of an unanticipated disease link, especially to a specific disease, is

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probably higher for genetic tests than for other biomedical tests. One past example is a polymorphism in the *APOE* gene (which encodes a protein important for lipid transport). Based on 2 loci, there are 3 polymorphic forms: APO E2, E3 and E4. The APO E4 variant was initially shown to be associated with limited differences in lipid profile but only later with late-onset familial Alzheimer's disease [15]. Thus, individuals who had previously been tested for a genetic variant that was associated with their lipid profile now retrospectively had information about their likelihood of suffering from the severer Alzheimer's disease. How can we deal with the risk of unanticipated future links of genetic test results to severe disease? A pragmatic solution would be to make mandatory genetic counselling necessary so that individuals are aware of this risk before deciding whether to proceed or not with a genetic test.

(3) A third difference is that genetic tests have more direct implications for relatives than other tests, as Green and Botkin [11] point out. Some non-genetic tests have important implications for others – for example, a positive HIV test result may not only affect the individual, but also have far-reaching implications for relatives, plus current and previous sexual partners. However, genetic tests are *always* also predictive for close relatives and this should be taken into account when performing genetic tests. Again, mandatory genetic counselling could be useful to at least ensure that individuals understand the implications of genetic test results for their relatives.

The first difference we have highlighted in particular, and its resultant consequences such as the potential selection of embryos, warrants the use of the term 'genetic exceptionalism'. Also, for now at least, scientists must accept that 'people see genetic information as special' [16], even if in reality the information obtained by genetic and non-genetic tests can in some instances be very similar.

How Powerful Are the Genetic Tests That Currently Exist?

By the end of 2007, there had been over 200 genetic variations associated with performance and health-related fitness phenotypes [17], and that number continues to increase although it has not been documented in the same comprehensive way in recent years. However, in many cases, there has still only been a single positive association with a relevant phenotype, and consistent replication of the reported associations is obviously needed to increase confidence in the associations.

Focusing initially on rare mutations, we are aware of just two that appear to have a powerful 'positive' influence on exercise-related phenotypes (although many rare mutations exist that have powerful 'negative' influences on exercise-related phenotypes). One rare mutation exists in the family of the Finnish cross-country skier Eero Antero Mäntyranta, where over 200 g of haemoglobin per litre of blood and extremely high haematocrit values of >60% were reported [18]. Erythropoietin (EPO) levels were normal but the mutation enhanced sensitivity to EPO. The responsible mutation in the EPO receptor (*EPOR*) gene was subsequently identified [19] as a premature stop

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codon that shortens the protein by 70 amino acids. A more active EPOR protein is the result and is likely to have contributed to Mäntyranta winning 3 gold and 4 other medals at the Olympic Games during the 1960s. Haematocrit in excess of 50% would attract investigation from the antidoping authorities, although the WADA 'Athlete Biological Passport' concept combined with DNA analysis may allow an athlete competing today with such a mutation to demonstrate that no erythropoiesis-stimulating agents had been used.

A second naturally occurring rare mutation, this time with profound effects on muscle growth, has been observed in the myostatin gene (*MSTN* [20]). The authors reported the existence of a boy who was 'extraordinarily muscular, with protruding muscles in his thighs and upper arm'. The boy was homozygous for an extremely rare G-to-A intronic mutation in the *MSTN* gene and his muscle tissue showed no evidence of functional MSTN protein. This observation in a human parallels the deliberate knockout of the myostatin gene in mice, which has resulted in pronounced skeletal muscle fibre growth [21]. However, it is not certain that health status (e.g. cardiac function) will not be compromised by the absence of functional MSTN protein, and there may be other detrimental changes such as changes in tendon properties [22]. Nevertheless, one possible kind of genetic test for physical performance could be to screen athletes for rare mutations such as those described in the *EPOR* and *MSTN* genes. The rarity and heterogeneity of such powerful mutations means that they would need to be identified using sequencing technology that allows base-by-base examination of relevant chromosomal regions, and even then would probably have a very low success or 'hit' rate. Nevertheless, transgenic mouse models suggest that there are multiple genes whose mutation can have large effects on performance [23], and it seems likely that some of these mutations occur in some humans. Thus, more athletes with rare, powerful mutations will probably be discovered. This information might help to explain the physiological capacity of those individuals, provide clues regarding the type of events in which they might excel and even provide information that might be useful in the individualization of training.

In contrast to rare, powerful mutations, there are many common polymorphisms that are usually less powerfully associated with performance-related phenotypes. Here, we will consider as an example just *ACTN3* R577X, while others are addressed in other reviews.

A common polymorphism exists in the *ACTN3* gene in which the element encoding arginine (R) may alternatively be a stop codon (X) that produces a truncated protein molecule with no known function. Studies of elite Australian [24] and Finnish [25] sprint/power athletes found none were of the XX genotype. An *ACTN3* knockout mouse displaying characteristics summarized as a fast-to-slow muscle phenotype change helps to explain mechanistic links between *ACTN3* genotype and physical performance phenotype [26, 27]. These data suggest it is virtually impossible to become an elite sprint or power athlete without the R allele of *ACTN3*, suggesting a powerful influence of the *ACTN3* common polymorphism. However, in the general

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population it appears that only at most ~2% of interindividual variability in muscle strength, sprinting speed and competitive racing distances are related to the *ACTN3* genotype [28–30], and this seems somewhat at odds with the striking absence of the XX genotype in most elite sprint/power athletes. This paradox may be analogous with a classic study demonstrating that while the maximal rate of oxygen uptake may have good statistical power in predicting endurance running performance amongst a wide range of running abilities, when a narrow (elite) range of performance is considered it is then running economy, a different phenotype, that becomes the dominant factor influencing performance [31]. Perhaps the *ACTN3* genotype (and thus the presence/absence of α-actinin-3 protein in muscle) is equivalent to running economy in that analogy, in that only amongst highly trained athletes does the practical significance of the *ACTN3* genotype increase to a meaningful extent. Nevertheless, even then, the *ACTN3* XX genotype does not seem to completely preclude success in power events [32]. So the practical use of an *ACTN3* genotype test to inform an individual (or his/her coach, for example) about future performance potential is thus still not clear, although of all common polymorphisms *ACTN3* currently shows the most potential in this regard. Despite scientific uncertainty, one can understand individuals interested in exercise and sport wishing to learn about their own genetic composition at this locus – even if this discrete variant only imparts a very small proportion of the total genetic influence. So the provision of a service for the testing of the *ACTN3* R577X polymorphism on a commercial basis could be seen as meeting an understandable public interest and providing information that has at least some replicated scientific evidence to justify the activity. Nevertheless, the predictive value of such tests in the context of training responses or talent identification in sport is virtually zero [1, 8].

It is our view that while *ACTN3* and other genotypes show promise, a large monogenic influence of a common polymorphism on physical performance or injury phenotypes is extremely unlikely. Future genetic testing of athletes will therefore need to account for a greater proportion of the genetic influence on interindividual variability via simultaneous consideration of genetic variation at a number of loci. The principle behind this polygenic approach has been demonstrated [33], although more research is needed before the application of genetic algorithms to athletes can proceed with a valid scientific basis. Major decision-making regarding the careers or training/medical environment of athletes, based largely on the genetic testing of those athletes, is not scientifically justified until more research is conducted and therefore would be unethical at the present time. An increased predictive power of genetic testing in athletes will be dependent upon the quality of the data that emerge from the future research that will itself be dependent on the application of more advanced technology such as cheap, fast, whole-genome sequencing.

It is therefore doubtful whether the body of knowledge is sufficiently strong for practical applications such as selection of talented athletes for intensive training, individualization of training regimens to improve performance or modulation of the

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training load to minimize injury risk. Perhaps at the most elite level of sports performance, where every little piece of information about an athlete is most likely to be considered sensibly in the context of much other data, some tentative conclusions might be reached and any implementation evaluated extremely closely. However, the careful wording of the previous sentence is very deliberate, and there is a requirement for greater replication of the >250 genotype-phenotype associations reported to date [9, 17, 34] before genetic testing in sport and exercise has more widespread utility. This is because the common polymorphisms identified to date only account, individually, for a small proportion of the interindividual variability in phenotype. To explain a larger proportion of the variability, either rare variants of large effect or favourable combinations of many common variants need to be identified. Evidence regarding rare variants of large effect is currently limited to very few documented examples [19, 20]. Using several common variants, elite athletes in certain sports have at least been shown to differ in polygenic profile from non-athletes and from elite athletes in other sports [35–38], and such differences will become clearer as broader panels of appropriate variants are included [33]. Quite recently, 21 single-nucleotide polymorphisms were identified that appear to capture the heritable component (approx. 50% of total interindividual variability) of the responsiveness to endurance training of the maximal rate of oxygen uptake phenotype [39]. While this observation also needs replication (and that is more easily written than conducted in practice), the applications of this kind of insight into an individual's potential to respond to training in a sporting context, as well as an exercise-health-fitness context, are obvious.

Who Should Be Able to Request Genetic Tests?

With an accumulating number of available genetic tests, a wide range of genetic testing scenarios seems inevitable in the sport and exercise context. The 5 examples below show different individuals (athletes, parents, coaches, physicians) requesting genetic tests either for themselves or for others for a variety of purposes:

(1) Genetic performance testing: parents might request genetic tests for genes that determine adult peak maximal oxygen uptake for their child in order to decide whether to send their offspring to a special sports school or not

(2) Genetic testing for personalized training programmes: a coach might request genetic tests for trainability polymorphisms in order to decide whether weightlifters should take part in a high-volume or high-intensity strength training programme (see Roth [40] for a more detailed debate)

(3) Genetic sports disease testing: sports associations and their physicians might use genetic tests to screen for variants associated with sudden death in order to identify individuals that are at high risk and to exclude such individuals from competing. A similar but non-genetic screening programme is performed in Italy [41] and has

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reduced sudden deaths but has also led to the exclusion of elite athletes from competitions

(4) Genetic sports injury testing: an individual could request a DTC genetic test for tendon gene variants to predict the frequency of injury in order to decide whether to embark on a career as a professional football player or not

(5) Genetic insurance risk testing: an insurance company might request genetic tests for injury genes in order to determine the insurance premium for a professional football player

At the moment, most people would probably accept that adults should not be prohibited from requesting genetic tests for performance or sport and health-related traits for themselves, in order to assist making life choices. We recommend, however, even in the case of DTC tests [42] such as those listed in table 1, that these tests are accompanied by some genetic counselling. This could include counselling about potential unanticipated associations with disease, implications for relatives and other information which has been summarized in a review on 'ideal' genetic counselling [43]. The other recommendation is that genetic tests should, for the time being at least, only be allowed to be requested by mature individuals (in the sense of mental capacity, in specific relation to the issue of genetic testing in sport) who understand the implications of a test.

Serious ethical concerns arise if genetic tests for an individual are requested by others. In the sport context this could be physicians, parents or coaches, and such tests could be used to discriminate in favour of or against athletes on the basis of performance-related or health-related genetic information. Some of these concerns are highlighted by a real case [44]: Eddy Curry was a professional NBA basketball player who missed games due to cardiovascular symptoms. His team (the Chicago Bulls) requested a genetic test for him based on the advice of a cardiologist. The athlete refused to do the test and was sold to the New York Knicks who did not request such a test. This is an example of an employer trying to force an employee to do a genetic test in order to then discriminate for or against the employee based on the test result. In this case one can see the team's perspective as an employer that has a duty of care that might want to prepare itself for an acute cardiovascular problem, yet on the other hand one can understand the athlete's desire not to know or have others know about a serious genetic condition.

The most serious ethical concern arises from the major fundamental difference between genetic and non-genetic testing which is that the DNA does not change throughout life and that therefore prenatal genetic tests could be performed to select an embryo with the 'best sport genotype' or to abort an embryo with the 'wrong sport genotype'. The legal prevention of such testing is important because there is evidence that some parents use prenatal information to decide about whether or not to abort a pregnancy. In India and China, non-genetic ultrasound scans have been used to determine the sex of an embryo, and this practice has greatly contributed to an estimated 80 million 'missing' females [45]. Similarly, it may be that some genetic tests (not

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limited to genetic sex tests), including genetic tests of sporting potential, would be used by some parents during pre-implantation genetic diagnosis or to decide whether or not to select an embryo instead of others.

Conclusions

The focus of this paper has been on the potential use of genetic tests to predict performance and/or the risk of exercise-related injury or illness. The knowledge base is expected to develop so that the prescription of training, nutrition and competition load, and the management of injury risk, can be conducted in a more individualized manner than is currently possible to improve both performance and athlete welfare [46]. Consequently, various people may wish to conduct a sport-related genetic test on themselves, or on another person, for a variety of reasons. An individual may seek personal genetic information to assist him/her with their own sporting participation and career, by identifying the most suitable type of sport. A sports coach may wish to test the members of a youth team to assist in selection for a professional career or to individualize training. A physician may want to predict the risk of injury or illness in an athlete and advise a coach regarding selection or preventative measures. An insurance company may seek to estimate the risk of career-threatening injury or illness to an athlete based partly on genetic information. However, despite the commercial availability of genetic tests today, the evidence available at present suggests that few, and probably none, of these or similar scenarios are scientifically justified – the genetic tests available at the moment are not powerful enough to provide valid data on which to base important decisions in sport.

As written recently [47], as the evidence base improves, we predict that the first evidence-based practical application of genomic information in the management of elite athletes will involve the modification of training in an attempt to reduce the likelihood of injury when an athlete is predicted from their genome to be at greater than average risk. Secondly, personalization of training programmes should become possible in sports where 2 or more dichotomous physiological characteristics combine to produce athletic performance. For example, in many team sports where both endurance and sprint ability are required, at a truly elite level (where physiological monitoring as well as strength and conditioning processes are of the highest standard) it should become possible to carefully modify the relative emphasis during training of the development of those two physiological characteristics according to genotype. Thirdly, and probably more distantly in the future, some selection processes in sport might become informed by genomic information, although even in those cases the genomic information will probably remain secondary to the more informative phenotypic information.

There are many challenging ethical issues regarding the genetic testing of athletes. The imposition of genetic tests on individuals by third parties, and particularly the

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imposition of genetic tests on young people, is potentially susceptible to abuse. We suggest that an individual must be able to consent to their own genetic test (i.e. not of another individual/employee/child), and this is only valid if he/she can demonstrate beforehand an understanding of the possible implications of the test result. We also recommend that an appropriate standard of genetic counselling is always provided. It is critical that these issues continue to be debated widely so that the tests already available, and the more powerful ones that are likely to emerge following improvements in knowledge and genetic technology, are only used in acceptable ways.

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