

GÉNÉTIQUE ET SPORT:

L'impact de l'hérédité sur
la performance sportive.

Intervenant :



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Le mardi
18 Mai
à 17H



Visioconférence

Webinar

Comité National Olympique Marocain (CNOM)

Mardi 18 mai 2021

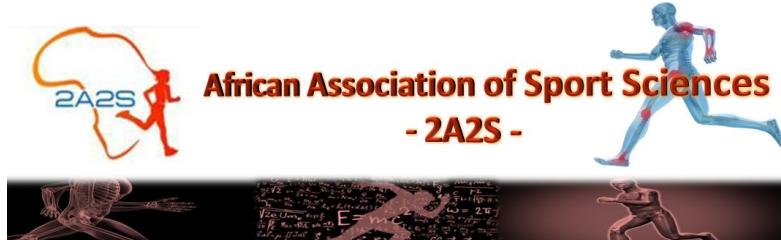


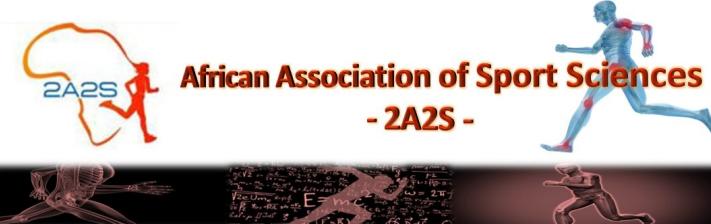
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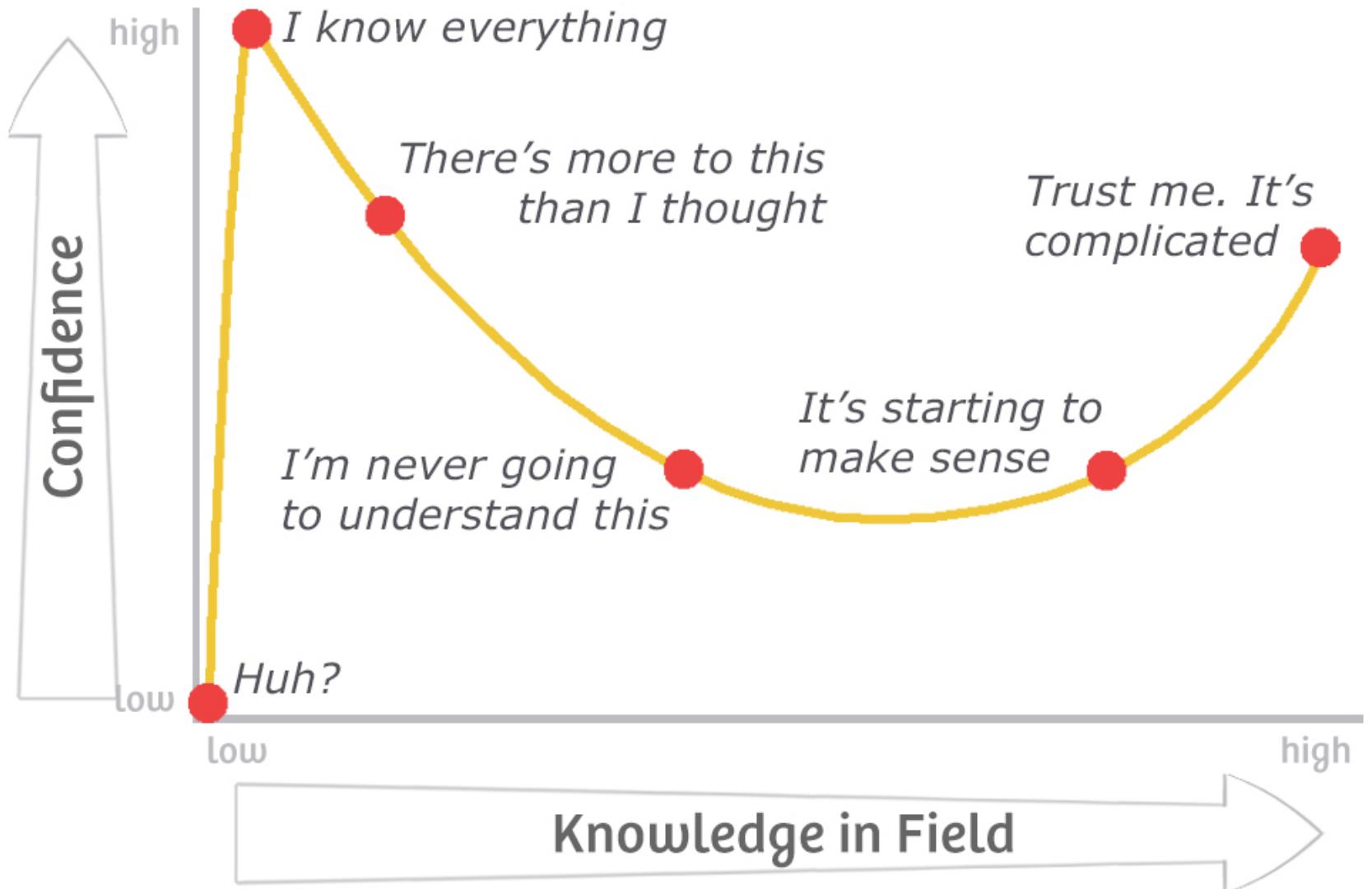


Génétique et Sport : L'impact de l'hérédité sur la performance sportive ?

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Dunning-Kruger Effect



Introduction

Performance Sportive = Trait Complexé

Atteindre Statut
Athlète Haut-Niveau

Génétique

Rôle +++

Influence
Prioritaire

Facteurs
Environnementaux

Nature
(Génétique)

Nurture
(Environnement)

Perf. Sportive

(Antero et al. *Front. Physiol.* 2018)

Hérédité
(Sexe, Génétique, Epigénétique)

Environnement
(Entraînement, Nutrition, Facteurs Sociodémographiques...)





A Medal in the Olympics Runs in the Family: A Cohort Study of Performance Heritability in the Games History

Juliana Antero^{1*}, Guillaume Saulière¹, Adrien Marck¹ and Jean-François Toussaint^{1,2,3}

Conclusion: Having a kinship with a former Olympic medallist is associated with a greater probability for an Olympian to also become a medallist, the closer an athlete is genetically to such kinship the greater this probability. Once in the OG, the genetic contribution to win a medal is estimated to be 20.5%.

Lien Parenté /
Médaillé Olympique → Probabilité Gain Médailles...



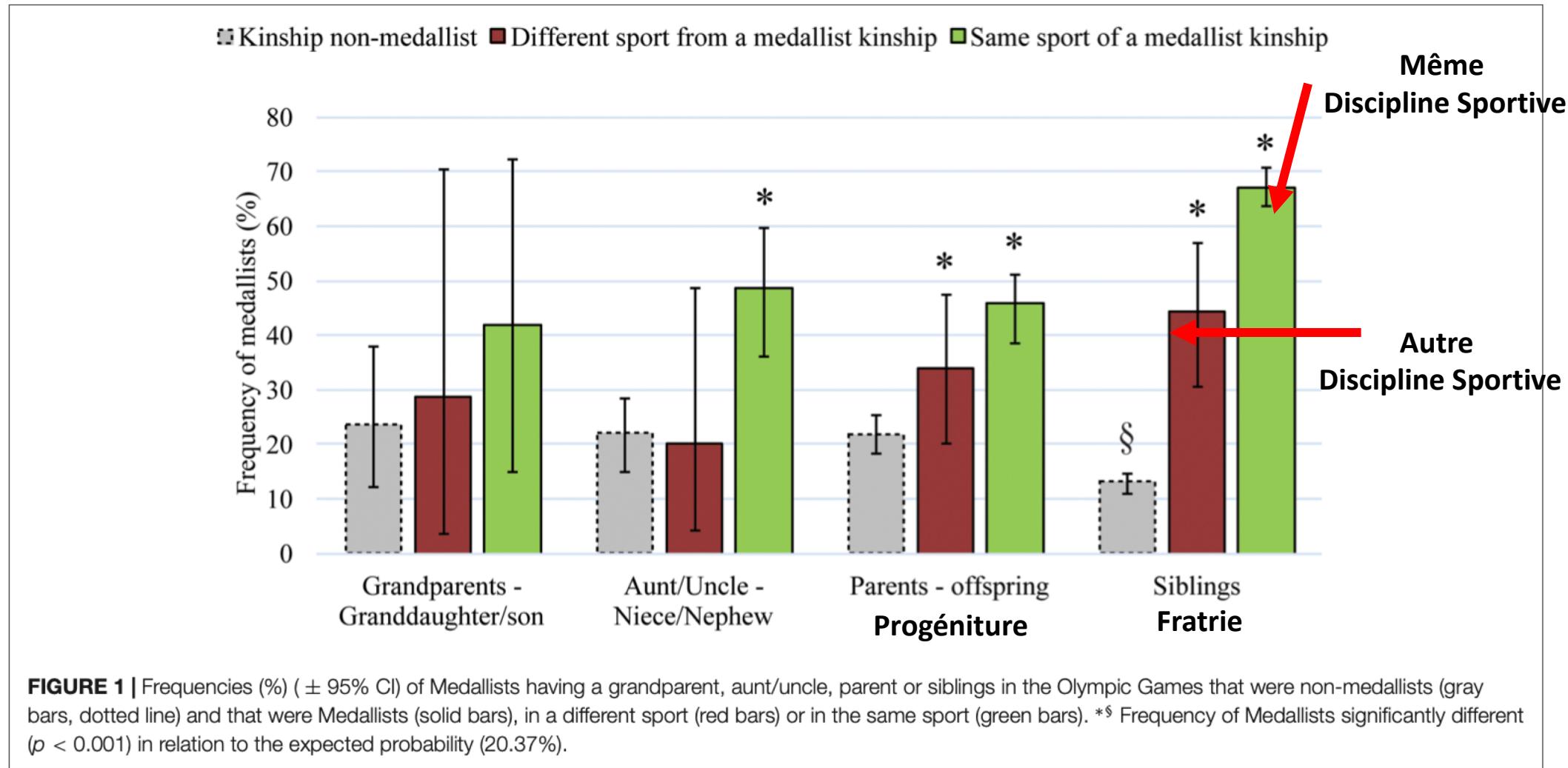


TABLE 1 | Frequency of medallists according to a kinship status with a former Olympic Medallist.

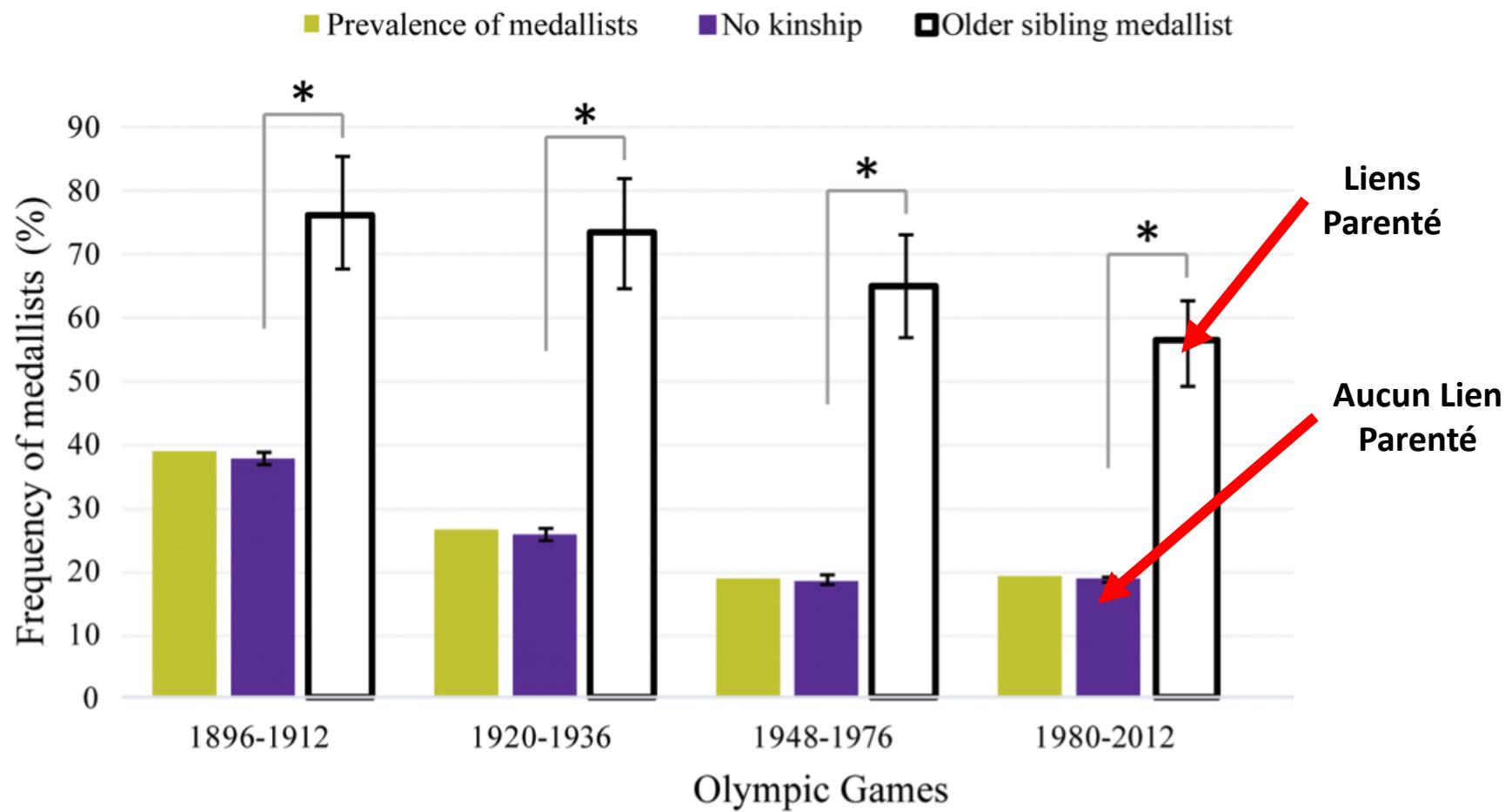


FIGURE 4 | Prevalence of Medallists in the Olympic Games according to four historical periods (yellow bars). The purple bars represent the frequency of Medallists (%) ($\pm 95\%$ CI) among Olympians with no kinship in the Games per period. The white bars represent the observed frequency of Medallists (%) ($\pm 95\%$ CI) among Olympians with a former sibling Medallist in the Olympics for each period. *The Medallist frequency was significantly different ($p < 0.001$) from the expected one.

Influence Génétique / Perf. Sportive → Inconnue !!!

Facteurs Héréditaires / VO₂max : Environ 50%

(Bouchard et al. MSSE. 1986 - 1998)

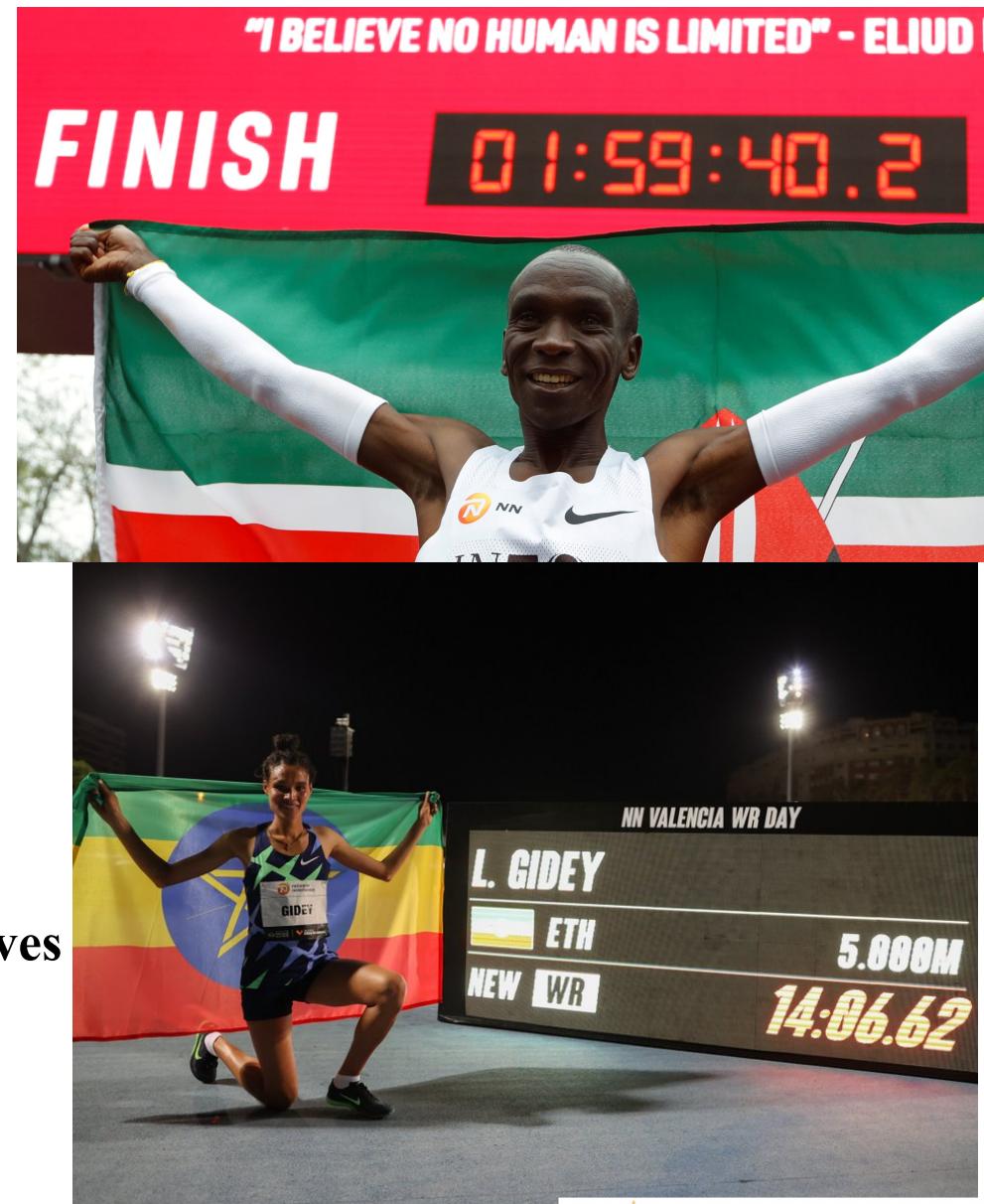
Nature
(Génétique) + Nurture
(Environnement) → Nécessaire → Perf. Sportives
Haut Niveau

Interaction
Champions
(Georgiades et al. BMG Genom, 2017)

Polymorphisme Génétique ↔ Certains Aspects
Exe. ou Perf. Sportives

Gènes Candidats
> 100 ↔ Identifications

(Ahmeton et al. Sc. Sport. Med., 2016)



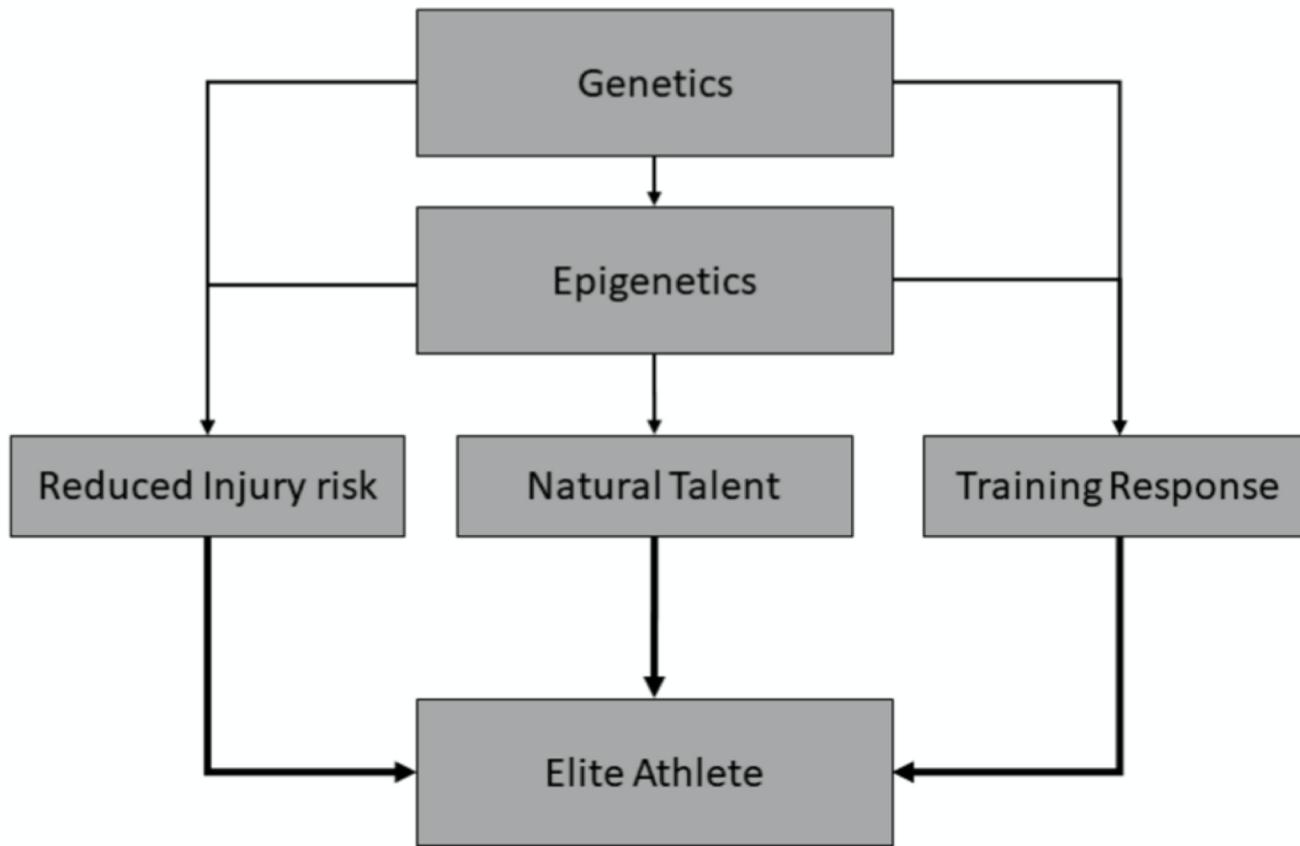


Figure 2. Influence of genetics and epigenetics on traits associated with elite performance. To succeed in sport, an athlete must possess genetic and epigenetic variations that might predispose to a natural talent trait (direct effect), and/or to enhanced response to physical training, and/or to reduced risk of injury (indirect effect).

Genetics and the Elite Athlete: Our Understanding in 2020

Rakesh John¹ · Mandeep Singh Dhillon² · Sidak Dhillon³

John et al. Sports. Med. 2020

Table 3 Timeline of genetic testing in sports

Sl no.	Year	Country	Sport	Sports association	Test
1	2001	Australia	Boxing	Professional Boxing and Martial Arts Board of Victoria	Compulsory genetic screening for APOE4 [75]
2	2005	Australia	Rugby	Sea Eagles (professional Rugby team based in Manly, Sydney)	Tested 18 of 24 players for 11 exercise-related genes [76]
3	2005	USA	Basketball	Chicago Bulls	Eddie Curry asked to undergo DNA test for hypertrophic cardiomyopathy [77]
4	2009	USA	American Football	National Football League (NFL)	DNA samples analysed from NFL linemen—current and former [78]
5	2009	USA	Baseball	Major League Baseball	DNA tested for a prospective player from the Dominican Republic [79]
6	2010	USA	Athletics	National Collegiate Athletic Association	Mandatory sickle cell trait screening introduced after lawsuit [80]
7	2011	United Kingdom	Soccer	English Premier League	Players' DNA samples analysed at 100 genetic loci linked to performance and risk of injuries [81]
8	2011	USA	American Football	National Football League (NFL)	Sickle cell trait and G6PD screened under the 2011 NFL collective bargaining agreement [82]
9	2012	United Kingdom	Athletics	English Institute of Sport	Considers genetic testing to assess injury risk in England's Olympic and Paralympics athletes [83]
10	2014	United Kingdom	Soccer	Barclays Premier League	Tested DNA for 45 variants in 2 teams to adapt individual training programmes and prevent injuries [84]
11	2015	Uzbekistan	Various (swimming, soccer, rowing, etc.)	National Olympic Committee	Test for 50 gene variants to identify future champion athletes at the molecular level [85]
12	2018	China	Various	Ministry of Science and Technology/Chinese Academy of Sciences	Announces complete genome sequencing to identify athletes for Olympic Winter games 2022 to be held in Beijing [86]



Table 1. Characteristics of studies included (bold indicates gene of interest).

References	Participants	Study design	Genes and SNPs measured	Outcome(s)
Ahmetov et al., 2015	Russian endurance athletes (n=219; 2 marathon runners), power athletes (n=230), Russian controls (n=192) and European controls (n=1367)	GWAS	NFIA-AS2 rs1572312 C/A TSHR rs7144481 T/C RBFOX1 rs7191721 G/A	C alleles of NFIA-AS2 rs1572312 and TSHR rs7144481 associated with elite endurance athlete status including marathon runners.
Amir et al., 2007	Israeli elite marathon runners (n=79), elite power athletes (n=42) and sedentary controls (n=247)	Case-control	ACE I/D rs4646994	D allele associated with elite marathon athlete status.
Ash et al., 2011	Ethiopian elite endurance runners (n=76), demographically matched controls (n=410), controls from general Ethiopian population (n=317), power athletes (n=38)	Case-control	ACE I/D rs4646994; A22982G rs4363	No association with elite Ethiopian runners.
Döring et al., 2010	Caucasian male elite endurance athletes (n=316; 39 runners) and Caucasian male sedentary controls (n=304)	Case-control	HIF1A Pro582Ser; rs11549465; C/T rs17099207 G/A; rs1951795 C/A; rs1158358 C/G; rs2301113 A/C; rs11549467 G/A	Pro582 C allele of rs11549465 and A allele of rs17099207 associated with elite endurance runners.
He et al., 2015	Chinese elite endurance runners (n=235) and Chinese controls (n=504)	Case-control	PPARGC1 α (41 SNPs) PPARGC1 β (43 SNPs) PPRC1I (4 SNPs); TFAM (3 SNPs); TFB1M (7 SNPs); TFB2M (3 SNPs); NRF1 (14 SNPs); GABPA (2 SNPs); GABPA (5 SNPs); ERR α (4 SNPs); SIRT1 (7 SNPs)	No significant association between proliferator-activated receptor γ (PGC)-related genes and elite endurance running status after adjusting for multiple comparisons.
Martinez et al., 2009	Hispanic marathon runners (n=784; 393 3 rd percentile and 388 lowest 3 rd percentile finishers)	Case-control	AQP1 rs1049305 C/G	C allele associated with elite performance in Hispanic marathon runners.
Myerson et al., 1999	Elite runners (n=91; 79 Caucasian) and British controls (n=1906)	Case-control	ACE I/D rs1049305 C/G	I allele positively associated with elite endurance running performance.
Papadimitriou et al., 2018	1,5k, 3k, 5k, and 42k m running times of 698 male and female Caucasian endurance athletes	Cohort	ACTN3 R577X ACE I/D	No association between ACTN3 or ACE I/D genotype and running performance at any distance.
Posthumus et al., 2011	Caucasian male triathlon (incl. 42.2km run) finishers (n=313)	Cohort	COL5A1 <i>Bst</i> UI RFLP rs12722 T/C	T allele associated with faster time to complete running component (42.2km) of triathlon.
Sawczuk et al., 2013	Polish elite endurance athletes (n=123; 12 marathon runners) and sedentary controls (n=228)	Case-control	ADRA2A rs553668 C/T	No association with elite endurance athlete status including marathon runners.
Stebbins et al., 2018	Male marathon runners (n=141) and recreationally active men (n=137)	Cohort	TTN rs10497520	TTN gene is associated with shorter skeletal muscle fascicle length and conveys an advantage for marathon running performance in trained men.
Tobina et al., 2010	Japanese male elite endurance runners (n=37) and non-athlete controls (n=335)	Case-control	ACE I/D rs4646994	Frequency of the ACE I/D genotype was lower in elite endurance runners than controls. The D allele was associated with faster marathon-running speed.
Tsianos et al., 2010	Greek Mount Olympus marathon runners (n=438)	Cohort	ACTN3 rs1815739 AMPD1 rs17602729 BDKRB2 rs1799722 ADRB2 rs1042713 PPARGC1α rs8192678 PPARα rs4253778; rs6902123 rs1053049; rs2267668 APOE rs7412; rs429358	BDKRB2 rs1799722, ADRB2 rs1042713 and AMPD1 rs17602729 associated with endurance running performance.
Wolfarth et al., 2008	Caucasian male elite endurance athletes (n=316; 39 runners) and sedentary male controls (n=299)	Case-control	NOS3 Glu298Asp rs1799983 G/T (CA) _n repeats; 27-bp repeats 4B/4A	164 bp allele of (CA) _n repeats associated with elite endurance runners.

NFIA-AS2, nuclear factor I A- antisense RNA 2; TSHR, thyrotropin receptor precursor; RBFOX1, RNA binding protein fox-1 homolog; ACE, angiotensin-converting enzyme; HIF1A, hypoxia-inducible factor 1-alpha; PPARGC1 α , peroxisome proliferator-activated receptor gamma coactivator 1-alpha; PPARGC1 β ,

Genes and Elite Marathon Running Performance: A Systematic Review

Hannah J. Moir ¹✉, Rachael Kemp ^{1,2}, Dirk Folkerts ^{1,3}, Owen Spendiff ¹, Cristina Pavlidis ⁴ and Elizabeth Opara ¹



Table 4 Gene variants for endurance athlete status (see Ahmetov and Fedotovskaya, 2012)

Gene	Location	Polymorphism	Endurance-related marker	Studies with positive results		Studies with negative or controversial results	
				Number of studies	Total number of studied athletes	Number of studies	Total number of studied athletes
<i>ACE</i>	17q23.3	Alu I/D (rs4646994)	I	16	1310	11	1263
<i>ACTN3</i>	11q13.1	R577X (rs1815739 C/T)	577X	3	518	11	2382
<i>ADRA2A</i>	10q24–q26	6.7/6.3 kb	6.7-kb	1	148	–	–
<i>ADRB2</i>	5q31–q32	Gly16Arg (rs1042713 G/A)	16Arg	2	629	–	–
<i>ADRB3</i>	8p12–8p11.1	Trp64Arg (rs4994 T/C)	64Arg	1	100	1	81
<i>AQP1</i>	7p14	rs1049305 C/G	rs1049305 C	1	784	–	–
<i>AMPD1</i>	1p13	Gln12X (rs17602729 C/T)	Gln12	2	231	–	–
<i>BDKRB2</i>	14q32.1–q32.2	+9/-9 (exon 1) rs1799722 C/T	-9 rs1799722 T	2 1	524 316	1 –	74 –
<i>CKM</i>	19q13.32	A/G NcoI (rs8111989 T/C)	rs1803285 A	1	176	3	581
<i>COL5A1</i>	9q34.2–q34.3	rs12722 C/T (BstUI)	rs12722 T	2	385	–	–
<i>COL6A1</i>	21q22.3	rs35796750 T/C	rs35796750 T	1	661	–	–
<i>EPAS1</i> (<i>HIF2A</i>)	2p21–p16	rs1867785 A/G rs11689011 C/T	rs1867785 G rs11689011 T	1	451	–	–

Table 4.2 Gene variants for power/strength athlete status (see Ahmetov and Fedotovskaya, 2012)

Gene	Location	Polymorphism	Power/ strength- related marker	Studies with positive results		Studies with negative or controversial results	
				Number of studies	Total number of studied athletes	Number of studies	Total number of studied athletes
<i>ACE</i>	17q23.3	Alu I/D (rs4646994)	D	6	255	5	365
<i>ACTN3</i>	11q13.1	R577X (rs1815739 C/T)	Arg577	11	1350	4	368
<i>AGT</i>	1q42.2	Met235Thr (rs699 T/C)	235Thr	1	63	–	–
<i>CKM</i>	19q13.32	A/G NcoI (rs8111989 T/C)	rs1803285 G	1	74	–	–
<i>AMPD1</i>	1p13	Gln12X (rs17602729 C/T)	Gln12	2	463	–	–
<i>HIF1A</i>	14q21– q24	Pro582Ser (rs11549465 C/T)	582Ser	2	211	1	81
<i>IL1RN</i>	2q14.2	VNTR 86 bp (intron 2)	<i>IL1RN</i> *2	1	205	–	–
<i>IL6</i>	7p21	–174 C/G (rs1800795 C/G)	rs1800795 G	1	53	1	81
MtDNA loci	MtDNA	Haplogroups constructed from several MtDNA polymorphisms or single polymorphisms	F m.204C Non-L/U6	1 1 1	60 85 119	– – –	– – –
<i>MTHFR</i>	1p36.3	A1298C (rs1801131 A/C)	rs1801131 C	1	77	–	–
<i>MTR</i>	1q43	A2756G (rs1805087 A/G)	rs1805087 G	1	77	–	–

(Wang et al. *Advances in Genetics*, 2013)

Gène Particulier



ACTN3

Code

(Sarzynski et al. MSSE, 2016)

(Jacob et al. Sports, 2018)

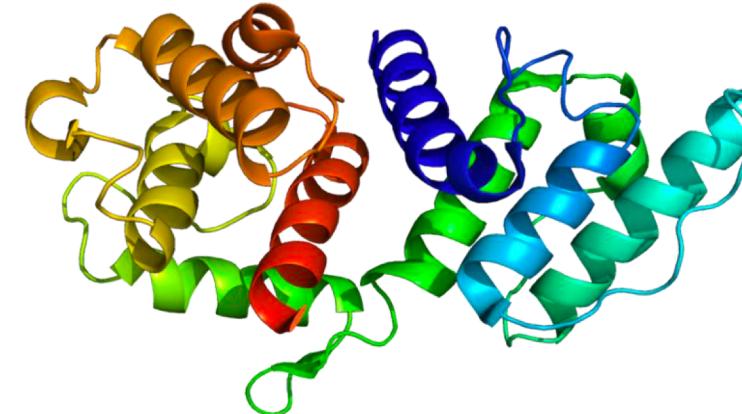
Protéine α -actinine-3



Rôle Clé



Production Force
Sarcomères



Gène ACTN3

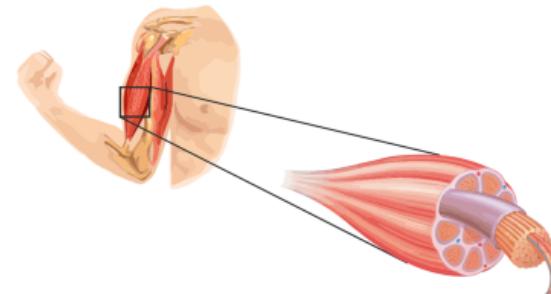
Expression

Protéine: Articule + Stabilise

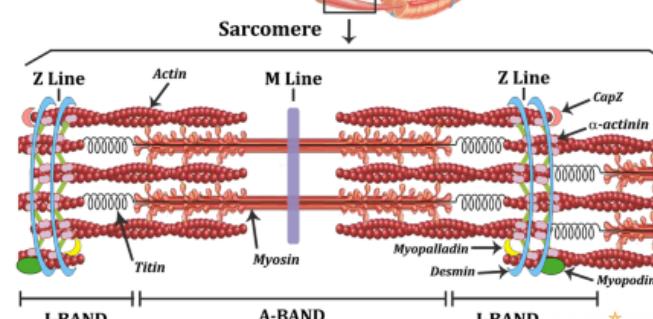
Production Contraction
Rapides + Explosives



Filament Actine
Disque Z



Actin-binding domain



(Mc Arthur et al. Bio Essays, 2004)

Expression α -actinine-3 : Uniquement FM Type II

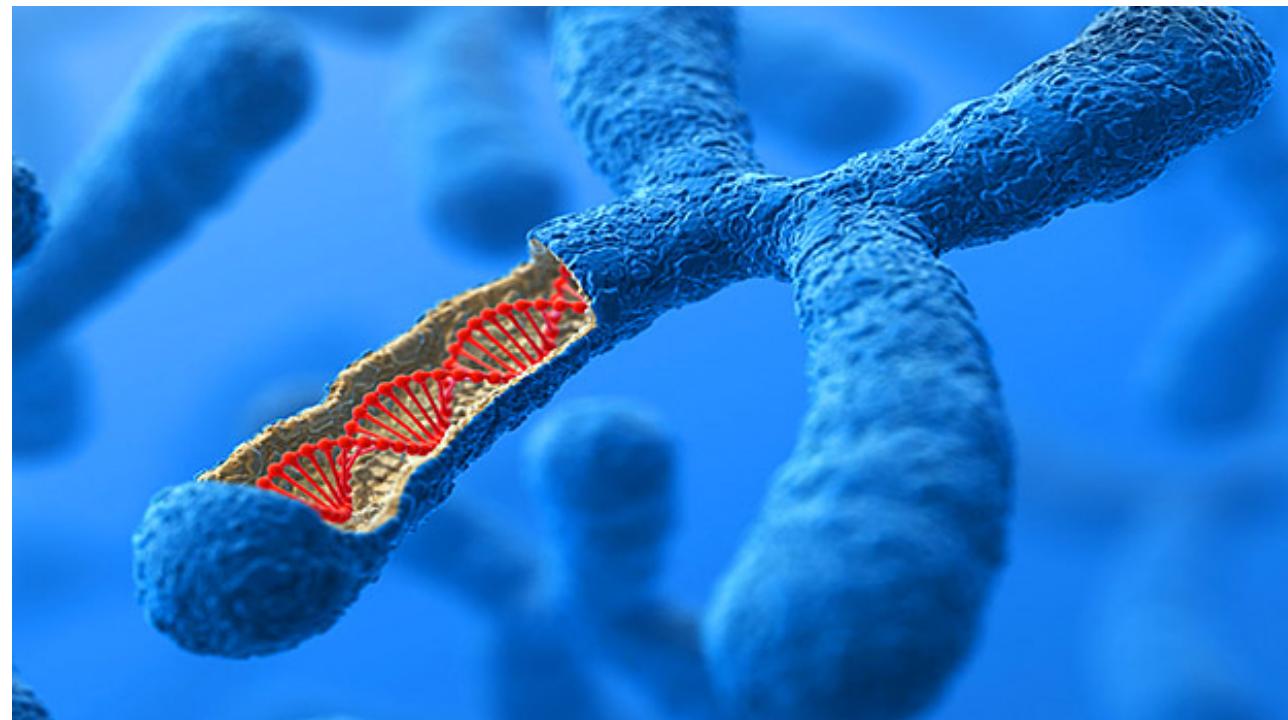
(Houweling et al. Hum. Mutat, 2018)

Isoforme: α -actinine-2 (81% Identique + 91% Similaire)

Expression Tout Types FM

Table 1 List of studies exploring correlation of ACTN3 gene with sports performance

Year	Study authors	Population tested	Number of athletes tested (athletes/controls)
2003	Yang [9]	Australia	301/436
2005	Niemi [20]	Finnish	68/120
2007	Yang [21]	Ethiopia	76/198
		Kenya	284/158
		Nigeria	62/60
2007	Paparini [17]	Italian	42/102
2008	Papadimitriou [16]	Greek	101/181
2008	Druzhevskaya [22]	Russia	486/1197
2008	Ahmetov [6]	Russia	456/1211
2010	Doring [23]	German, Finnish and North American	305/292
2010	Muniesa [24]	Spanish	141/123
2010	Ruiz [25]	Spanish	153/100
2010	Shang [26]	China	250/450
2011	Chiu [15]	Taiwan	168/603
2011	Gineviciene [27]	Lithuania	193/250
2012	Kikuchi [28]	Japan	135/333



ACTN2 + ACTN3 : Rôles Différents / Muscle Squelettique

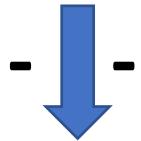
(Del Coso et al. EJAP, 2019)

(North et al. Nuromuscular Dis. 1996 ; Nature Genet. 1999)

p.R577XX (rs1815739)



Polymorphisme Nucléotidique



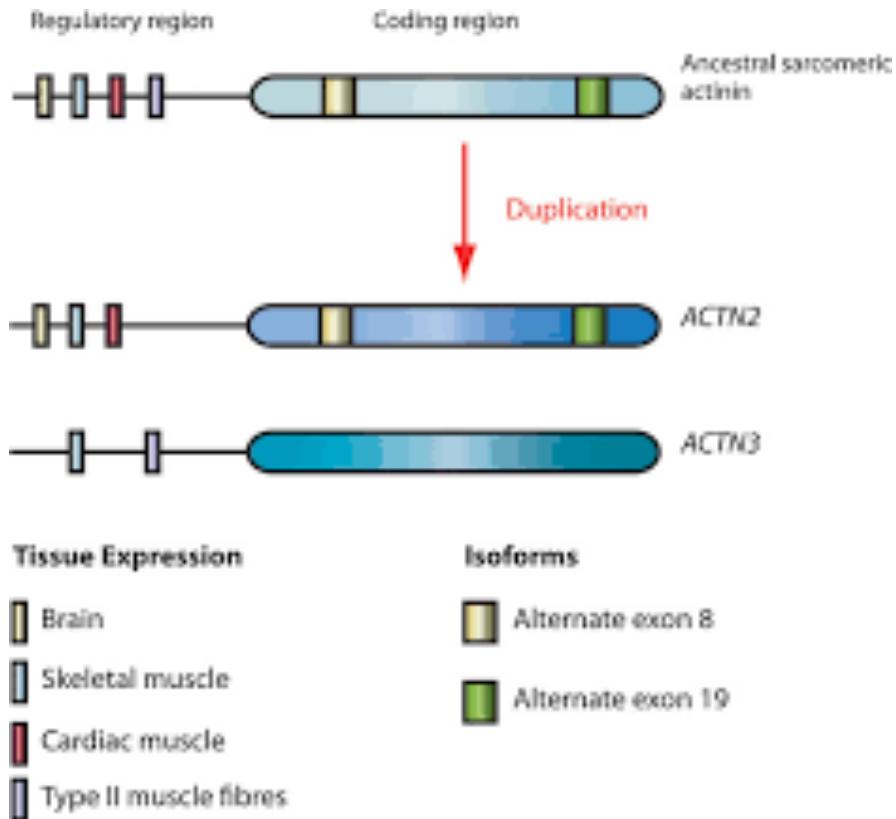
Expression Gène Protéine α -actinine-3

Arginine (R) —————> Code Stop Prématuré (X)

Ind. Homozygotes
(Génotype 577 XX) Déficit α -actinine-3
Ind. ACTN3 XX

Ind. RR ou RX —————> Expression Fonctionnelle
 α -actinine-3

(Scott et al. MSSE, 2010; Yang et al. MSSE, 2007)



More than a “speed gene”: *ACTN3* R577X genotype, trainability, muscle damage and the risk for injuries

α -actinin-3 is a bundling protein that binds and cross-links the ends of F-actin filaments to the sarcomere.

α -actinin-3 is only expressed in type II skeletal muscle fibers.

α -actinin-3 is encoded by *ACTN3* gene. A common stop-codon polymorphism (R577X) in this gene was discovered in humans.

Homozygosity for the X allele (577XX) results in the absence of α -actinin-3.

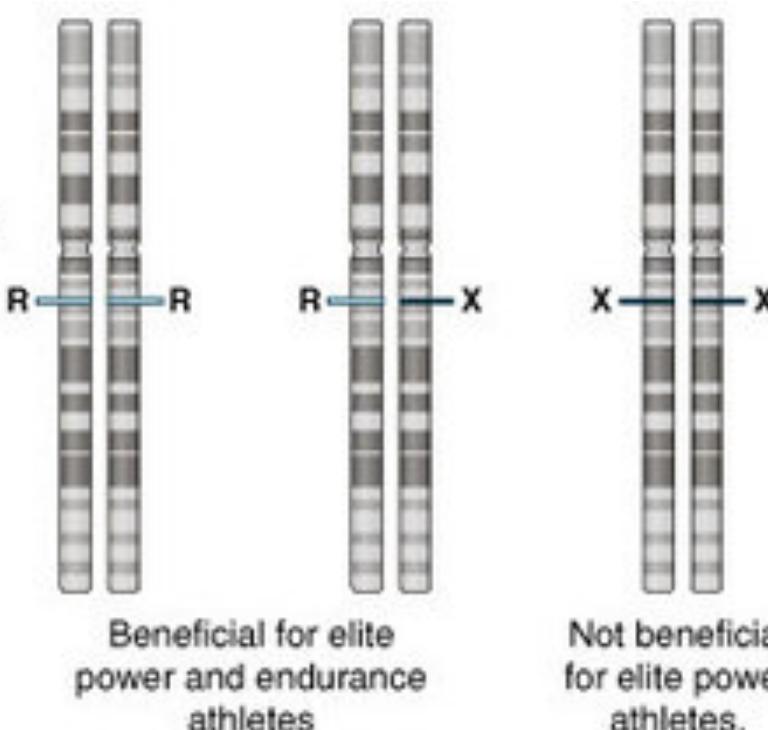


Chromosome 11

Research suggests that elite athletes who rely on the power of fast-twitch fibers in their muscles, like sprinters, share a common genotype. These fibers contain a protein produced by the R allele (version) of the ACTN3 gene.

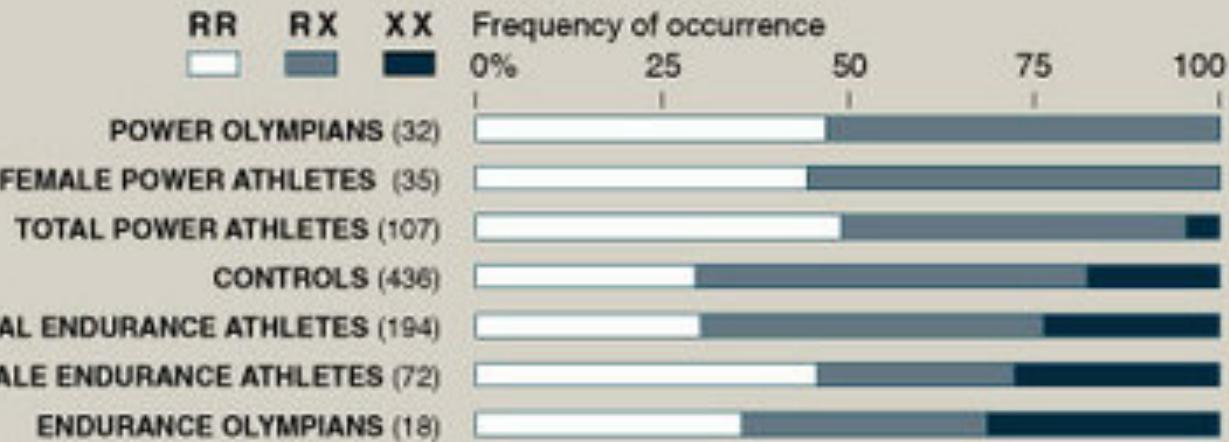
ACTN3

Possible variations (genotypes) of the ACTN3 gene.

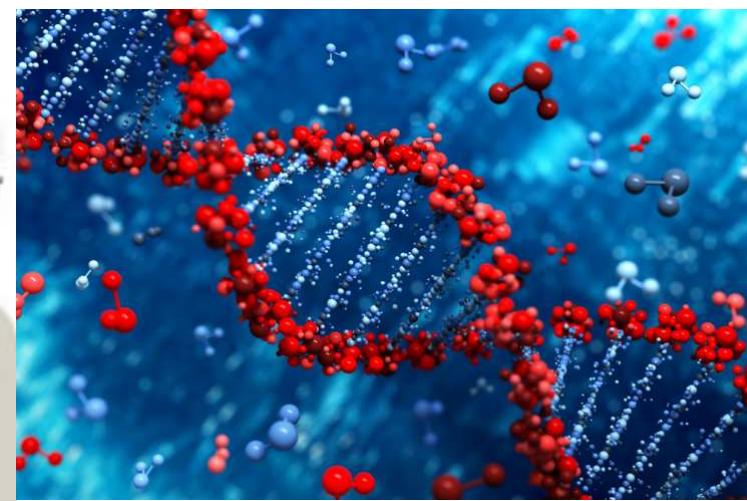
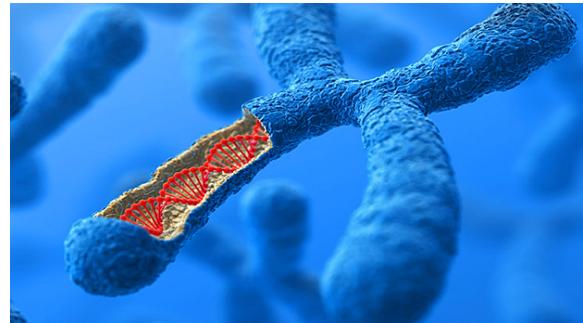


Genotype frequency among elite power/sprint athletes and elite endurance athletes.

Confidence intervals are 95%.



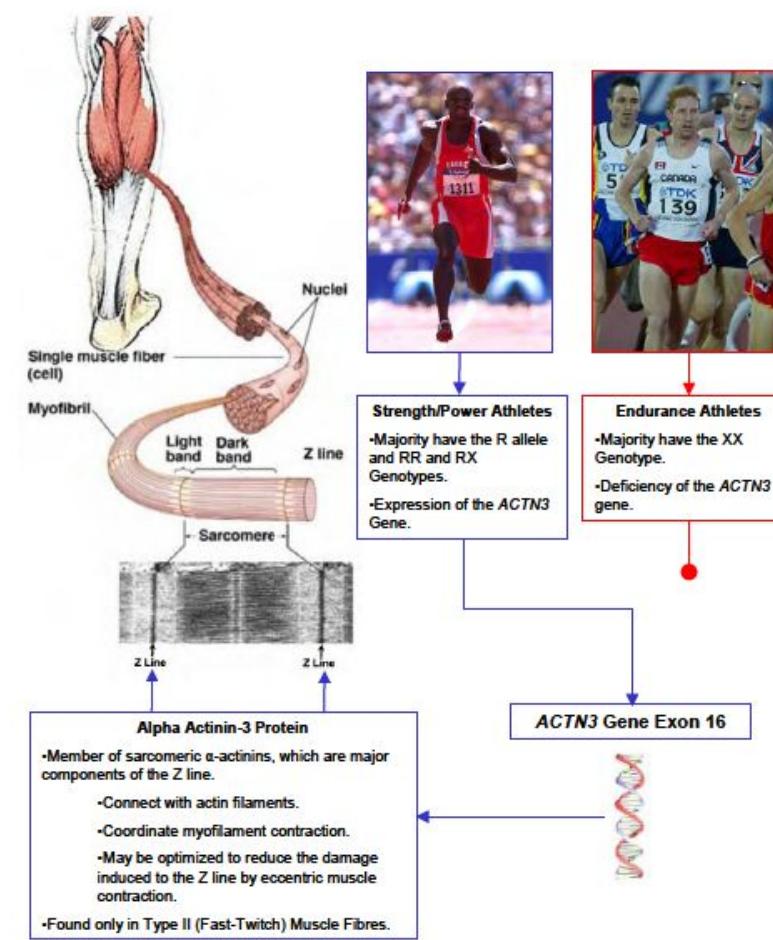
Sources: Stephen M. Roth, Ph.D., University of Maryland; American Journal of Human Genetics



Composition Sarcomères + Fonction Musculaire Contrôle / ACTN3 (Hogarth et al. *Hum. Mol. Genet.*, 2016)

Génotype ACTN3 XX Sous Représenté Ath. Élites Spé. Puissance + Explosivité (Huweling et al. *Hum. Mutat.*, 2018)

ACTN3 XX → Carence α -actinine-3 → Effet --- Fonction Fibres Muscu. II
Rôle
Ne Peut Être Compensée / Sur-Présentation α -actinine-2 (Baltazar-Martins et al. *Sports*, 2020)



(Baltazar-Martins et al. *Sports*, 2020)

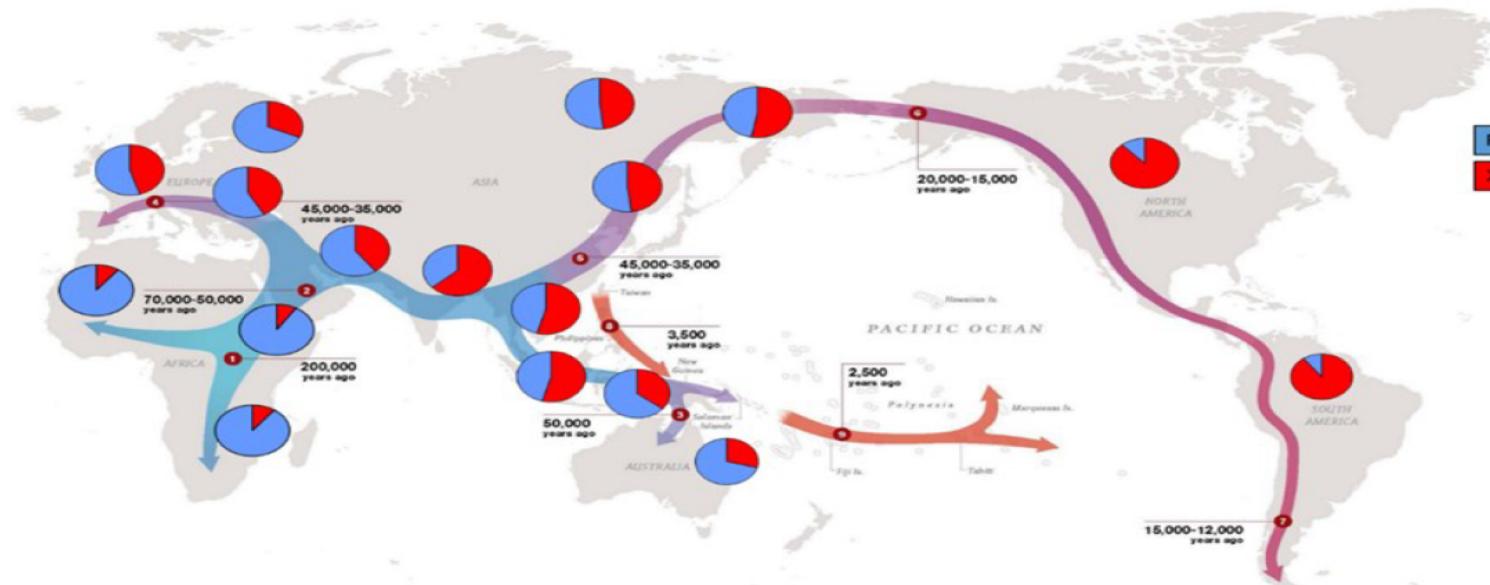
20% Population
Mondiale

Génotype XX



% / Zones Géographiques

25% Asiatiques - 18% Caucasiens – 11% Ethiopiens
3% Afro-Américains - 1% Kenyans



ACTN3 rs1815739:C>T

(Houweling et al. Hum. Mutat., 2018)

Carence α -actinine-3 / Perfs. Sportives

Génotype
ACTN3 XX

Sous
Représenté

Ath. Élites Inter. / Non-Ent.

(Young et al. Am J Hum Genet, 2003)

Allèle R + Génotype RR

Fréquence >>>
Ath. Sprint + Sports Puissance

(Eynon et al. Sports Med, 2009-2013; Alfred et al. Hum Mutat, 2011)

Pas Fréquente : Sport Puissance + Facteurs Techniques

ACTN3
 α -actinine-3

Important

+++ Sport Puissance, Sprint...

--- Sport Puissance + Facteurs Techniques



Table 2 a. Case control studies with the *ACTN3 R577X* polymorphism in sprint/power oriented athletes and **b.** Case control studies with the *ACTN3 R577X* polymorphism in endurance athletes.

Sprint/Power Athletes					Athletes Genotype%			Controls Genotype%				
Country/ Ethnicity	Gender	Sport	P	N	RR	RX	XX	N	RR	RX	XX	Reference
Australian	M	Short distance Swimmers, Track cyclists>400, Rowers<2000m, Short distance Skiers	<0.001	72	53	39	8	134	30	54	16	Yang et al., 2003
	F		<0.01	35	43	57	0	292	30	54	16	
Finnish	M&F	Power oriented Track & Field athletes	<0.03	23	48	52	0	120	45	46	9	Niemi & Majaama 2006
Greek	M&F	Power oriented Track & Field - Mainly Sprinters (100m-400m)	<0.02	73	48	36	16	181	26	54	18	Papadimitriou et al., 2008
USA	M&F	Bodybuilders, Powerlifters	0.005	75	31	63	7	876	38	46	16	Roth et al., 2008
Russian	M	Speed Skiers, Gymnasts, Bodybuilders , Hockey players, Powerlifters, Footballers, Speed Skaters; Swimmers; Sprint Track & Field athletes, Volleyball players, Weightlifters, Wrestlers	<0.0001	363	38	56	6	524	37	47	16	Druzheveskaya et al., 2008
	F		0.067	123	46	48	6	673	37	51	13	
Israeli	M&F	Power oriented Track & Field athletes- Mainly Sprinters (100m-400m)	<0.0001	55	38	42	20	240	20	62	18	Eynon et al. 2009
Italian	M&F	Artistic Gymnasts	0.04	35	49	49	3	53	32	49	19	Massidda et al., 2009

(Houweling et al. Hum. Mutat., 2018)

Polish	M&F	Power oriented Track & Field athletes, Short distance Swimmers, Weightlifters	0.008	178	40	52	8	254	35	49	15	Cieśczyk et al., 2011
Taiwanese	M	Short distance Swimmers	NS	37	39	48	14	306	32	49	20	Chui et al., 2011
	F		<0.05	44	46	43	11	306	32	49	20	
Japanese	M&F	Wrestlers	0.028	52	27	62	11	333	27	45	28	Kikuchi et al., 2012
Korean	M	Gymnasts, Sprinters, Throwers, Speed Skaters, Weightlifters and Taekwondo athletes	NS	47	21	57	21	361	29	53	18	Hong et al., 2013
	F		0.028	37	46	51	3	361	32	50	18	
Japanese	M	Power oriented Track & Field athletes - Mainly Sprinters (100m-400m)	0.002*	134	25	58	17	649	21	53	26	Mikami et al., 2013
Korean	M&F	Weightlifters, Speed Skaters, Sprinters and Short distance Swimmers	<0.05	121	40	48	12	854	30	51	19	Kim et al., 2014
Chinese	M&F	Power oriented Track & Field athletes, Track Cyclists, Weightlifters	<0.001	59	49	46	5	50	26	40	34	Yang et al., 2017
Nigerian	M&F	Power oriented Track & Field athletes	NS	62	87	13	0	60	83	17	3	Yang et al., 2007
Jamaican	M&F	Power oriented Track & Field athletes	NS	86	75	22	3	232	75	22	2	Scoot et al., 2010
USA	M&F	Power oriented Track & Field athletes	NS	79	70	28	2	126	66	30	4	Scoot et al., 2010

* In Japanese cohort the statistical significant difference was detected in RR+RX sprinters vs. Control group.

(Houweling et al. Hum. Mutat., 2018)



Carence α -actinin-3



Défavorable Sport Puissance Sprint...



(Houweling et al. *Hum Mutat*, 2018)

ACTN3 : Gène Vitesse

Allèle R : Fréquence >>

(Scott et al. *MSSE*, 2010)



Détenteurs + Détentrices
Record Monde Sprint



Ind. RR
Non-Élites



Valeurs Force >>
Volume Muscu. >>
Réponse Ent. >> / XX

(Del Coso et al. *Genes*, 2019; Broos et al. *EJAP*, 2015;
Walsh et al. *JAP*, 2008; Gentil et al. *JSSM*, 2011)



Composition Fibres Musc. : Similaire (Norman)et al. *JAP*, 2014)



Section Fibres Type II >> RR / XX (Broos et al. *PlosOne*, 2016)



اللجنة الوطنية الأولمبية المغربية
COMITÉ NATIONAL OLYMPIQUE MAROCAIN

Ent. Musculation
Hte Intensté



Puiss. + Perf. Muscu. >> RR / XX

(Demonicco et al. A Biol. Sci. Med. Sci. 2007; Jones et al. Biol Sports, 2016;
Montgomery et al. Nature, 1998)

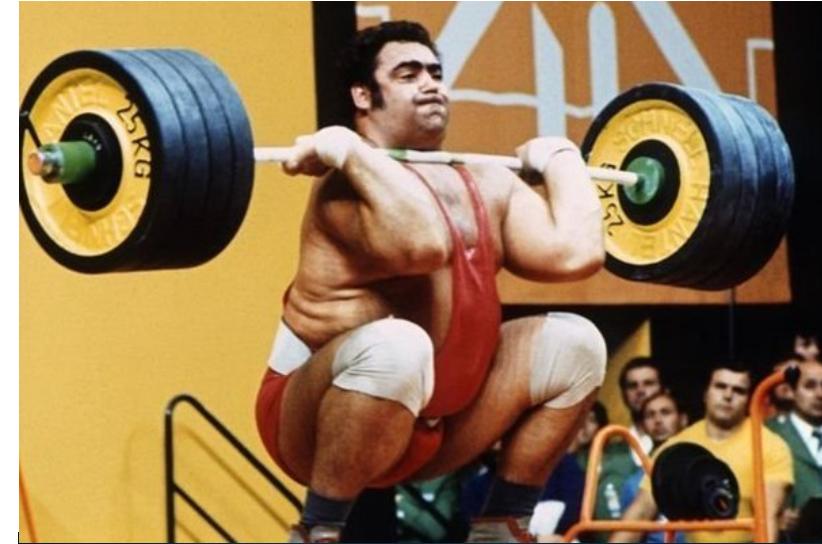
Synthèse Protéique



Ind. Déficients
 α -actinine-3

Ind. XX : Très Bonne Rép. Ent. Endurance +. Force Faible Intensité

(Montgomery et al. Nature, 1998)



Ind. RR



Rép. Ent. Force >>



Perf. >> Sprint + Force

(Pickering et al. Front Physiol, 2017)



Ent. Spécifique : Permet-il Compensation
Diff. Perf. Anaérobies entre Génotypes ACTN3 ???



Perf. Sportives

Influencent

Plusieurs Facteurs

Génotype ACTN3 : Fréquence >> Ind. Spécialistes Endurance

(Yang et al. Am J Hum Genet, 2003)



Données Récentes
Ath. Internationaux
(1/2 Fond, Fond, Marathon, Triathlon etc.)



Absence
Association

(Eynon et al. Sports Med. 2009; Head et al. PlosGenet, 2015;
Friedlander et al. PlosOne, 2013; Papadimitriou et al. IJSM, 2008)

Étude / Records ½ Fond
Papadimitriuo et al. BMC Genom, 2018

A blue arrow pointing from the text above to the result below.

Absence
Association

Déficience α -actinine-3



Pas
Avantages / Endurance



		Endurance Athletes				Athletes Genotype%			Controls Genotype%				
Country/ Ethnicity	Gender	Sport	P	N	RR	RX	XX	N	RR	RX	XX	Reference	
Australian	M	Long distance Swimmers, Endurance Cyclists, Rowers>2000m, Cross-country skiers	NS	118	28	53	19	134	30	54	16	Yang et al., 2003	
	F		<0.05	75	20	50	30	292	30	50	20		
Finnish	M&F	Endurance Track & Field athletes		NS	52	50	40	10	1060	43	48	9	Niemi & Majaama 2006
Spanish	M&F	Long distance Rowers, Long distance cyclists, Long distance runners		NS	139	27	45	27	103	29	57	14	Lucia et al., 2006
Greek	M&F	Endurance Track & Field athletes – Mainly long distance runners		NS	20	50	25	25	81	26	56	18	Papadimitriou et al., 2008
Russian	M	Race walkers, Biathletes, Endurance Cyclists, Long distance Rowers, Long distance swimmers, Triathletes, Cross-country skiers	NG†	293	40	53	7	532	36	47	17	Ahmetov et al., 2010	
	F		NG	163	37	59	4	69	37	50	13		
Israeli	M&F	Endurance Track & Field athletes – Mainly long distance runners		<0.006	54	19	46	35	240	20	62	18	Eynon et al. 2009
American, Finnish, German	M	Biathletes, Triathletes, Long distance cyclists, Long distance runners, Long distance rowers		NS	316	29	50	21	304	32	51	18	Doring et al., 2010
Chinese	M	Long distance rowers, Long distance cyclists, Long distance runners and Long distance swimmers	NS	132	37	51	12	450	35	48	17	Shang et al., 2010	
	F		<0.05	118	19	60	21	450	35	48	17		
Russian	M&F	Long distance Rowers, Speed skaters, Race endurance walkers, Cross country Skiers, Long distance swimmers		NS	70	44	56	0	354	35	41	23	Eynon et al. 2012
Polish, Spanish, Russian	M&F	Long distance Cyclists, Long distance Rowers, Long distance Runners		NS	284	37	51	12	808	32	51	18	Eynon et al., 2012
Koreans	M	Badminton Players, Table Tennis Players, Hockey Players and Handball Players	NS	41	46	44	10	188	29	53	18	Hong et al. , 2013	
	F		NS	25	24	48	28	173	32	50	18		
Japanese	M&F	Endurance Track & Field – Mainly long distance athletes		NS	165	23	54	23	649	21	53	26	Mikami et al., 2013
Estonians	M&F	Cross Country skiers and Biathletes		NG	58	33	58	9	222	76	16	8	Mägi et al., 2016
Chinese	M&F	Long distance runners		NS	44	32	36	32	50	26	40	34	Yang et al., 2017

* In Israeli cohort an Endurance athletes vs. Sprinters statistical significant detected difference ($P<0.005$) was detected on top of Endurance athletes vs. Controls significant difference.

† In Russian cohort none of the males highly elite endurance athletes had the ACTN3 577XX genotype.

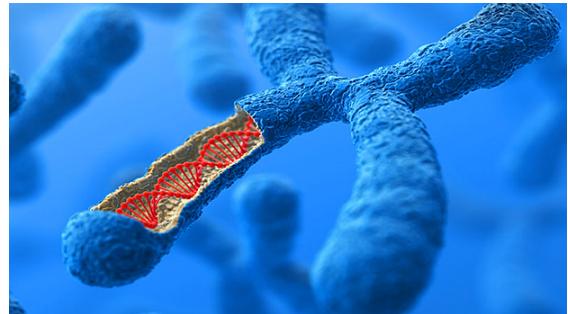
(Huweling et al. Hum. Mutat., 2018)

Modèle Animal

Souris ACTN3 (KO) → Déficit α -actinine-3



(Mac Arthur et al. *Nature Genet*, 2007)



Xⁿ Force << + Masse Maigre << / Souris Normales

(Seto et al. *J Clin Invest.* 2013)

↓ Taille Fibres Type II (Quinlan et al. *Hum Mol Genet.* 2010;
Mac Arthur et al. *Hum Mol Genet.* 2008)

→ Phénotype Métab. Aérobie

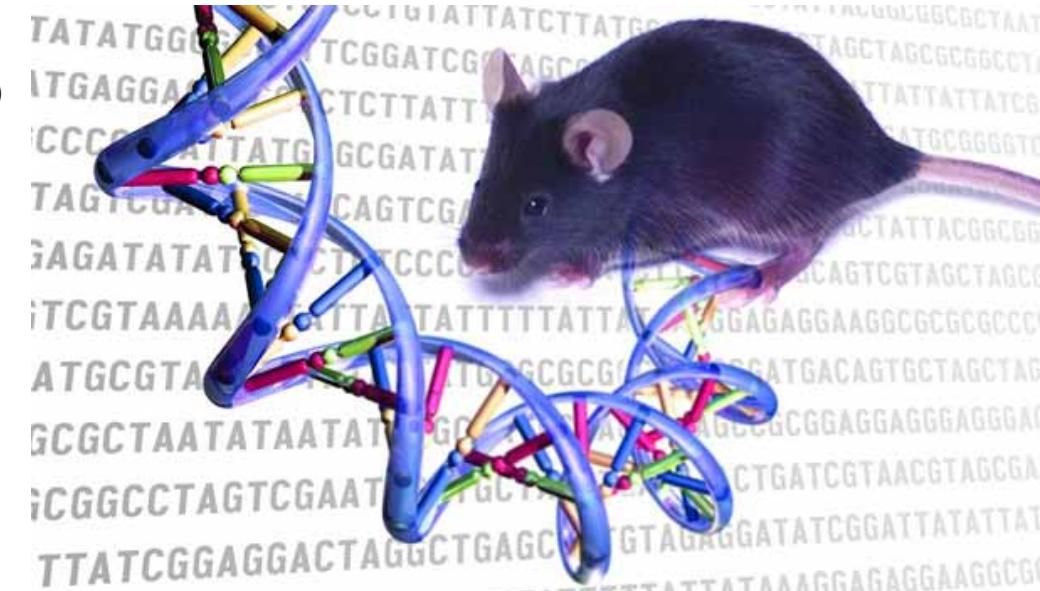
↑ Stockage Gly. + Act. Enz. Oxy. Mitoch.

↑ Act. Calcineurine (Garton et al. *Hum Mol Genet.* 2014)

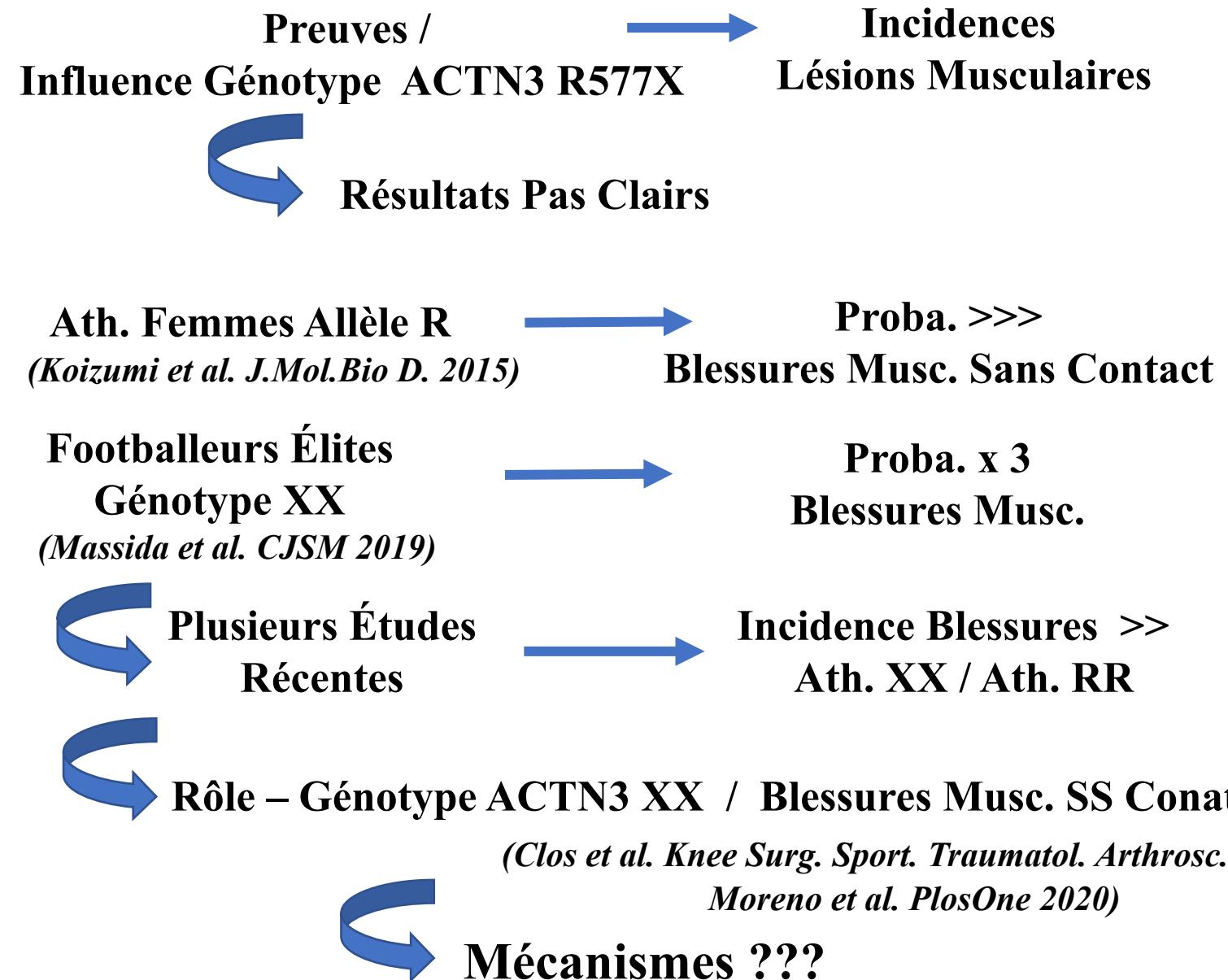


Pas de RéPLICATION chez l'Homme

(Papadimitriou et al. *Sci Rep.* 2019)



Carence α -actinine-3 / Epidémiologie Blessures





Ind. XX :

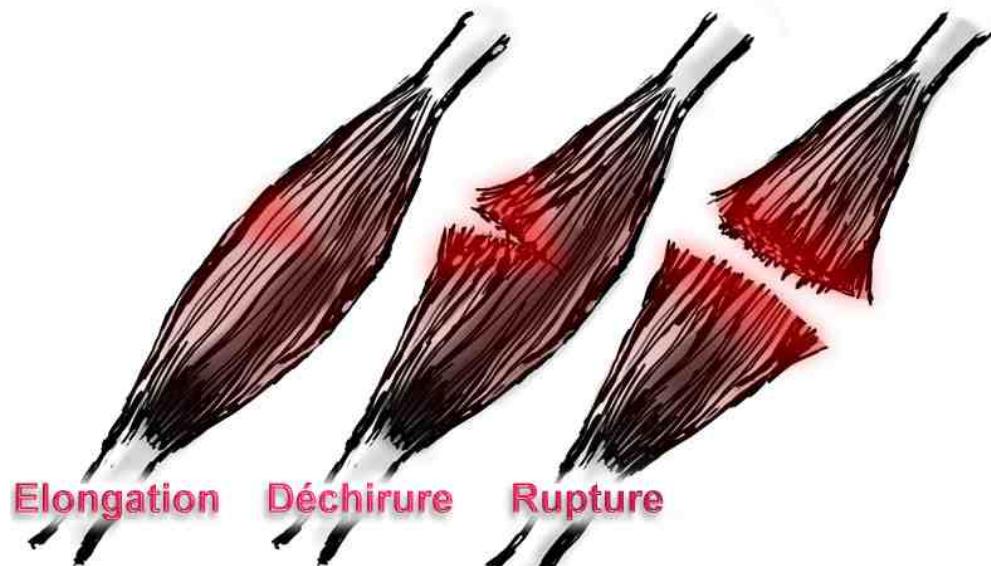
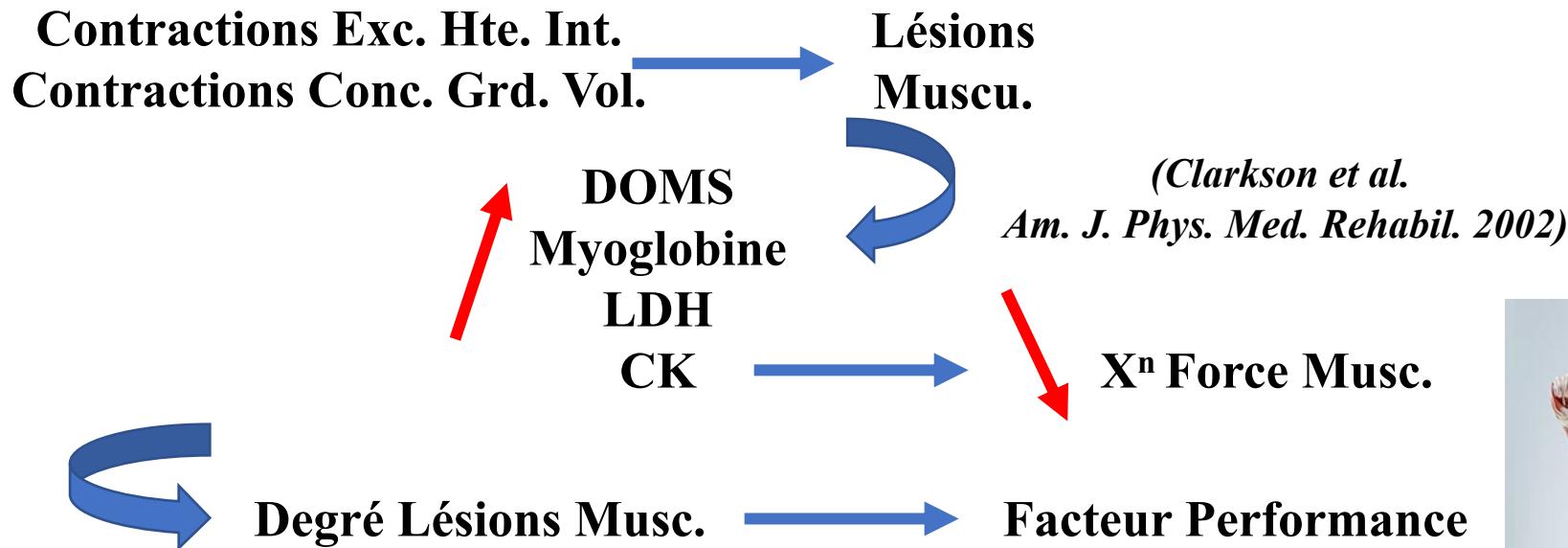
- Entorse Cheville >>
- Blessures Ligamentaires >>
*(Kim et al. J. Exerc. Nutr. Biochem. 2014;
Qi et al. Genet Mol Res. 2016; Shang et al. JSS 2015;)*

Femmes XX : Densité Minérale Osseuse << RR

(Min et al. J. Phys. Ther. Sci. 2016)



Carence α -actinine-3 / Lésions Musc. Induites / Exe.



Carence α -actinine-3 → Résistance Fibres Musc.
/ Contractions Exc. + Conc.

Ind. XX → Marqueurs Lésions Muscu. >> Ind. Allèle R
(DOMS, CK)

(*Vincent et al. JAP 2010; Pimenta et al. EJAP 2012; Del Coso et al. EJAP 2019*)

Clarkson et al. JAP (2005) &
Broos et al. EJSS (2019) → Pas Association
Génotype ACTN3 / ↑ Lésions Muscu.

Ind. XX → Récupération + Rapide → S'entraîner ++

(*Venckunas et al. APNM 2012*)

Carence α -actinine-3 → Lésions Muscu. >>

Récupération + Rapide ???





ACTN3: More than Just a Gene for Speed

Craig Pickering^{1,2*} and John Kiely¹

TABLE 1 | Studies examining the interaction between ACTN3 genotype and exercise adaptation.

Study	Method	Sample characteristics	Main outcome
Clarkson et al., 2005a	12 weeks progressive resistance exercise training on non-dominant arm. Progression from 3 sets of 12 repetitions to 3 sets of 6 repetitions, with concurrent increase in load.	602 (355 females) aged 18–40 (<i>n</i> = 133 XX genotype).	In females, the X allele was associated with greater absolute and relative improvements in 1RM vs. RR genotypes.
Pereira et al., 2013	12-week high-speed power training programme. Progression from 3 sets of 10 repetitions @ 40% 1RM to 3 sets of 4 repetitions @ 75% 1RM.	139 Older (mean = 65.5 years) Caucasian females (<i>n</i> = 54 XX genotype).	RR genotypes exhibited greater performance improvements (maximal strength, CMJ) compared to X allele carriers.
Erskine et al., 2014	9-week unilateral knee extension resistance training programme.	51 previously untrained young males (<i>n</i> = 7 XX genotype).	Responses to resistance training were independent of ACTN3 genotype.
Silva et al., 2015	18-week (3 sessions per week) endurance training programme, comprised primarily of 60-min running, individually controlled by heart rate monitor use.	206 male Police recruits (<i>n</i> = 33 XX genotype).	At baseline, XX genotypes had greater VO ₂ measure scores than RR genotypes. Following training, this difference disappeared; i.e., RR had greater improvements than XX.
Delmonico et al., 2007	10-week (3 session per week) unilateral knee extensor strength training comprised of 4–5 sets of 10 repetitions.	155 (<i>n</i> = 86 females) older (50–85 years) subjects (<i>n</i> = 39 XX genotype).	Change in absolute peak power greater in RR vs. XX (<i>p</i> = 0.07) for males. Relative peak power change greater in RR vs. XX (<i>p</i> = 0.02).

TABLE 2 | Studies examining the interaction between *ACTN3* genotype and exercise recovery.

Study	Method	Sample characteristics	Main outcome
Pimenta et al., 2012	Eccentric-contraction based training session.	37 male professional soccer players based in Brazil. ($n = 9$ XX genotype).	Greater creatine kinase (CK) activity in XX genotypes vs. RR.
Clarkson et al., 2005b	50 maximal eccentric contractions of the elbow flexor.	157 male ($n = 78$) and female subjects of various ethnicities ($n = 115$ Caucasians; $n = 48$ XX genotype).	No association of R577X with increases in CK and myoglobin (Mb) following eccentric exercise.
Vincent et al., 2010	4 × 20 maximal single leg eccentric knee extensions.	19 healthy young males ($n = 10$ XX genotype).	XX genotypes had greater peak CK activity post-training compared to RR genotypes, and reported greater increases in muscle pain.
Venckunas et al., 2012	Two bouts of 50 drop jumps.	18 young males ($n = 9$ XX genotype).	RR showed greatest decrease in voluntary force, and slower recovery, compared to XX genotypes.
Djarova et al., 2011	Resting blood sample.	31 South African Zulu males ($n = 14$ Cricketers and $n = 17$ controls). No XX genotypes.	R allele associated with lower CK levels (RR vs. RX).
Del Coso et al., 2017b	Marathon race, pre- and post-race Counter Movement Jump (CMJ).	71 experienced runners ($n = 8$ XX genotype).	X allele carriers had higher CK and Mb levels post-race compared to RR homozygotes. X allele carriers also had a greater reduction in leg muscle power compared to RR genotypes.
Del Coso et al., 2017a	Triathlon competition (1.9 km swim, 75 km cycle, 21.1 km run), pre- and post-race CMJ.	23 healthy, experienced triathletes ($n = 19$ males, $n = 5$ XX genotype).	X allele carriers had a more pronounced jump height reduction compared to RR genotypes. In X allele carriers, there was a tendency toward higher post-race Mb concentrations ($P = 0.10$) and CK concentrations ($P = 0.06$) compared to RR homozygotes.
Belli et al., 2017	37.1 km adventure race (22.1 km mountain biking, 10.9 km trekking, 4.1 km water trekking, 30 m rope course).	20 well trained athletes ($n = 15$ males; $n = 4$ XX genotype).	XX genotypes had higher concentrations of serum Mb, CK, lactate dehydrogenase (LDH) and AST compared to R allele carriers.



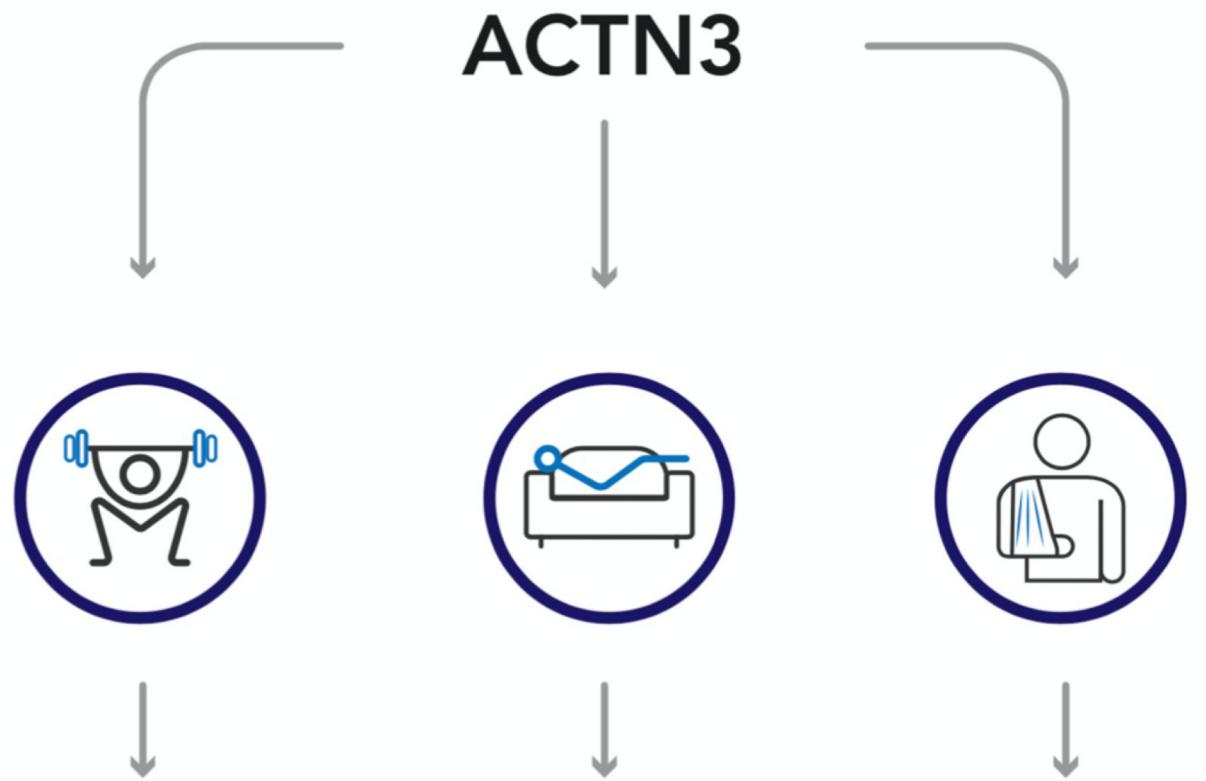
ACTN3: More than Just a Gene for Speed

Craig Pickering^{1,2*} and John Kiely¹

¹ School of Sport and Wellbeing, Institute of Coaching and Performance, University of Central Lancashire, Preston, United Kingdom; ² Exercise and Nutritional Genomics Research Centre, DNAFit Ltd, London, United Kingdom

TABLE 3 | Studies examining the interaction between ACTN3 genotype and sports injury.

Study	Method	Sample characteristics	Main outcome
Iwao-Koizumi et al., 2015	Sports injury data survey.	99 female students ($n = 34$ XX genotype).	R allele associated with an increased odds ratio (OR) of 2.52 of muscle injury compared to X allele.
Deuster et al., 2013	Controls—lower body exercise test. Cases—anonymous blood or tissue sample collected after an exertional rhabdomyolysis (ER) incident.	134 controls and 47 ER patients ($n = 38$ XX genotype)	XX genotypes 2.97 times more likely to be to ER cases compared to R allele carriers.
Qi et al., 2016	Ankle sprain case-control analysis.	100 patients with non-acute ankle sprain vs. 100 healthy controls ($n = 89$ XX genotype).	Significantly lower frequency of RR genotype in ankle sprain group compared to controls ($p = 0.001$).
Kim et al., 2014	Ankle injury case-control analysis.	97 elite ballerinas and 203 normal female adults ($n = 65$ XX genotype).	XX genotypes 4.7 times more likely to suffer an ankle injury than R allele carriers.
Shang et al., 2015	Ankle injury case-control analysis.	142 non-acute ankle sprain patients and 280 physically active controls ($n = 87$ XX genotype). All military recruits.	RR genotype and R allele significantly under-represented in the acute ankle injury group.
Massidda et al., 2017	Case control, genotype-phenotype association study.	257 male professional Italian soccer players and 265 non-athletic controls.	XX players were 2.6 times more likely to suffer a sports injury than RR genotypes. Severe injuries were also more likely in X allele carriers compared to RR genotypes.



(Pieckering & Kiely, *Front. Physiol.* 2017)

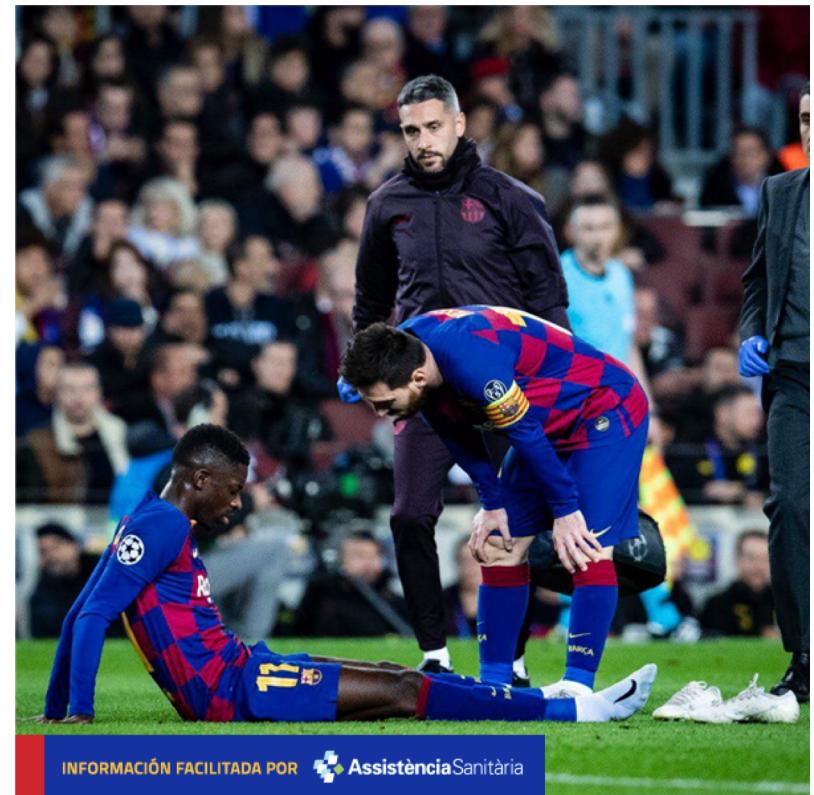


FIGURE 1 | A summary of the potential wider implications of ACTN3 genotype on outcomes from exercise.



More than a 'speed gene': *ACTN3* R577X genotype, trainability, muscle damage, and the risk for injuries

Juan Del Coso¹ · Danielle Hiam² · Peter Houweling³ · Laura M. Pérez^{4,5} · Nir Eynon^{2,3} · Alejandro Lucía⁴

European Journal of Applied Physiology

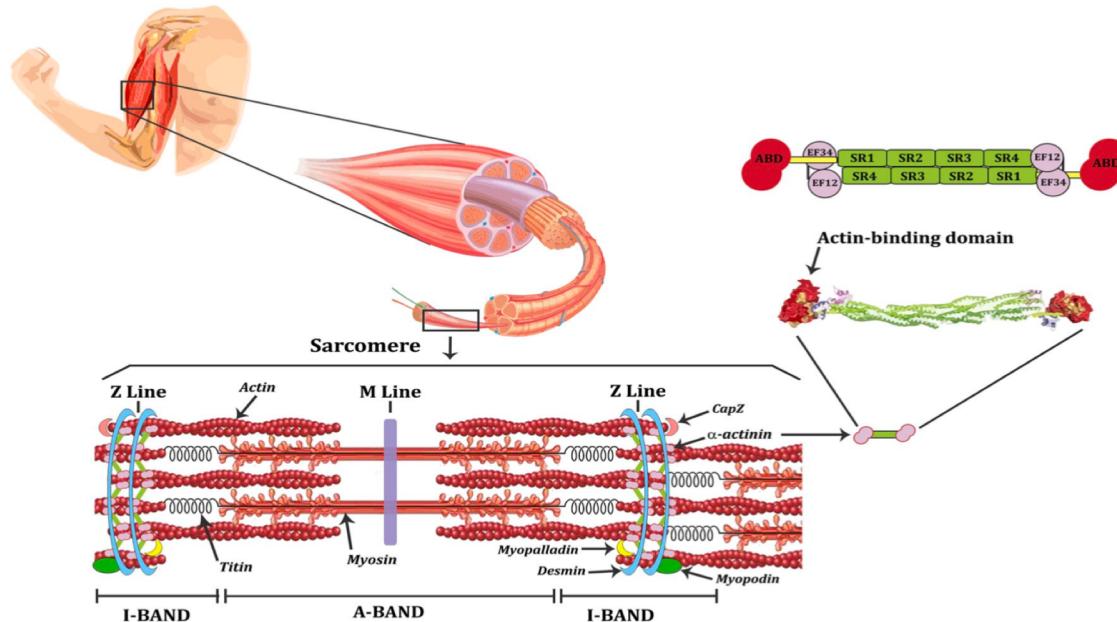


Fig. 1 Localisation of α -actinin in skeletal muscle. The sarcomeric α -actinins are essential for the contractile apparatus at the Z-line because they bind and cross-link the ends of F-actin filaments from adjacent sarcomeres. While the expression of α -actinin-2 is ubiquitous in all types of muscle fibers, α -actinin-3 is restricted to fast type II fibers, suggesting a different physiological role of each isoform for

muscle contraction. α -actinins are antiparallel homodimers of more than 200 kDa, comprising an actin-binding domain (ABD), a central domain of four spectrin-like repeats (SR1-4), and a C-terminal calmodulin-like domain with two pairs of EF hand motifs (EF). Adapted from (Ribeiro Ede et al. 2014)



More than a “speed gene”: ACTN3 R577X genotype, trainability, muscle damage and the risk for injuries

α -actinin-3 is a bundling protein that binds and cross-links the ends of F-actin filaments to the sarcomere.

α -actinin-3 is only expressed in type II skeletal muscle fibers.

α -actinin-3 is encoded by ACTN3 gene. A common stop-codon polymorphism (R577X) in this gene was discovered in humans.

Homozygosity for the X allele (577XX) results in the absence of α -actinin-3.



XX and RR individuals have a similar muscle fiber type composition.



XX are more prone to muscle damage during eccentric exercise and weight-bearing endurance exercise.



XX individuals have lower values of muscle strength and power than R-allele carriers.



The response to strength and endurance training is similar in XX, RX and RR.



XX genotype is much less frequent in sprint- and power based sports than RR.



In animals, XX have higher endurance capacity but this positive phenotype has not been replicated in human studies.



XX have a higher likelihood of ligament injuries during exercise but not of muscle injury.

XX have lower levels of bone mineral density but there is no data to relate this phenotype with a higher risk of bone injury during exercise.

(Del Coso et al. EJAP, 2019)

Fig. 2 Most common phenotypes related to α -actinin-3 deficiency due to homozygosity for the X allele in the ACTN3 R577X polymorphism

Association between ACTN3 R577X genotype and risk of non-contact injuries in trained athletes: A systematic review

Hassane Zouhal, Juan Del Coso, Ayyappan Jayavel, Claire Tourny, Guillaume Ravée, Nidhal Jebabli, Cain C. T. Clark, Benjamin Barthélémy, Anthony C. Hackney,*; Abderraouf Ben Abderrahman,*



Association between ACTN3 R577X genotype and risk of non-contact injury in trained athletes: a systematic review

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Complete List of Authors:	ZOUHAL, Hassane; EA Jayavel, Ayyappan; SRM Institute of Science and Technology Tourny, Claire; University of Rouen Ravé, Guillaume; Toulouse Football Club Del Coso, Juan; Camilo Jose Cela Univ jebabli, nidhal; Sciences Faculty of Bizerte, Department of Biology; High Institute of Sports and Physical Education of Kef, University of Jendouba, Kef, Tunisia., Research Unit, Sportive Performance and Physical

Zouhal et al. Coming Soon... JSHS...





Genetic testing for exercise prescription and injury prevention: AIS-Athlome consortium-FIMS joint statement

Nicole Vlahovich¹, David C. Hughes^{1,8}, Lyn R. Griffiths², Guan Wang³, Yannis P. Pitsiladis^{3,4,5}, Fabio Pigozzi^{4,5}, Nobert Bachl^{5,6} and Nir Eynon^{7*}

From 34th FIMS World Sports Medicine Congress
Ljubljana, Slovenia. 29th September – 2nd October 2016



Review

Can Genetic Testing Identify Talent for Sport?

Craig Pickering ¹ , John Kiely ¹, Jozo Grgic ², Alejandro Lucia ^{3,4} and Juan Del Coso ^{5,*}

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Problèmes du Testing Génétique dans le Sport

Problème de Taille de Cohorte ...

Problème de Homogénéité de Cohorte ...

Tests Génétiques Non-Valides Scientifiquement ...

REVIEW

Open Access



CrossMark

Genetic testing for exercise prescription and injury prevention: AIS-Athlome consortium-FIMS joint statement

Nicole Vlahovich¹, David C. Hughes^{1,8}, Lyn R. Griffiths², Guan Wang³, Yannis P. Pitsiladis^{3,4,5}, Fabio Pigozzi^{4,5}, Norbert Bachl^{5,6} and Nir Eynon^{7*}

From 34th FIMS World Sports Medicin Ljubljana, Slovenia. 29th September –

Abstract

Background: There has been considerable growth in basic knowledge and understanding of how genes are influencing response to exercise training and predisposition to injuries and chronic diseases. On the basis of this knowledge, clinical genetic tests may in the future allow the personalisation and optimisation of physical activity, thus providing an avenue for increased efficiency of exercise prescription for health and disease.

Results: This review provides an overview of the current status of genetic testing for the purposes of exercise prescription and injury prevention. As such there are a variety of potential uses for genetic testing, including identification of risks associated with participation in sport and understanding individual response to particular types of exercise. However, there are many challenges remaining before genetic testing has evidence-based practical applications; including adoption of international standards for genomics research, as well as resistance against the agendas driven by direct-to-consumer genetic testing companies. Here we propose a way forward to develop an evidence based approach to support genetic testing for exercise prescription and injury prevention.

Conclusion: Based on current knowledge, there is no current clinical application for genetic testing in the area of exercise prescription and injury prevention, however the necessary steps are outlined for the development of evidence-based clinical applications involving genetic testing.

Review

Can Genetic Testing Identify Talent for Sport?

Craig Pickering ¹ , John Kiely ¹, Jozo Grgic ², Alejandro Lucia ^{3,4} and Juan Del Coso ^{5,*} 

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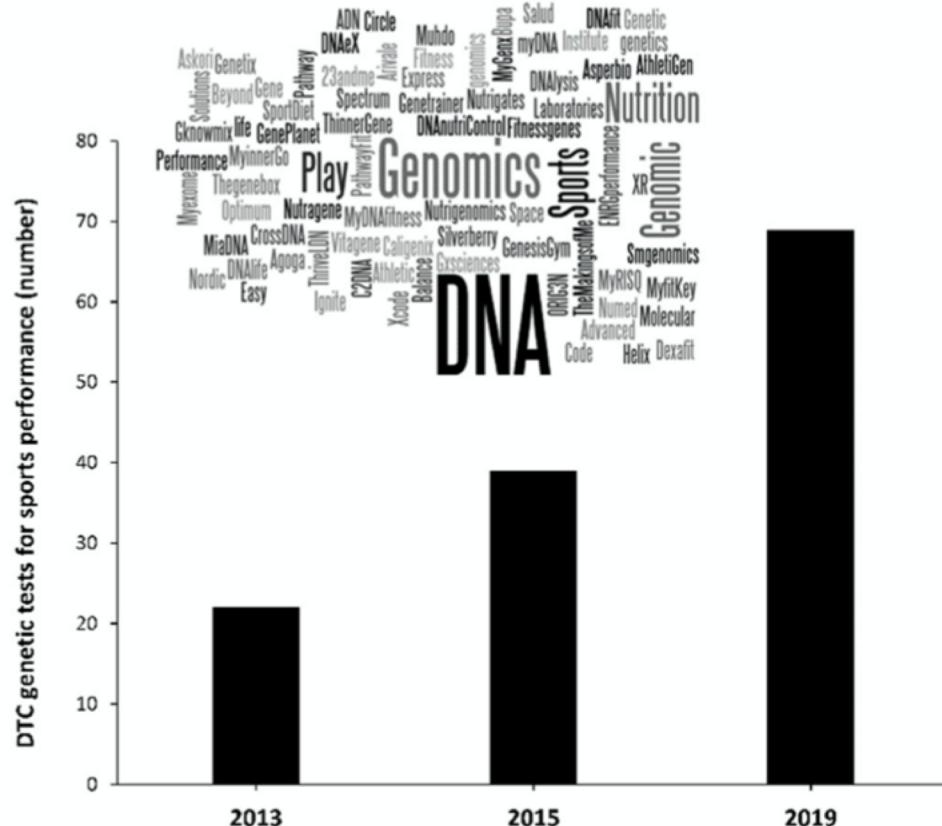


Figure 1. Number of companies that offer direct-to-consumer (DTC) genetic testing marketed as being related to sport performance, exercise performance and sports injury risk. Data in 2019 has been obtained by using the search terms “genetic”, “test”, “exercise” and “sport” in two popular search engines (Google and Bing) replicating the procedures followed by Williams et al., in 2013 [23] and Webborn et al., in 2015 [21].

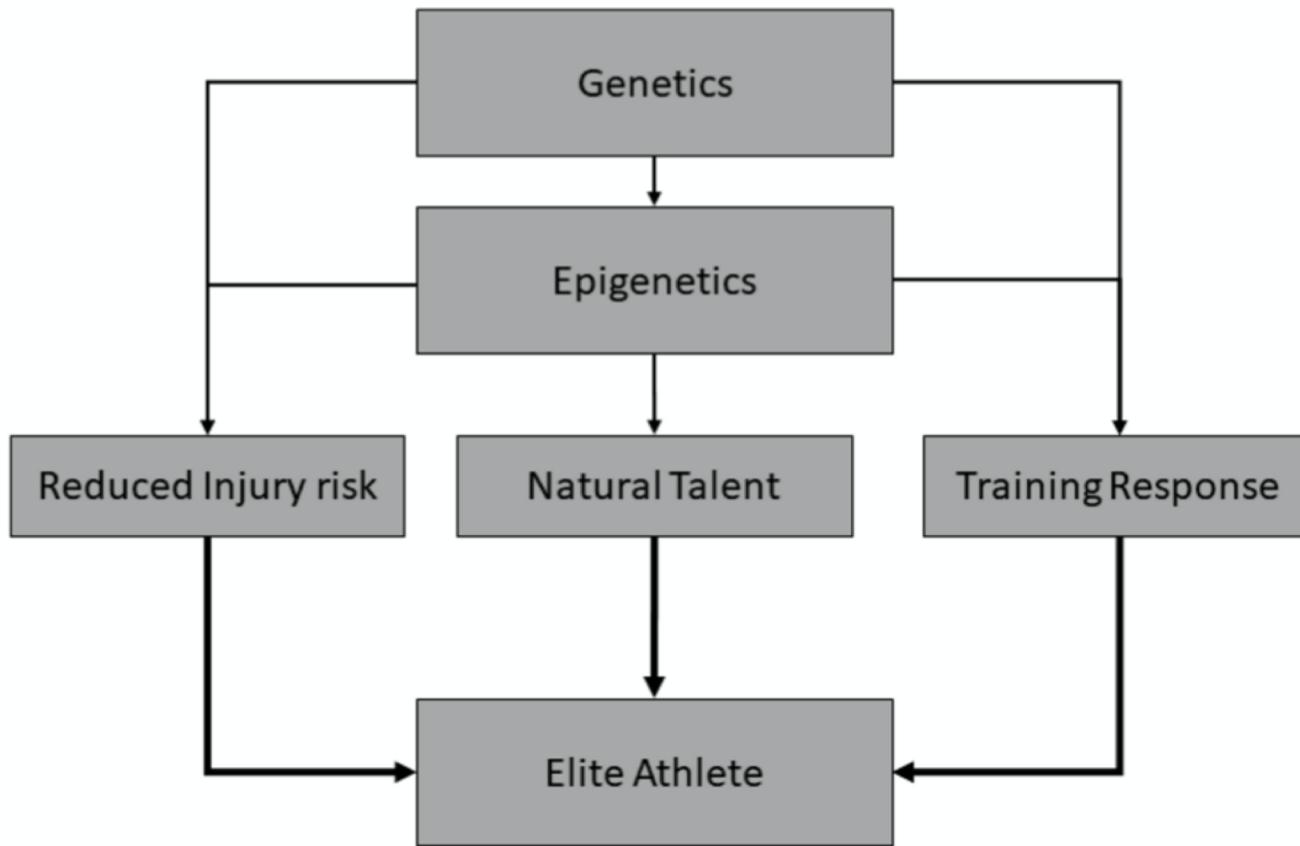


Figure 2. Influence of genetics and epigenetics on traits associated with elite performance. To succeed in sport, an athlete must possess genetic and epigenetic variations that might predispose to a natural talent trait (direct effect), and/or to enhanced response to physical training, and/or to reduced risk of injury (indirect effect).

Conclusion

Carence α -actinine-3
Homzygotie XX
Polymorphisme ACTN3 R577X

Altérations Physiologiques + Structurelles
Fibres Musculaires Type II

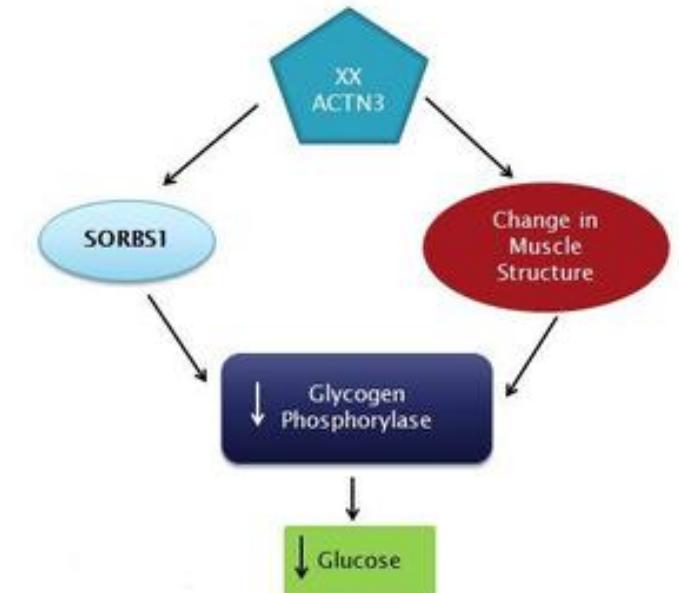
Effets - - / Perfs. Sportives
Puissance + Explosivité

Ath. XX

Proba. Blessures % Muscu. + Ligamentaires

Carence α -actinine-3

Capacité Endurance



NON
Polymorphisme ACTN3 R577X → Détection Talents

Perf. Sportives = Interactions Multifactorielles Complexes

(Baltazar-Martins et al. Sports 2020)

Effect of ACTN3 on sport performance, injury epidemiology and exercise-induced muscle damage

Discussion

Effect of ACTN3 Genotype on Sports Performance, Exercise-Induced Muscle Damage, and Injury Epidemiology

Gabriel Baltazar-Martins ¹✉, Jorge Gutiérrez-Hellín ²✉, Millán Aguilar-Navarro ^{1,2}✉, Carlos Ruiz-Moreno ¹✉, Víctor Moreno-Pérez ³, Álvaro López-Samanes ²✉, Raúl Domínguez ⁴✉ and Juan Del Coso ^{5,*}✉

- Morphology¹

Changes induced by the ACTN3 R577X polymorphism

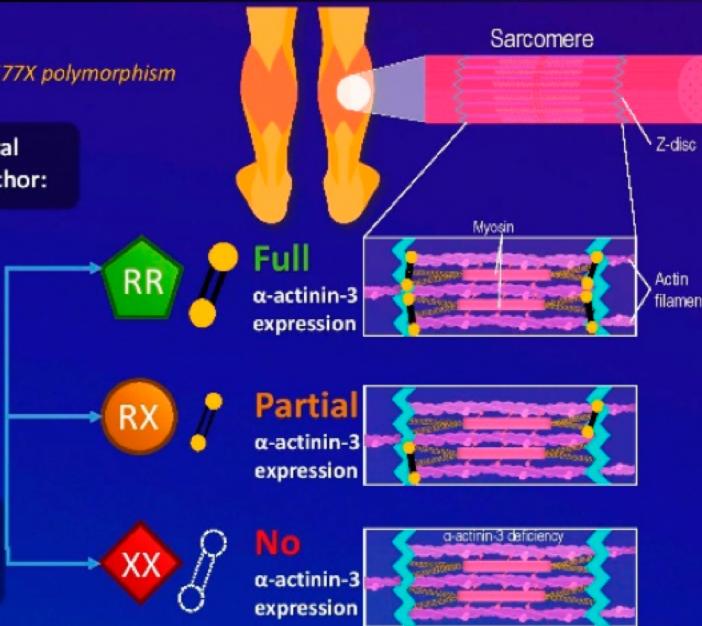
α -actinin-3 is a structural protein that helps to anchor:

Actin filaments

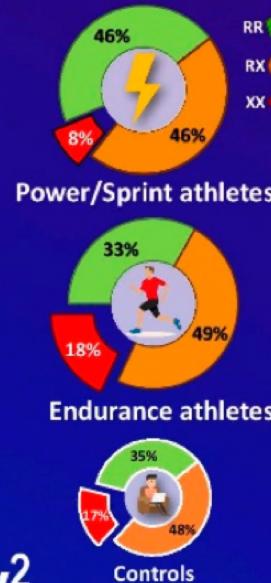
to the Z-disc

Z-disc

R577X polymorphism in the gene that codifies α -actinin-3 (ACTN3) changes the expression...



- Frequency² - of ACTN3 genotypes in sport



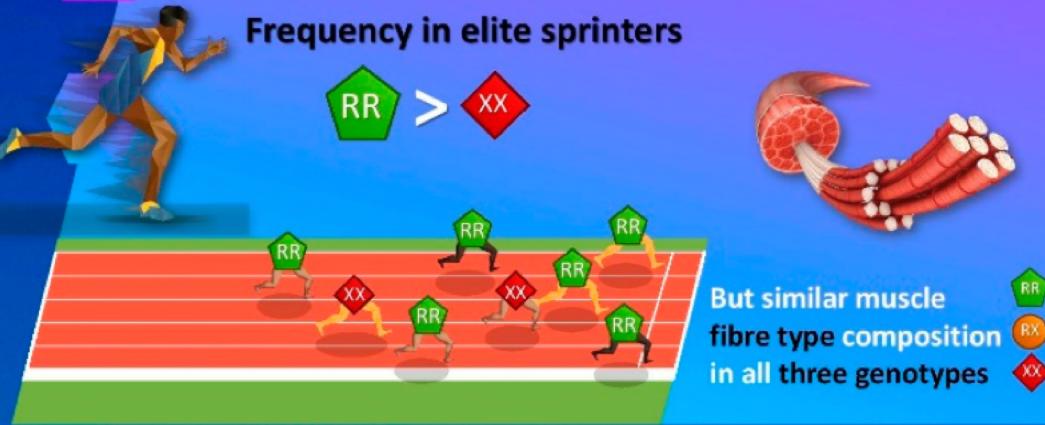
- Knock-out mice² - Evidence obtained with Actn3 knockout mice



01 Sports performance & trainability²

Frequency in elite sprinters

RR > XX



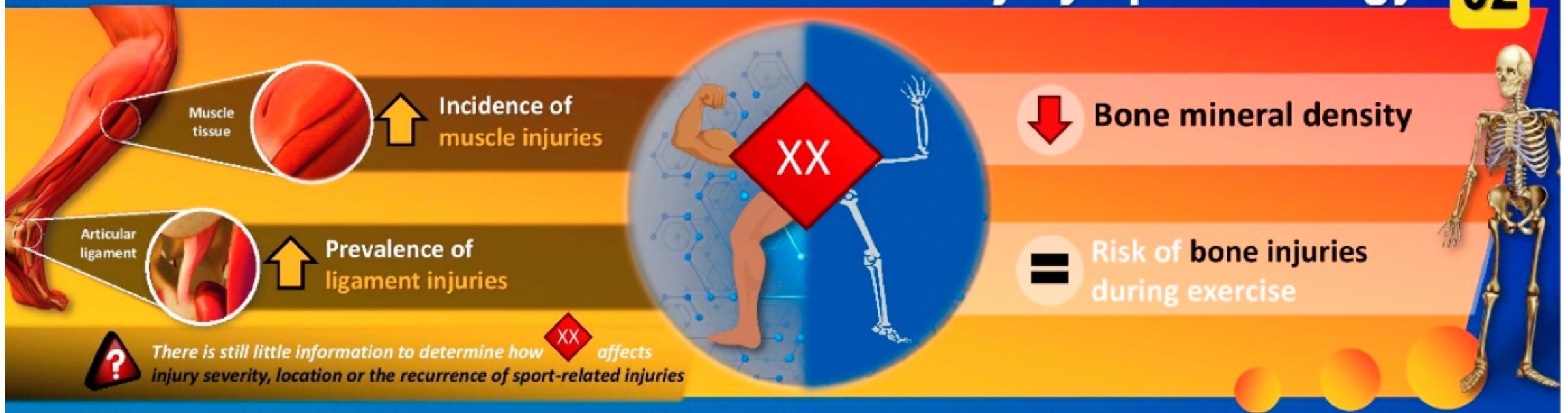
Muscle strength and power



But...

Similar response to strength and endurance training in all genotypes

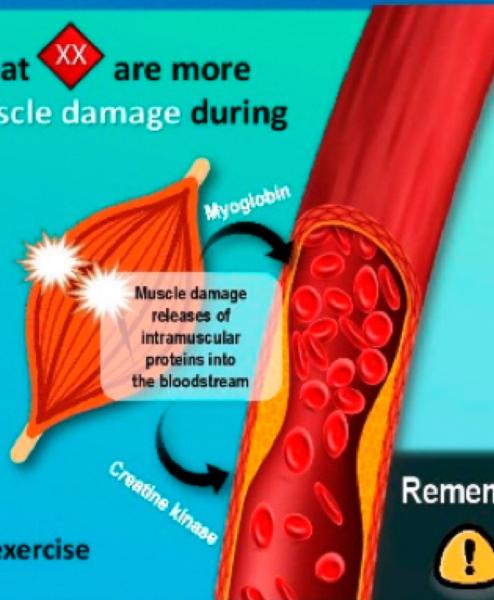
Injury epidemiology¹ 02



03

Exercise-induced muscle damage¹

- XX Most research indicates that XX are more prone to high levels of muscle damage during endurance exercise
- R-allele is considered protective against damaging exercise
- But...



- XX might be able to undertake more frequent training sessions due to a faster recovery after exercise



The current information on ACTN3 R577X should not be used to detect sports talent with direct-to-consumer genetic testing



Remember... One single gene polymorphism will not predict athletes' success or injury

Future studies should focus in real sporting contexts to increase their applicability

1. Del Coso et al., More than a 'speed gene': ACTN3 R577X genotype, trainability, muscle damage, and the risk for injuries. Eur J Appl Physiol (2019)
2. Houweling et al., Is evolutionary loss our gain? The role of ACTN3 p.Arg577Ter (R577X) genotype in athletic performance, ageing, and disease. Hum Mutat (2018)

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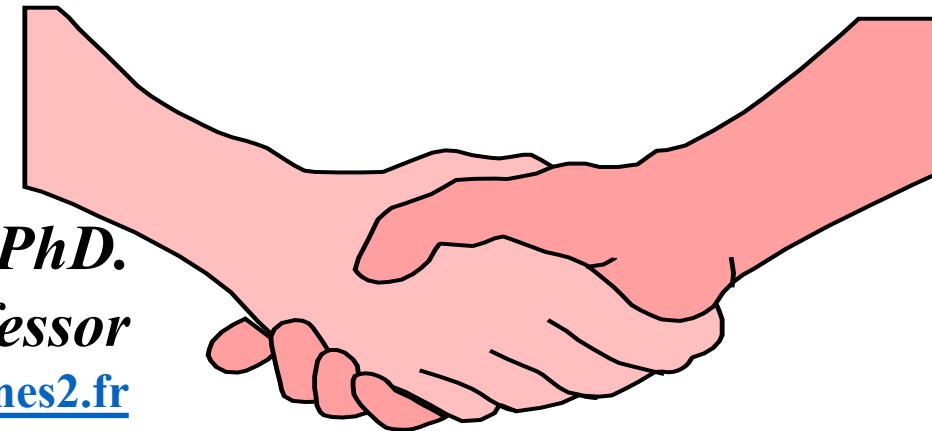


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MERCI POUR VOTRE ATTENTION



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Des questions??



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