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Human and African ape myosin heavy chain content and the evolution of hominin skeletal muscle

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ABSTRACT

Humans are unique among terrestrial mammals in our manner of walking and running, reflecting 7 to 8 Ma of musculoskeletal evolution since diverging with the genus *Pan*. One component of this is a shift in our skeletal muscle biology towards a predominance of myosin heavy chain (MyHC) I isoforms (i.e. slow fibers) across our pelvis and lower limbs, which distinguishes us from chimpanzees. Here, new MyHC data from 35 pelvis and hind limb muscles of a Western gorilla (*Gorilla gorilla*) are presented. These data are combined with a similar chimpanzee dataset to assess the MyHC I content of humans in comparison to African apes (chimpanzees and gorillas) and other terrestrial mammals. The responsiveness of human skeletal muscle to behavioral interventions is also compared to the human-African ape differential. Humans are distinct from African apes and among a small group of terrestrial mammals whose pelvis and lower limb muscle is slow fiber dominant, on average. Behavioral interventions, including immobilization, bed rest, spaceflight and exercise, can induce modest decreases and increases in human MyHC I content (i.e. -9.3% to 2.3%, $n = 2033$ subjects), but these shifts are much smaller than the mean human-African ape differential (i.e. 31%). Taken together, these results indicate muscle fiber content is likely an evolvable trait under selection in the hominin lineage. As such, we highlight potential targets of selection in the genome (e.g. regions that regulate MyHC content) that may play an important role in hominin skeletal muscle evolution.

1. Introduction

Humans are unique among African apes (i.e. chimpanzees and gorillas) and other primates in the size and shape of our lower back, pelvis, and lower limbs. Our suite of musculoskeletal traits interact so as to enhance our bipedal locomotor capabilities as compared to living African apes (e.g. Sockol et al., 2007; O'Neill et al., 2022), facilitating long-distance, overground travel and other long duration, muscle-driven activities. While skeletal traits are important determinants of locomotor performance and are under selection in the earliest hominins (e.g. Haile-Selassie, 2001; Lovejoy et al., 2009), skeletal muscle tissue also plays a fundamental role in the mechanics and energetics of movement. Yet, its contribution to hominin locomotor evolution is still not well understood. This is due to the limitations of the hominin fossil record and the near absence of comparative studies of human skeletal muscle biology, beyond individual-muscle mass and architectural measurements (e.g. Thorpe et al., 1999; Zihlman and Bolter, 2015).

Measurements of pulling (Bauman, 1923, 1926; Finch, 1943; Edwards and Clarke, 1965; Bozek et al., 2014) and jumping (Scholz et al., 2006) tasks in humans and chimpanzees indicate that chimpanzee skeletal muscle can outperform human skeletal muscle on a mass-specific basis, by about 1.5 times, on average (O'Neill et al., 2017). While direct measurements of the contractile characteristics of single muscle fibers (i.e. maximum isometric forces, maximum shortening velocities) indicate that humans and chimpanzees are quite similar, these two species differ substantially in their distribution of myosin

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heavy chain (MyHC) isoforms throughout their skeletal muscle (O'Neill et al., 2017). Indeed, while human skeletal muscles possess a predominance of MyHC I (i.e. slow fibers), the same muscles in chimpanzees possess about half as much, instead exhibiting a predominance of MyHC II (i.e. IIa, IId; fast fibers). This difference is relevant to locomotor performance capabilities, as MyHC isoform content affects whole-muscle contractile mechanics in both in vitro experiments (e.g. James et al., 1995; see also Schiaffino and Reggiani, 2011) and Hill-based muscle model simulations of maximum dynamic force and power (e.g. O'Neill et al., 2017; Mayfield et al., 2022). In particular, the MyHC isoform content of a muscle can influence its rate of contraction in response to a neural signal, as well as the shape of its force-velocity relationship (e.g. James et al., 1995). The metabolic cost of isometric force production and fatigability varies among muscle fibers of different MyHC content, with whole muscles that exhibit a predominance of slow fibers having the lowest costs and highest fatigue resistance (e.g. Harridge et al., 1996). As such, the predominance of MyHC I content within human skeletal muscle may reflect a shift within the hominin lineage, affecting both the mechanics and energetics of locomotor performance.

Still, it remains unclear whether the predominance of MyHC II or fast fibers is a characteristic of the pelvis and hind limb muscles of African apes as a group or simply a characteristic of chimpanzees alone. Direct measurements of skeletal muscle MyHC content of a gorilla species would help address this and further contextualize human patterns within the larger ape and primate clades. Gorilla skeletal muscle measurements also provide an important assessment of the size independence of human and African ape MyHC content. Whereas chimpanzee body masses are smaller than humans on average, both Western and Eastern gorillas can exceed human mean body mass by more than two times (Smith and Jungers, 1997). As such, commonalities among chimpanzees and gorillas would suggest that any human-African ape MyHC isoform composition differential is likely untethered from the increase in hominin body mass over the past 7 to 8 million years (Ma) (e.g. Grabowski et al., 2015; Ruff et al., 2018), which likely began with a common ancestor of the *Pan* and *Homo* lineages that was similar in size to chimpanzees (Grabowski and Jungers, 2017; Grabowski et al., 2018).

Understanding how humans and African apes compare to other terrestrial mammals across a wide body mass range is also needed to provide broader comparative context to human MyHC I content. Since 1973, the skeletal muscle fiber composition (defined based on mATPase, immunohistochemistry, MyHC content, RNA expression, etc.) of several non-ape primate species have been studied (Supplementary Materials Table 1), but only macaques (Acosta and Roy, 1987), galagos (Ariano et al., 1973; Sickles and Pinkstaff, 1981), slow lorises (Ariano et al., 1973; Sickles and Pinkstaff, 1981), and mouse lemurs (Petter and Jouffroy, 1993) have representative sampling across their pelvis and hind limbs (i.e. $n \geq 8$ muscles). An initial assessment of these and other studies indicated that the percent MyHC I or slow fiber content increases with larger body mass in terrestrial mammals, albeit with considerable interspecific variation (O'Neill et al., 2017; see Supplementary Materials Table 1). However, a more comprehensive sampling of the currently available literature across the terrestrial mammalian size range will further clarify the extent to which humans or African apes depart from this size-scaling pattern and help identify what other terrestrial mammals are slow fiber dominant.

Of course, skeletal muscle fiber composition is expected to be responsive to age and some behavioral interventions, although the magnitude of this effect is difficult to determine from one or two studies alone. Human muscle fiber composition has been measured in the pelvis and lower limb muscles of both young (Johnson et al., 1973: 22 yrs) and older adults (Tirrell et al., 2012: 83 yrs), and has been subject to a broad range of behavioral interventions, from immobilization to increased exercise. While muscle mass is exceptionally responsive to these factors (e.g. D'Antona et al., 2006; Handsfield et al., 2017), the responsiveness of muscle fiber composition may be quite modest by comparison. A recent meta-analysis of decreased activity levels (e.g. bed rest, leg unloading, detraining) on human lower limb muscle found a trivial 1–2% decrease in MyHC I content, on average ($n = 451$ subjects; Vikne et al., 2020). It is possible that increased activity levels due to exercise or strength training may have a more substantial effect on MyHC I content, but there is no comparable survey of the existing human experimental data. Such data would provide greater insight into the extent to which the human-African ape differential in MyHC isoform composition is attributable to behavioral shifts in life or may be better understood as an evolvable musculoskeletal trait under selection between species.

Here, we combine new MyHC isoform content data from pelvis and hind limb muscles of a Western gorilla (*Gorilla gorilla*) with existing chimpanzee (*Pan troglodytes*) data, as well as comprehensive data collation and meta-analysis of skeletal muscle fiber composition studies from 1965 to 2022 to better understand the distinctiveness of human skeletal muscle MyHC I content. Based on these results, we suggest that the substantial MyHC I content in human pelvis and lower limb skeletal muscle may be best understood as an evolvable musculoskeletal trait under selection in the hominin lineage, perhaps for reducing muscle metabolism and enhancing fatigue resistance to aerobic muscle contractile behavior. We hypothesize that molecular mechanisms that underlie muscle fiber composition are potential targets for selection during hominin evolution. Given the importance of MyHC gene regulation during muscle fiber development (Hagiwara et al., 2007; Hennebry et al., 2009; Schiaffino et al., 2015), it is likely that species-specific differences in adult MyHC content, such as those observed between humans and African apes, are due to species-specific changes in regions of the genome that regulate the expression of MyHC genes and their MyHC isoforms. As such, we highlight potential targets of selection in the genome (e.g. enhancer regions, a specific type of regulatory element) that may play an important role in hominin skeletal muscle evolution.

2. Materials and methods

2.1. *Gorilla gorilla* muscle MyHC content

The MyHC isoform distribution of *Gorilla gorilla* was determined for samples (10–20 mg) of 35 pelvis and hind limb muscles from one adult, female. The animal had been living in a zoo and died of natural causes prior to muscle sampling. After death, the cadaveric remains were kept fresh frozen at −20 °C until dissection. The pelvis and hind limb were free of visible pathology. Prior to dissection, the specimen was CT scanned using a Philips-Gemini TF64. Serial scans of each bone were collected at a slice thickness of 0.67 mm with 0.35 overlap (voltage: 120 kV; current 320 mA). The CT scanner output a stack of DICOM image files that were imported, rendered, and measured in Mimics Research 19.0 (Materialise n.v., 2016). Femoral head superior-inferior diameter (FHSI) predicted an adult body mass of 85.3 kg using a gorilla-specific reference sample, although an African ape reference sample prediction was similar (FHSI: 41.33 mm; African Ape Eqn: 83.7 kg; Burgess et al., 2018).

To determine MyHC isoform composition, the skin and fascia were removed around the pelvis and hind limb, then individual muscles were identified. A 2 cm × 0.5 cm × 0.5 cm muscle tissue sample was taken from two locations of each muscle in the same manner as a previous study (e.g. O'Neill et al., 2017). The MyHC isoform expressed in each sample was identified using SDS-PAGE. The composition, preparation, staining and densiometric scanning of the gels were identical to those described previously (O'Neill et al., 2017). The amount of each MyHC isoform in the sample that expressed multiple isoforms was calculated as a percentage of the total amount of MyHC. The three MyHC isoforms that were detected on protein gels were identified based on commonalities with previous human and chimpanzee gels (O'Neill et al., 2017).

The distribution of MyHC isoforms within 35 pelvis and hind limb muscles of the gorilla was compared using an analysis of variance (ANOVA), with Tukey HSD post-hoc pairwise comparisons between MyHC isoforms. Two-sample *t*-tests were used to conduct pairwise comparisons between the average fraction of MyHC I in the gorilla mean and the individual-subject means for the chimpanzee and two human datasets. For interspecific comparisons, the mean MyHC I content across all pelvis and hind/lower limb muscles was calculated for each individual, then the between-individual mean and standard deviation were determined. This reflects the variance in mean MyHC I content between individuals studied in each species. Two human datasets were used, representing both young (22 yrs.; Johnson et al., 1973, $n = 14$ muscles) and old adults (83 yrs.; Tirrell et al., 2012, $n = 37$ muscles), and permitting an initial assessment of age effects on mean MyHC I content across the pelvis and lower limb.

2.2. Terrestrial mammal muscle fiber composition comparisons

2.2.1. Eligibility criteria and study selection

Published, peer-reviewed data were compiled for meta-analysis between June 1, 2021 and November 30, 2022 following a structure similar to Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) (Moher, 2009), facilitating transparency and ease of reproducibility. Terms relating to mammalian skeletal muscle fiber composition (red, Type 1, β, MHC I, MyHC I, slow twitch, fatigue resistant, slow oxidative, slow fiber, slow myosin isozyme) were queried using academic search systems (Google Scholar, PubMed, and JSTOR) and library databases for relevant primary articles. Reference lists in relevant articles were thoroughly investigated for eligible studies. No restrictions were set on the date of publication.

Eligible studies were published in the English language and provided muscle fiber composition data from at least one skeletal muscle from a species belonging to class Mammalia. Any data collected after a behavioral intervention (e.g. % fiber content after a treadmill running regime) were excluded.

2.2.2. Data extraction

The following data were recorded from the text, tables, figures, and supplementary materials of included studies when available: sampled species' common name, scientific name, sex, age, method for classification of muscle fiber composition, slow muscle fiber terminology used (e.g. MyHC I, MHC I, Type I, beta, slow oxidative, red or slow twitch), number of individuals sampled, average body mass (kg), muscle(s) sampled and average percent slow fiber content (% fibers).

In most studies, body mass was reported; for those studies that did not report a body mass the species mean was taken from Clarke et al. (2010) or Genoud et al. (2018). When muscle fiber content was recorded as the percentage of fast muscle fibers within a skeletal muscle, the proportion of slow muscle fibers was derived as 100 minus the total proportion of fast muscle fibers. If slow muscle fiber content was reported from multiple sampling sites across a single muscle (e.g. superficial and deep), the average across the sampling sites was recorded as the percent slow muscle fiber content of that muscle.

Given that most studies were published between 1965 and 1999, binomial and common names were updated when necessary to reflect the current understanding of phylogenetic relationships. Taxonomic data (i.e. class, infraclass, magnorder, superorder, order, suborder, infraorder, parvorder, clade, superfamily, family, subfamily, tribe, and subspecies) provided by NCBI Taxonomy (Schoch et al., 2020) was recorded for each species when available.

For interspecific comparisons a minimum sampling threshold of 8 pelvis and hind/lower limb muscles per species was considered representative. Studies meeting the minimum sampling threshold were used for two analyses: (i) one comparing the average slow fiber content across all measured pelvis and hind/lower limb muscles per species and (ii) one comparing the mean slow fiber content across a set of 8 matched pelvis and hind/lower limb muscles per species, which controlled for individual muscle variation. The matched muscle condition included muscle composition measurements from the *mm. gluteus medius*, *biceps femoris*, *semimembranosus*, *semitendinosus*, *vastus lateralis*, *extensor digitorum longus*, *gastrocnemius*, and *tibialis anterior*. This subset of muscles represented the three main anatomical regions (i.e. pelvis, thigh, leg) while permitting the greatest number of species to be included. When multiple studies existed for the same species, slow fiber content was averaged by muscle across studies and the average of recorded body masses was used as the pooled species average body mass. This both increases the number of animals sampled and permits the inclusion of data from multiple labs and techniques, which should reflect measurement reproducibility.

2.2.3. Interspecific scaling analyses

To incorporate the potential statistical non-independence of species due to shared common ancestry, the scaling relationship of muscle slow fiber content with $\log_{10}$ body mass was evaluated using phylogenetic generalized least squares (PGLS). The phylogenetic structure of the analyzed species was taken from published mammalian trees (Upham et al., 2019). The PGLS parameters were estimated using the Comparative Analyses of Phylogenetics and Evolution in R package (Orme et al., 2013) with the parameter lambda (λ) fixed at 0 (star phylogeny) and 1 (Brownian motion) and empirically estimated using a maximum-likelihood (ML) approach (Pagel, 1999). The three different model fits (i.e. 0, 1, ML) were compared using a likelihood ratio test. Human, chimpanzee and gorilla MyHC I content z-scores were calculated as $z = (x_i - \mu_i)/\sigma$, where x_i is the average fraction of MyHC I of species i, μ_i is the i species mean predicted from the regression fit, and σ is the standard deviation of the sample. To detect regression fit outliers, phylogenetic residuals were studentized by dividing the residual by the square root of their variance. Studentized residuals greater than an absolute value of 3 were considered outliers (Jones and Purvis, 1997). Phylogenetic residuals were also standardized by dividing the residual by the square root of the expected value.

2.3. Human intervention muscle fiber content comparisons

2.3.1. Eligibility criteria and study selection

Humans are the best-studied species in terms of the response of muscle fiber content to behavioral interventions and are of clear, direct relevance for hominin locomotor evolution. As such, published, peer-reviewed data were compiled for meta-analysis between June 1 and November 30, 2022 following a structure similar to PRISMA (Moher, 2009). Terms relating to human exercise (human exercise, human running, human training, strength training, endurance training, sprint training, detraining, cycling) and skeletal muscle fiber composition (red, Type 1, β, MHC I, MyHC I, slow twitch, fatigue resistant, slow oxidative, slow fiber, slow myosin isozyme) were used to query academic search systems (Google Scholar, PubMed, JSTOR) and library databases for relevant primary articles. Reference lists in relevant articles were thoroughly investigated for eligible studies. No restrictions were set on the date of publication.

Eligible studies were published in the English language and provided muscle fiber composition data from human lower limb muscles both before and after a behavioral intervention. This permitted a change in mean slow fiber content (%) over time to be calculated. As such, only longitudinal studies were included; all cross-sectional studies were excluded from consideration. Interventions that included a countermeasure (e.g. bed rest with exercise or bed rest with nutritional countermeasure; Trappe et al., 2008) were also excluded, although the mean effects of these countermeasures all fall within the range determined here. No criteria were set on participant sex as no significant sex-based differences in skeletal muscle response to training have been identified (Short et al., 2005; Kojić et al., 2021).

2.3.2. Data extraction

The following data were recorded from the text, tables, figures, and supplementary materials of included studies when available: intervention type, intervention duration (hours, days, weeks, months), type(s) of exercise participants were subjected to, skeletal muscle sampled, number of participants, participant sex, average participant mass (kg), average participant age (years), average pre-intervention skeletal muscle slow fiber content (% fiber), average post-intervention skeletal muscle slow fiber content (% fiber), standard deviation, and method for classification of muscle fiber composition. Study results were then categorized into one of nine distinct behavioral interventions based on the activity under investigation: bed rest, immobilization, environmental, spaceflight, endurance training, strength training, sprint training, dynamic training, and detraining. See definitions of each intervention in Table 3.

When muscle fiber content was recorded as the percentage of fast muscle fibers within a skeletal muscle, the proportion of slow muscle fibers was derived as 100 minus the total proportion of fast muscle fibers. If multiple intervention time points were reported along a time series, only slow fiber content at the first and last time points were recorded.

2.3.3. Statistical analyses

The delta of each study was calculated as the mean difference in slow fiber content at the start and end of each unique behavioral intervention for each studied lower limb muscle. For each of the nine intervention categories, a pooled intervention effect size was calculated across studies. This was done as a weighted average based on sample size, such that studies with a larger number of subjects had a larger weight on the intervention mean. The weighted intervention mean across all lower limb muscles and the weighted intervention mean of *m. vastus lateralis* alone were calculated. A negative delta indicated a decrease in slow fiber content, while a positive delta indicated an increase in slow fiber content.

The weighted intervention means were then compared to the mean difference in slow fiber content between humans and African apes (gorillas and chimpanzees) for all studied pelvis and hind/lower limb muscles, as well as for the *m. vastus lateralis* alone. For these muscles the human average was taken from Tirrell et al. (2012) and Johnson et al. (1973) and compared to that of chimpanzees (O'Neill et al., 2017) and the gorilla (this study) to determine the degree of difference between humans and each African ape.

3. Results

3.1. Gorilla MyHC isoform content is similar to chimpanzees

The distribution of MyHC isoforms within 35 pelvis and hind limb muscles of the gorilla indicate a predominance of MyHC II fibers, with a significant bias towards MyHC IId, on average ($F_{(2,114)} = 11.55$, $p = 0.000027$; Fig. 1A; Table 1). The MyHC IId content was significantly higher than MyHC I ($p = 0.00022$) or MyHC IIa ($p = 0.00015$). There are significant differences between African apes and humans (H) in mean MyHC I content across the pelvis and hind/lower limb ($F_{(3,122)} = 96.93$, $p < 0.0001$). Specifically, chimpanzees (C) and gorillas (G) were similar ($p = 0.6702$), while both species differed from young (G v. H: $p = 0.00012$; C v. H: $p = 0.00075$) and old adult humans (G v. H: $p = 0.00011$; C v. H: $p = 0.00012$) (Fig. 1B). The difference between the old and young adult humans was not significant ($p = 0.147$).

Muscle-matching across species to the young human muscle count ($n = 14$ muscles, Johnson et al., 1973) results in similar species-mean differentials (G: 29.7 ± 8.1%; C: 33.4 ± 11.9%; H: 61.8 ± 14.6%, 55.8 ± 5.7%) as in the full, unmatched accounting. All three species exhibit a similar pattern of African ape-human differentiation across the three regions within the pelvis and hind/lower limb (pelvis, thigh, leg) (Fig. 1C). Among the two human datasets, the older adults exhibit a larger fraction of MyHC I isoforms in their pelvis and thigh muscles than the younger adults, while the leg musculature is similar between groups.

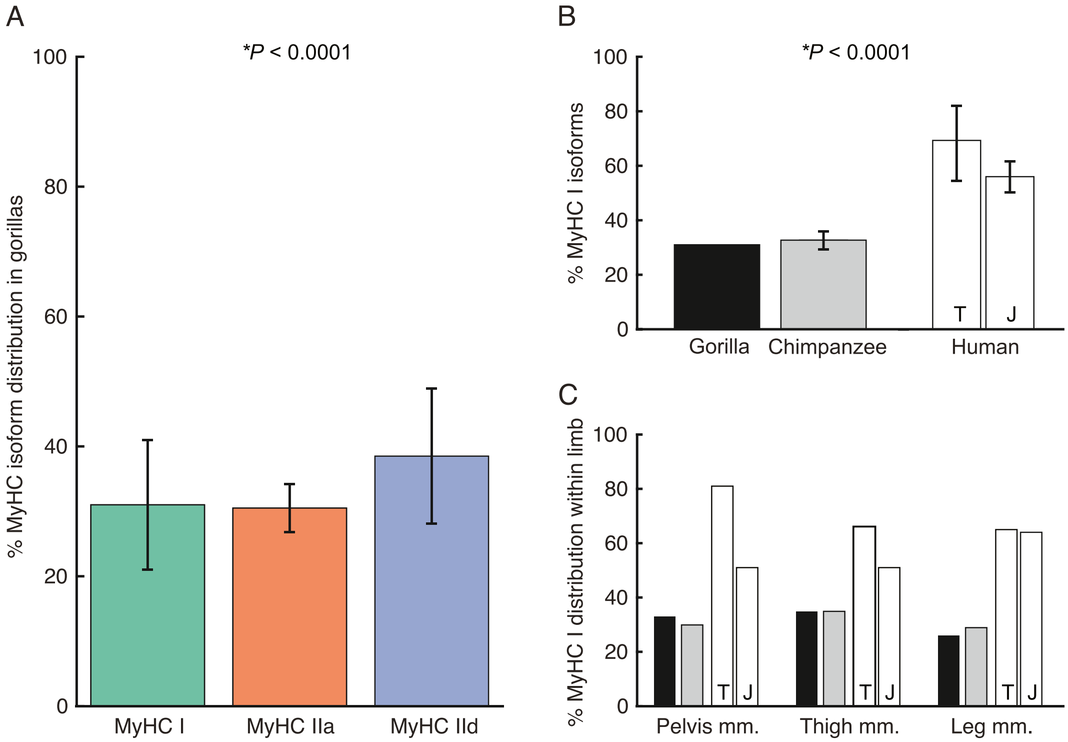

Fig. 1. MyHC isoform distributions of gorilla, chimpanzee and human skeletal muscles. (A) Gorilla exhibits a MyHC II dominant distribution among the three MyHC isoforms across 35 skeletal muscles. P value is from an ANOVA. (B) Humans exhibit a significant bias towards slow MyHC I fibers in their skeletal muscle with measurements ranging from the between-subjects mean ± s.d. of (i) 69.0 ± 13.7% ($n = 37$ muscles, Tirrell et al., 2012; T) to (ii) 55.6 ± 5.7% ($n = 14$ muscles, Johnson et al., 1973; J). This differentiates humans (T: $n = 6$; J: $n = 6$) from the between-subject mean ± s.d. of 31.5 ± 3.3% in chimpanzees ($n = 3$) and 30.8% in the gorilla ($n = 1$). (C) The predominance of slow MyHC I fibers in human skeletal muscle is distinct from African apes for all major anatomical regions, including the pelvis, thigh and leg.

Table 1
Mean myosin heavy chain (MyHC) isoform content of 35 pelvis and hind limb muscles of *Gorilla gorilla* ($n = 1$).

Muscle	MyHC I (%)	MyHC IIa (%)	MyHC IId (%)
Adductor brevis	26.9	31.9	41.3
Adductor longus	45.6	41.4	13.1
Adductor magnus			
Adductor magnus ischiocondylaris	53.5	25.8	20.8
Adductor magnus pubofemoralis	34.7	37.6	27.8
Biceps femoris			
Biceps femoris, long head	40.9	25.2	34.0
Biceps femoris, short head	26.7	28.5	44.9
Extensor digitorum longus	26.1	28.8	45.3
Extensor hallucis longus	31.4	26.2	42.6
Flexor digitorum fibularis	15.5	27.2	57.4
Flexor digitorum tibialis	17.7	27.1	55.2
Gastrocnemius lateralis	20.2	35.2	44.7
Gastrocnemius medialis	22.1	31.6	46.3
Gemellus inferior	17.2	32.4	50.5
Gemellus superior	27.4	30.1	42.7
Gluteus maximus			
Gluteus maximus ischiofemoralis	39.4	22.9	37.7
Gluteus maximus proprius	27.2	33.0	39.9
Gluteus medius	33.0	32.0	35.1
Gluteus minimus	29.5	30.2	40.4
Gracilis	24.8	32.5	42.7
Iliopsoas			
Iliacus	33.9	30.7	35.4
Psoas major	20.6	29.5	49.9
Obturator externus	29.9	30.1	40.1
Obturator internus	23.2	27.0	49.8
Pectineus	30.1	31.9	38.0
Peroneus (fibularis) brevis	26.7	33.6	39.8
Peroneus (fibularis) longus	21.3	32.9	46.0
Piriformis	39.4	34.1	26.6
Quadratus femoris	50.9	29.2	20.0
Rectus femoris	28.4	30.1	41.5
Sartorius	26.3	34.4	39.4
Semimembranosus	38.4	26.6	35.2
Semitendinosus	26.7	31.4	41.9
Soleus	45.7	25.9	28.5
Tensor fascia lata	26.2	33.0	40.9
Tibialis anterior	21.2	34.5	44.5
Tibialis posterior	32.3	30.6	37.2
Vastus intermedius	55.3	33.8	11.0
Vastus lateralis	28.3	27.1	44.7
Vastus medialis	36.8	28.2	35.0
Mean	30.8	30.6	38.6
Standard deviation	9.8	3.7	10.2

3.2. Humans are distinct from African apes and most other terrestrial mammals in muscle slow fiber content

A total of 373 terrestrial mammal muscle fiber composition studies were identified. Of these, 108 were excluded because: (i) muscle fiber composition data were not provided ($n = 73$), (ii) muscle fiber composition data provided were ambiguous ($n = 14$), (iii) muscle fiber composition data were provided for an unidentified muscle ($n = 2$), (iv) muscle fiber composition data were provided for cardiac fibers ($n = 2$), (v) muscle fiber composition data were provided for single muscle fibers ($n = 3$), (vi) muscle fiber composition data were provided for a mammal under experimental conditions ($n = 4$), (vii) the study duplicated another dataset ($n = 2$), (viii) the source was secondary ($n = 7$), or (ix) the source was a published abstract ($n = 1$). The remaining 265 studies were published between 1965 and 2022. Skeletal muscle fiber composition data were collated for 175 species spanning 15 mammalian orders (see Supplementary Materials Table 1).

Of these, 35 species across 12 mammalian orders met the minimum sampling threshold of 8 hind/lower limb muscles (Table 2), ranging in size from a Dsinezumi shrew (0.0094 kg) to an African savanna elephant (1542 kg). The total number of pelvis and hind/lower limb muscles sampled was 8 to 37 muscles per species, with humans and African apes being the best represented species. Twelve of the studies meeting the minimum sampling threshold included data for the 8 matched pelvis and hind/lower limb muscles (i.e. *mm. gluteus medius*, *biceps femoris*, *semimembranosus*, *semitendinosus*, *vastus lateralis*, *extensor digitorum longus*, *gastrocnemius*, *tibialis anterior*). As such, the reduced, muscle-matched sample included 21 species, spanning the same size range.

PGLS scaling analyses revealed that greater log$_{10}$ body mass predicted higher hind/lower limb slow fiber content across both the larger, unmatched (coefficient ± s.e. 7.51 ± 2.36, $\lambda = 0.74$, 95% CI [0.12, 0.94], $r^2 = 0.21$, $t_{1,33} = 3.18$, $p = 0.003$) (Fig. 2A) and smaller muscle-matched (estimate±s.e. 10.83 ± 3.61, $\lambda = 0.54$, 95% CI [NA, 0.91], $r^2 = 0.29$, $t_{1,19} = 3.00$, $p = 0.007$) (Fig. 2B) datasets. In both cases, the ML model fit was significantly different from a star phylogeny in the unmatched, but not the matched sample ($\lambda = 0$; $p = 0.0461$ and $p = 0.1253$, respectively) and from Brownian motion in both samples ($\lambda = 1$; $p = 0.0001$ and $p = 0.0008$). Humans exhibit a positive *z*-score relative to this size-scaling relationship (2.23), whereas African apes exhibit negative *z*-scores (C: -0.66; G: −1.08). This pattern is similar for both the unmatched and muscle-matched datasets.

Only four terrestrial mammal species are slow fiber dominant (i.e. ≥ 50% slow fibers) in their pelvis and hind/lower limb muscles (i.e. humans, slow lorises and two sloths) in the unmatched interspecific sample. However, none of these species – including humans – were determined to be outliers with respect to the studentized residuals of the size-scaling relationship. In the reduced, muscle-matched sample, humans are the only primate that are slow fiber dominant, with the substantial human-African ape differential being maintained (Fig. 2B).

3.3. Human behavioral interventions have a small impact on muscle slow fiber content

A total of 256 human intervention studies were identified. Of these, 131 studies were excluded because: (i) muscle fiber composition data were not provided ($n = 28$), (ii) pre- or post-intervention muscle fiber composition data were not provided ($n = 62$), (iii) pre- or post-intervention muscle fiber composition data were ambiguous ($n = 7$), (iv) muscle fiber composition data were provided for muscles other than the lower limb ($n = 6$), (v) muscle fiber composition data provided focused on the effect of aging ($n = 3$), (vi) the study provided a duplicated dataset ($n = 2$), and (vii) the source was secondary ($n = 23$). In addition, two studies quantified the change over time in fiber composition in persons with permanent loss of muscle innervation due to catastrophic injury (Lotta et al., 1991; Burnham et al., 1997). These studies were not included in the meta-analysis given their distinct difference from all other studies. The remaining 123 studies were published between 1973 and 2019. There were a total of 2033 participants across these 123 studies, with a mean reported age and body mass of 32.9 ± 17.4 years and 72.8 ± 9.3 kg. The total number of participants in each intervention category were: bed rest ($n = 153$), immobilization ($n = 179$), environmental ($n = 30$), spaceflight ($n = 21$), endurance training ($n = 313$), strength training ($n = 1018$), sprint training ($n = 92$), dynamic training ($n = 96$), and detraining ($n = 131$) (Table 3; see category definitions therein).

The effect of each intervention category on lower limb muscle slow fiber content ranged from −9.3 ± 6.9% in spaceflight to 2.3 ± 5.7% in endurance training (Table 3; Fig. 3A). Comparisons based on the *m. vastus lateralis* alone were similar, albeit with a slightly smaller range (−7.3 ± 1.4% to 2.4 ± 6.4%; Fig. 3B). Overall, these pooled intervention effect sizes are substantially lower than the degree of difference observed between the hind/lower limb muscles of humans and chimpanzees (31.1 ± 9.6%) and humans and the gorilla (31.3 ± 9.6%). This is also the case when looking at the *m. vastus lateralis* alone (H v. C: 11.0 ± 4.2%; H v. G: 17.1 ± 4.2%).

Table 2

Studies meeting the minimum threshold ($n \geq 8$ hind/lower limb muscles) for use in interspecific size scaling analysis of terrestrial mammals. Species colored by taxonomic order (Aigner et al., 1993; Armstrong and Phelps, 1984; Armstrong et al., 1982; Burkholder et al., 1994; Delp and Duan, 1996; Edgerton et al., 1975; Eng et al., 2008; Goto et al., 2013a; Goto et al., 2013b; Hansen et al., 1987; Ichikawa et al., 2019; Jouffroy et al., 2003; Kawai et al., 2009; Konno and Watanabe, 2012; Mashima et al., 2019; Mattson et al., 2002; Rivero et al., 1999; Sahd et al., 2022; Spainhower et al., 2021; Summerbell et al., 2000; Suzuki, 1990; Suzuki and Tamate, 1988; Suzuki et al., 1999; Talmadge et al., 1996; Zhong et al., 2008).

Order	Common name	Scientific name	No. of subjects	Average body mass (kg)*	No. of muscles	Average slow fiber content (%)	References
Artiodactyla	Japanese black cattle	*Bos taurus*	3	680*	8	30.6	Mashima et al., 2019
	Corriedale sheep	*Ovis aries*	13	51.5	14	35.0	Suzuki and Tamate, 1988; Konno and Watanabe, 2012
	Pig, De-Kalb strain	*Sus scrofa domesticus*	5	107.5	15	28.5	Suzuki et al., 1999
Carnivora	Dog	*Canis lupus familiaris*	3	25.3	31	44.5	Armstrong et al., 1982
	Cheetah	*Acinonyx jubatus*	2	36	23	22.7	Goto et al., 2013b
	Cat	*Felis catus*	4	3*	28	25.8	Ariano et al., 1973; Talmadge et al., 1996
Didelphimorphia	Virginia opossum	*Didelphis virginiana*	7	2.488*	10	43.3	Hansen et al., 1987
Diprotodontia	Brush-tailed bettong	*Bettongia penicillata ogilbyi*	1	1.018	8	20.0	Zhong et al., 2008
Eulipotyphla	Japanese water shrew	*Chimarrogale platycephalus*	1	0.0385	16	0.0	Ichikawa et al., 2019
	Dsinezumi shrew	*Crocidura dsinezumi*	1	0.0094	16	0.0	Ichikawa et al., 2019
	Asian house shrew	*Suncus murinus*	7	0.0707	21	0.0	Suzuki, 1990; Ichikawa et al., 2019
	Japanese shrew mole	*Urotrichus talpoides*	2	0.0162	16	0.0	Ichikawa et al., 2019
	Small Japanese mole	*Mogera imaizumii*	1	0.065	16	0.0	Ichikawa et al., 2019
	Japanese mole	*Mogera wogura*	2	0.111	16	0.0	Ichikawa et al., 2019
Lagomorpha	New Zealand White rabbit	*Oryctolagus cuniculus domesticus*	1	2.65	8	13.0	Aigner et al., 1993
Perissodactyla	Horse	*Equus ferus caballus*	6	482	13	24.6	Kawai et al., 2009
Pilosa	Brown-throated sloth	*Bradypus variegatus*	5	3.74	12	89.2	Spainhower et al., 2021
	Hoffmann's two-toed sloth	*Choloepus hoffmanni*	4	4.875	12	62.8	Spainhower et al., 2021
Primates	Crab-eating macaque	*Macaca fascicularis*	3	4.6	9	40.8	Acosta and Roy, 1987
	Gray mouse lemur	*Microcebus murinus*	12	0.0645	15	18.7	Petter and Jouffroy, 1993
	Senegal bushbaby	*Galago senegalensis*	15	0.2405	33	17.7	Ariano et al., 1973; Edgerton et al., 1975; Sickles and Pinkstaff, 1981
	Western gorilla	*Gorilla gorilla*	1	85.3	35	30.8	THIS STUDY
	Human	*Homo sapiens*	12	69.9	37	65.4	Johnson et al., 1973; Tirrell et al., 2012
	Chimpanzee	*Pan troglodytes*	3	26.5	35	31.5	O'Neill et al., 2017
	Sunda slow loris	*Nycticebus coucang*	4	1.16*	32	56.3	Ariano et al., 1973; Sickles and Pinkstaff, 1981
Proboscidea	African savanna elephant	*Loxodonta africana*	1	1542*	14	47.6	Goto et al., 2013a
Rodentia	Cape dune mole-rat	*Bathyergus suillus*	5	2	19	33.4	Sahd et al., 2022
	Natal mole-rat	*Cryptomys hottentotus natalensis*	6	0.097	20	27.6	Sahd et al., 2022
	Cape mole-rat	*Georychus capensis*	6	0.18	20	21.4	Sahd et al., 2022
	Guinea pig	*Cavia porcellus*	1	0.629	22	17.4	Ariano et al., 1973
	Syrian hamster	*Mesocricetus auratus*	3	0.146	19	14.3	Mattson et al., 2002
	Small five-toed jerboa	*Allactaga elater*	2	0.12	9	29.3	Jouffroy et al., 2003
	Swiss Webster mouse	*Mus musculus*	12	0.0246	26	6.4	Burkholder et al., 1994
	Sprague Dawley rat	*Rattus norvegicus domestica*	16	0.3267	33	14.3	Ariano et al., 1973; Armstrong and Phelps, 1984; Delp and Duan, 1996; Eng et al., 2008
Scandentia	Common treeshrew	*Tupaia glis*	8	0.123	30	17.8	Sickles and Pinkstaff, 1981

*Body mass from Clarke et al. (2010) or Genoud et al. (2018).

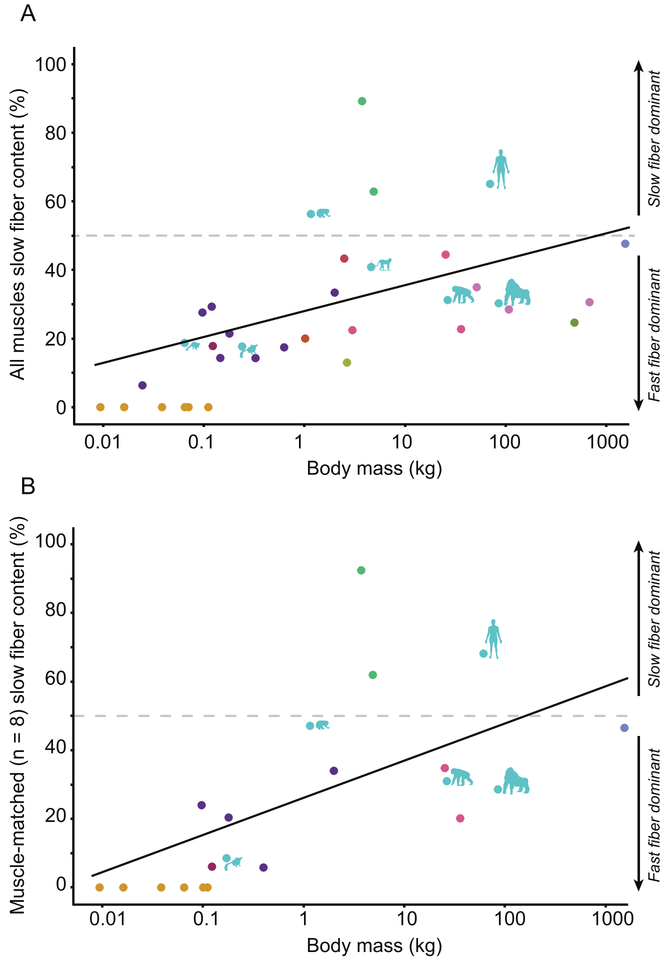

Fig. 2. Size scaling of slow fiber distribution across body size. (A) The relationship between $\log_{10}$ body mass and average percent slow fiber content from all available pelvis and hind/lower limb muscles ($n = 35$ species). (B) The relationship between $\log_{10}$ body mass and average percent slow fiber content from eight matched pelvis and hind/lower limb muscles (*mm. gluteus medius*, *biceps femoris*, *semimembranosus*, *semitendinosus*, *vastus lateralis*, *extensor digitorum longus*, *gastrocnemius*, *tibialis anterior*) ($n = 21$ species). Dotted line represents a slow fiber composition of 50%, above which denotes species that are slow fiber dominant. The solid line represents the slope and intercept of the PGLS regression of $\log_{10}$ body mass on slow fiber content. Data points are colored by taxonomic order and are matched to Table 2. Species belonging to order Primates are distinguished with icons.

4. Discussion

4.1. Humans MyHC I dominance is distinct from African apes and evolved within the hominin lineage

Humans are distinct from both gorillas and chimpanzees in the mean MyHC I isoform content of their pelvis and hind/lower limb skeletal muscles, while the two African apes are nearly identical across the same muscles. This reinforces the view that the predominance of MyHC I likely evolved within the hominin lineage (O'Neill et al., 2017), sometime since the *Pan-Homo* divergence 7 to 8 Ma (Langergraber et al., 2012). This substantial human-African ape contrast appears robust whether young or old adult human samples are used, and is evident across pelvis, thigh, and leg muscles.

Across terrestrial mammals, skeletal muscle slow fiber content increases with body mass, albeit with substantial interspecific variation. This is consistent with an earlier assessment (O'Neill et al., 2017) and confirms that almost all terrestrial mammals studied to date are fast fiber dominant, on average. The chimpanzee and gorilla data indicate that African apes are most similar to most other terrestrial mammals in this regard, including other primates such as macaques, galagos and mouse lemurs. Human slow fiber dominance is therefore an exception to this pattern, which appears to be maintained in both young (22 yrs.; Johnson et al., 1973) and old adults (83 yrs.; Tirrell et al., 2012). The absence of a significant age effect on slow fiber content is consistent with detailed cross-sectional studies of *m. vastus lateralis*, which previously reported a small, but nonsignificant increase from 10 to 85 yr olds (Lexell et al., 1988; Lexell and Downham, 1992). Still, there is marked variance in slow fiber content among individual muscles, with most of the muscles studied herein recruited during walking and running (e.g. Cappellini et al., 2006). Whether there are age-related shifts between fast (e.g. MyHC IIa and IId) or between hybrid fibers (e.g. MyHC IIa/IId) in humans requires further assessment.

The skeletal muscles of slow lorises (*Nycticebus coucang*) and sloths (*Bradypus variegatus*, *Choloepus hoffmanni*) are also slow fiber dominant on average, but this is almost certainly due to ecological factors that are distinct from those of humans. Whereas human walking and running capabilities likely benefit from an enhanced capacity for repetitive, low-cost contractile behavior, neither the slow loris nor the sloth have much need for frequent, overground travel. Instead, their commonalities may reflect a shared reliance on fatigue-resistant, low-force contractile behavior, used in the context of crypsis and 'slow climbing' (slow loris: Rassmusen and Nekaris, 1998; Nekaris, 2001, 2014) or extended tree hanging (sloth: Urbani and Bosque, 2007; Granatosky et al., 2018).

4.2. Human MyHC I content is an evolved trait with modest responsiveness to behavioral interventions

A -9 to 2% shift in muscle slow fiber content in response to a wide range of behavioral interventions is quite modest when compared to the average 31% interspecific differences between humans and African apes (Fig. 3A, Table 2; O'Neill et al., 2017). There is of course variance among individuals in average lower limb slow fiber content, with Johnson et al. (1973) exhibiting less between-subjects variance than Tirrell et al. (2012) for the same number of individuals (i.e. J: s.d. = 5.7%; T: s.d. = 13.7%; Fig. 1B). Yet, neither of these human datasets overlap the chimpanzees or gorilla. This is important since the average MyHC I shifts reported here control for between-subject or between-muscle variance by sampling longitudinal studies alone, in contrast to cross-sectional comparisons (e.g. sprinters *vs.* marathoners) that have the potential to be misleading in regard to responsiveness. Indeed, these results imply that the human-African ape contrast in MyHC I content is an evolved trait, not simply a reflection of increased or decreased activity level during a lifetime – distinct from the level of plasticity that influences muscle size (e.g. D'Antona et al., 2006; Handsfield et al., 2017) or even some skeletal parameters (e.g. cortical bone distribution; Ruff et al., 2006).

Among the 2033 subjects and 9 behavioral groups studied to date, only endurance training (e.g. running or cycling) and strength training (e.g. weightlifting) are associated with an increase in skeletal muscle slow fiber content, although the magnitude of this effect is quite small (i.e. 1.5–2.3%, Table 3). Longitudinal comparisons of different behavioral interventions in other taxa (e.g. mouse models) may provide additional insights into this pattern; however, these studies often focus on MyHC II, due to its much greater prevalence in small animals (e.g. Allen et al., 2001; see also Fig. 2). All other behavioral interventions decrease skeletal muscle slow fiber content, on average. This is important since the African ape, macaque and human data indicate that the shift within the hominin lineage was an increase in MyHC I isoform content, regardless of whether the last common ancestor of the *Pan* and *Homo* lineages was more similar to African apes or a generalized arboreal ape in its locomotor behavior (e.g. Lovejoy et al., 2009; Pilbeam and Lieberman, 2017).

The timing of the shift towards MyHC I dominant skeletal muscle

Table 3
Human intervention studies.

Intervention [a]	No. of studies	No. of subjects	Average Mass (kg)	Age (yrs)	Muscles [b]	Duration (days)	Weighted Delta (%) [c]	Standard Deviation	References
Bed rest	18	153	73.3	32.6	VL, SL	14–112	−5.6	9.4	Arentson-Lantz et al., 2016; Bamman et al., 1998; Blottner et al., 2020; Borina et al., 2010; Bosutti et al., 2016; Chopard et al., 2005; Dalla Libera et al., 2009; Dudley et al., 1989; Ferretti et al., 1997; Gallagher et al., 2005; Krainski et al., 2014; Larsson et al., 1996; Salanova et al., 2014; Trappe et al., 2001, 2004, 2007, 2008; Yamashita-Goto et al., 2001
Immobilization	11	179	74.6	30.2	VL, unknown leg m.	14–42	−3.9	3.5	Andersen et al., 1999; Berg et al., 1993, 1997; Deschenes et al., 2002; Hather et al., 1992; Hortobágyi et al., 2000; Hvid et al., 2010; Labarque et al., 2002; Veldhuizen et al., 1993; Vigelsø et al., 2015; Yasuda et al., 2005
Environmental	3	30	77.8	26.8	VL	21–40	−3.2	5.2	Debevec et al., 2018; Esbjörnsson et al., 1993b; Green et al., 1989
Spaceflight	3	21	76.1	42.0	VL, SL, GS	5–182	−9.3	6.9	Edgerton et al., 1995; Trappe et al., 2001, 2009
Endurance training	25	313	71.1	29.4	VL, SL, GS, quadriceps, unknown leg m.	1–168	2.3	5.7	Andersen and Henriksson, 1977a, 1977b; Ball et al., 1983; Baumann et al., 1987; Campbell et al., 1979; Denis et al., 1984; Eriksson et al., 1973; Esbjörnsson et al., 1993a; Gehlert et al., 2012; Gollnick et al., 1973; Green et al., 1991; Hardin et al., 1995; Houston et al., 1979; Howald, 1982; Ingjer, 1979; Jansson et al., 1978; Karavirta et al., 2011; Klausen et al., 1981; Kraemer et al., 1995; Krotkiewski et al., 1983; Luden et al., 2012; Putman et al., 2004; Sipila et al., 1997; Trappe et al., 2006; Vigelsø et al., 2015
Strength training	58	1018	71.7	36.5	VL	14–365	1.5	4.4	Aagaard et al., 2003; Adams et al., 1993; Andersen et al., 1994a; Andersen and Aagaard, 2000; Bamman et al., 2007; Bickel et al., 2011; Bishop et al., 1999; Cadefau et al., 1990; Campos et al., 2002; Carroll et al., 1998; Costill et al., 1979; Daugaard et al., 2000; Dons et al., 1979; Fry et al., 1994; Green et al., 1999; Häkkinen et al., 1981, 1990, 2001, 2002; Harber et al., 2004; Hather et al., 1991; Hepple et al., 1996; Hickson et al., 1994; Hikida et al., 2000; Holm et al., 2008; Hortobágyi et al., 2000; Hostler et al., 2001; Houston et al., 1983; Hvid et al., 2010; Karavirta et al., 2011; Kosek et al., 2006; Kraemer et al., 1995; Kryger and Andersen, 2007; Labarque et al., 2002; Larsson, 1982; Lexell et al., 1995; Malisoux et al., 2006; Martel et al., 2006; Pareja-Blanco et al., 2017; Parente et al., 2008; Pellegrino et al., 2016; Putman et al., 2004; Schuenke et al., 2012; Simoneau et al., 1985; Sipila et al., 1997; Slivka et al., 2008; Snijders et al., 2019; Staron et al., 1990, 1991, 1994, 2012; Terzis et al., 2008; Thorstensson et al., 1976; Trappe et al., 2000; Widrick et al., 2002; Williamson et al., 2000, 2001; Winchester et al., 2008
Sprint training	10	92	74.8	30.3	VL	1–91	−2.1	6.8	Allemeier et al., 1994; Christensen et al., 2011; Esbjörnsson et al., 1993a; Harber et al., 2012; Jansson et al., 1978, 1990; Konopka et al., 2011; Linossier et al., 1997; Parcell et al., 2005; Pereira Sant'Ana et al., 1997
Dynamic training	7	96	76.5	28.3	VL	70–1460	−1.6	4.5	Andersen et al., 1994b; Green et al., 1979; Hickson et al., 1988; Karavirta et al., 2011; Kraemer et al., 1995; Larsson and Ansved, 1985; Putman et al., 2004
Detraining	16	131	74.4	24.1	VL, GS	14–1460	−2.5	4.2	Andersen and Aagaard, 2000; Christensen et al., 2011; Dahlström et al., 1987; Denis et al., 1984; Green et al., 1980; Häkkinen et al., 1981; Hortobágyi et al., 1993; Houston et al., 1979, 1983; Howald, 1982; Klausen et al., 1981; Larsson and Ansved, 1985; Linossier et al., 1997; Madsen et al., 1993; Snijders et al., 2019; Terzis et al., 2008

[a] During bed rest the participants were confined to a bed at a hospital or research center and monitored continuously. During immobilization one of the participants' legs were prevented from weight-bearing to reduce muscle activity while participants continued their habitual daily activities. During environmental the participants were subjected to various living conditions (e.g., reduced barometric pressure or hypoxia) in a controlled research chamber for varying amounts of time with or without supine leg training. During spaceflight the participants (astronauts) flew aboard the International Space Station and followed an individually structured

aerobic and resistance exercise countermeasure program. During endurance training the participants followed an aerobic training regimen, typically involving cycling or running exercises, aimed at increasing cardiovascular and/or muscular endurance. During strength training the participants followed various resistance training regimens, typically involving free weights and/or exercise machines, aimed at building muscle mass and improving muscle strength. During sprint training the participants followed a high intensity interval training regimen, typically involving a cycle ergometer, aimed at increasing cardiovascular health, muscle mass, and muscle power. During dynamic training the participants followed a combined endurance exercise and resistance training regimen. During detraining the participants ceased training/exercise after a period of vigorous training, but otherwise continued their habitual daily activities.

[b] Muscles measured before and after intervention. VL = vastus lateralis, SL = soleus, GS = gastrocnemius, quadriceps = undefined muscle of the quadriceps muscle group (*mm. vastus lateralis*, *vastus medialis*, *vastus intermedius*, *rectus femoris*), unknown leg m. = undefined muscle of the leg.

[c] Mean weighted delta = (end intervention value – start intervention value) · (no. of subjects in study / total no. of subjects per intervention). This weighting factors the number of subjects in each intervention study into the mean effect, such that larger samples have more weight in determining the mean delta.

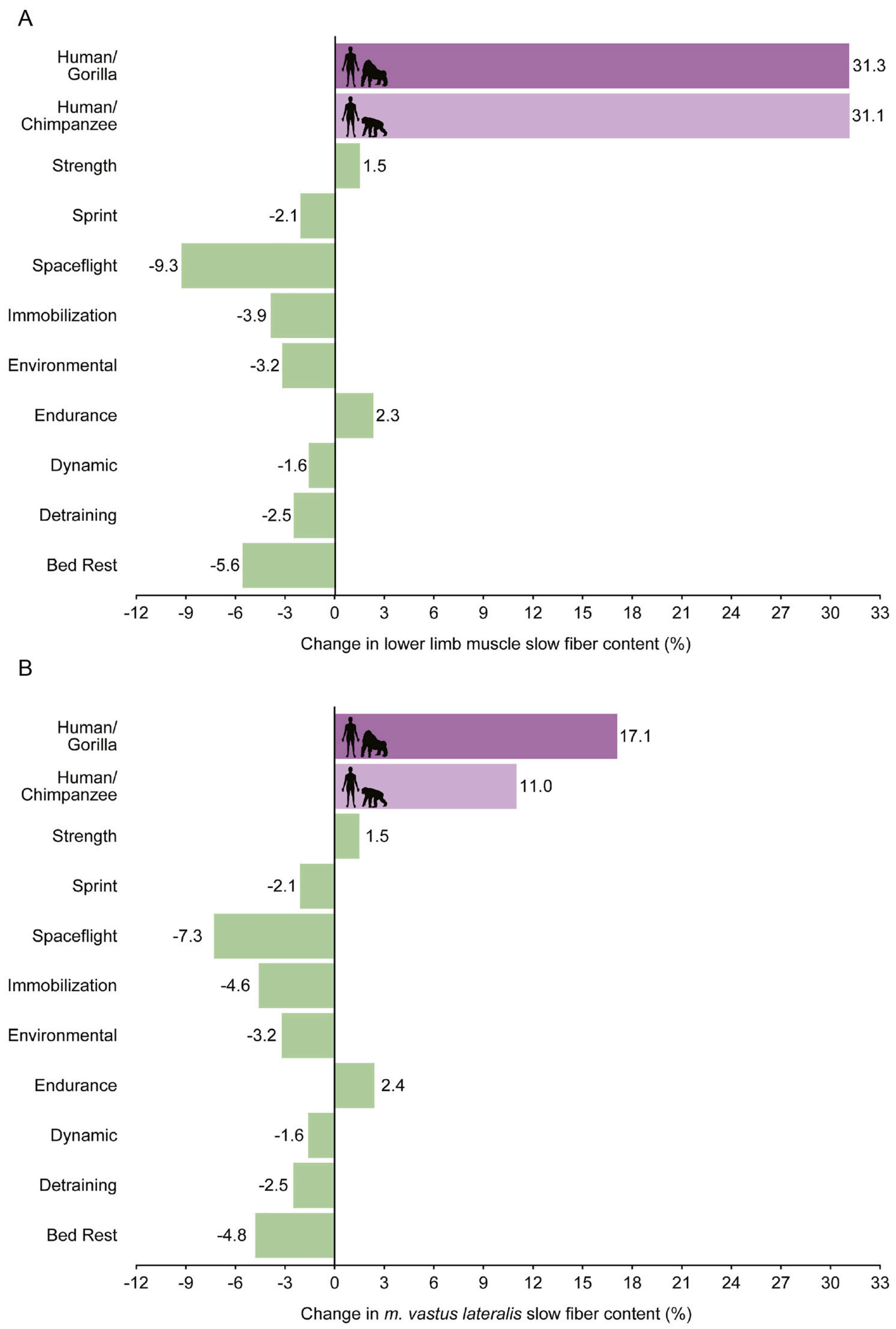

Fig. 3. Average change in lower limb muscle slow fiber content across 9 human intervention categories compared to the human/African ape differential. (A) Analysis of studies of lower limb muscle slow fiber content before and after a range of bed rest, immobilization, spaceflight and exercise interventions. (B) Analysis of studies of *m. vastus lateralis* slow fiber content before and after a range of bed rest, immobilization, spaceflight and exercise interventions. Strength and endurance training increased slow fiber content, while most other activities decreased slow fiber content, on average.

within the hominin lineage is difficult to establish. However, we anticipate this shift to have been concurrent with major transitions in locomotor behavior, daily travel distance, home range size or some combination thereof. The earliest australopithecines (e.g. *Australopithecus anamensis*, *Australopithecus afarensis*) exhibit changes to the pelvis and lower limb skeleton as compared to *Ardipithecus ramidus* (e.g. Ward et al., 1999; Lovejoy et al., 2009; Simpson et al., 2019), suggesting an adaptive shift towards greater overground locomotion as early as 4 Ma, at least in east Africa. Between 2.1 and 1.8 Ma, *Homo erectus* appears in east and south Africa (e.g. Herries et al., 2020; Hammond et al., 2021), east Europe (e.g. Ferring et al., 2011) and east Asia (e.g. Zhu et al., 2008; Zhu et al., 2018), indicating a global dispersal that must have involved substantial overground walking and running. This species would seem to benefit from a lower-cost, fatigue-resistant skeletal muscle design, although an earlier evolutionary shift or multiple, incremental shifts as part of ongoing selection for overground locomotion in the hominin lineage is also plausible. A better understanding of the molecular mechanisms that determine adult muscle MyHC content in primates and other mammals may provide additional information on the initial appearance, pleiotropic effects, or selective pressures acting on this trait within the hominin lineage.

4.3. Enhancers may play an important role in hominin skeletal muscle evolution

Our findings indicate that muscle fiber content is likely an evolvable trait that was under selection in the hominin lineage. MyHC isoforms expressed in mammalian skeletal muscle are encoded by specific MyHC genes (Schiaffino et al., 2015). While these genes, by nature of the proteins they encode, represent obvious candidates for selection in the hominin lineage, they are highly conserved across mammals (reviewed in Lee et al., 2019) and likely under heavy evolutionary constraint across species. Indeed, mutations in MyHC genes can have multiple effects (i.e. be pleiotropic) and are associated with human disease (e.g. Tajsharghi et al., 2010; Walsh et al., 2010; Colegrave and Peckham, 2014). Despite this, MyHC gene expression varies considerably across tissues (e.g. skeletal, cardiac, extraocular, and masticatory muscle), time points (e.g. embryonic, fetal, adult), and taxonomic lineages (e.g. small and large mammals) (Harrison et al., 2011; Smerdu and Cvetko, 2013; Lee et al., 2019). As such, regions of the genome that regulate the expression of these genes may better explain observed variation in slow fiber content across mammals (Fig. 2; see also Supplementary Materials Fig. 1) and make compelling candidates for understanding the shift in MyHC content in hominin skeletal muscle.

Indeed, phenotypic differences between humans and chimpanzees have long been attributed to species-specific mutations in non-coding regulatory regions of the genome (King and Wilson, 1975), which influence both where and when genes are expressed. Mutations in regulatory elements can change the spatiotemporal expression of genes during growth and development and lead to phenotypic variation and evolutionary divergence between closely related species (e.g. Haygood et al., 2007; Blekhman et al., 2008; McLean et al., 2011; Sumiyama and Saitou, 2011; Kamm et al., 2013; Boyd et al., 2015; Prescott et al., 2015; Indjeian et al., 2016; Kostka et al., 2018; Richard et al., 2020; Aldea et al., 2021; Johansson et al., 2022; Young et al., 2022). For example, the shapes of the human knee and pelvis, compared to those of African apes, have resulted from evolutionary selection on regulatory sequences unique to the individual skeletal elements of the knee (i.e. distal femur) (Richard et al., 2020) and pelvis (i.e. ilium) (Young et al., 2022). In line with these studies, here we hypothesize that natural selection has selected for human-specific variation in the non-coding regions of the genome that regulate the expression of fast MyHC II and slow MyHC I genes, rather than the MyHC genes themselves. The result of this selection would be increases in the amount of fatigue-resistant slow MyHC I muscle fibers in human lower limb muscles in order to facilitate repetitive, low-cost contractile behavior during walking and running.

Of particular interest are enhancers, a type of non-coding regulatory element that possess remarkable specificity in their control of gene expression. Enhancers can regulate gene expression in a tissue-specific or developmental stage-specific manner, leading to modularized effects on phenotype (reviewed in Hill et al., 2021). Previous research has also demonstrated that species-specific mutations within conserved enhancer regions can lead to evolutionary novelty (e.g. Prabhakar et al., 2008; Arnaud et al., 2011; McLean et al., 2011; Indjeian et al., 2016; Kvon et al., 2016) or convergence (e.g. Guerreiro et al., 2013; Sackton et al., 2019; LaPotin et al., 2022; Pereira et al., 2022). MyHC "super enhancers" have recently been identified in mouse skeletal muscle that regulate the expression of genes belonging to the fast and slow MyHC gene clusters (dos Santos et al., 2022; Long et al., 2022). Given that the temporal regulation of MyHC genes during development is critical for the stage-specific progression of primary myotubes to developmental (i.e. embryonic and fetal) and adult muscle fibers (Schiaffino et al., 2015), and the replacement of developmental isoforms (i.e. MyHC-emb and MyHC-neo) with adult slow (MyHC I) and fast (MyHC II) isoforms (Hagiwara et al., 2007; Hennebry et al., 2009), it is likely that species-specific differences in adult MyHC content, such as those observed between humans and African apes, are due to species-specific changes in MyHC enhancers (Fig. 4). Similarities in adult MyHC content, as seen in humans, sloths and slow lorises, may be due to functionally equivalent mutations in these evolutionarily conserved MyHC enhancers, although trait convergence may also have arisen via the evolution of novel, species-specific enhancers (e.g. Ordway et al., 2014; Boyd et al., 2015; Koshikawa et al., 2015; Signor et al., 2016; Letelier et al., 2018). A more comprehensive consideration of the molecular mechanisms involved in regulating muscle MyHC isoform content in humans and other mammals is needed to refine this understanding of skeletal muscle evolution and to reconstruct how and when these changes occurred.

5. Conclusions

Humans are distinct from African apes (chimpanzees and gorillas) and among a small group of terrestrial mammals whose pelvis and hind/lower limb skeletal muscle is slow fiber dominant, on average. Behavioral interventions, including immobilization, bed rest, spaceflight and exercise, can induce modest decreases and increases in human slow fiber content (i.e. -9.3% to 2.3%, $n = 2033$ subjects), but these shifts are much smaller than the mean human-African ape differential. The relative magnitude of the human-African ape differential in MyHC I content suggests that selection in the hominin lineage for low-cost, repetitive contractile behavior may underlie this difference. As a result, greater characterization of the regulatory landscape of muscles during muscle fiber development between species with divergent MyHC isoform composition is needed to reconstruct the evolutionary history of observed shifts in human skeletal muscle MyHC content.

Authors' contributions

MCO, SRQ, KNS conceived the project. SRQ, MCO, CO, PJR collected the data. SRQ, MCO implemented the statistical analysis. SRQ, TDC, KNS, MCO wrote the initial draft, and all authors contributed to revisions.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

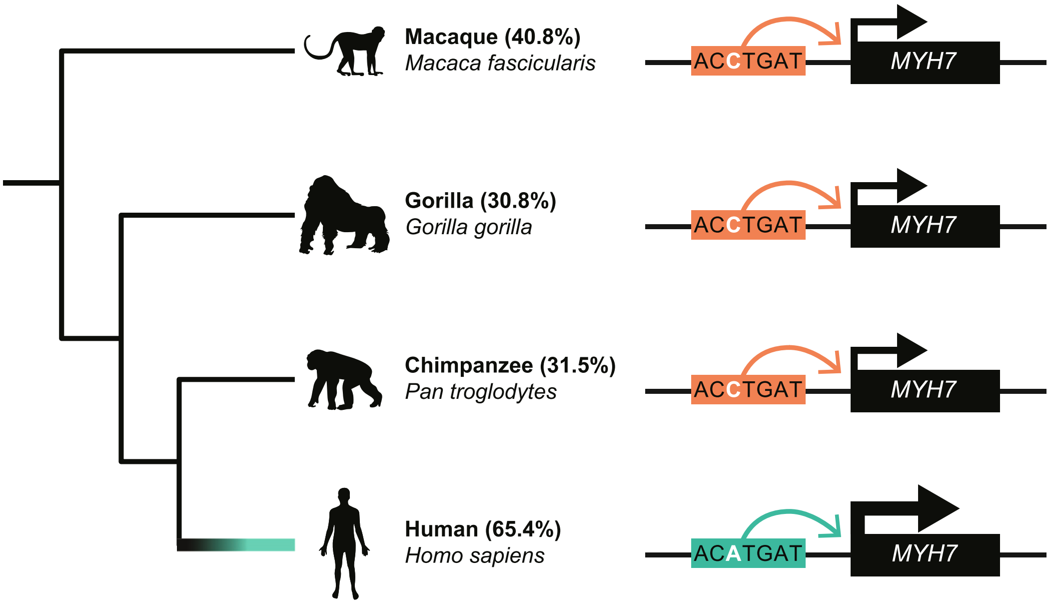

Fig. 4. One hypothesized regulatory mechanism underlying the observed variation in pelvis and hind/lower limb MyHC I content across species and human slow fiber dominance. The average, unmatched pelvis and hind/lower limb muscle slow fiber content for each species is given in parentheses. Here, the conserved enhancer (highlighted in orange or green) is shown to regulate the expression of *MYH7*, the gene encoding slow MyHC I. The non-human primates (orange enhancer) have identical DNA sequences within this conserved enhancer, reflecting similarities in muscle MyHC I content. Under this scenario, the hominin lineage acquired a mutation (or mutations) within a conserved enhancer (here represented in the green enhancer by a single C to A base pair change) after the *Pan*-*Homo* divergence, increasing the expression of *MYH7* and the proportion of slow MyHC I fibers within hominin pelvis and lower limb muscles. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Data availability

All data used in this manuscript are available in main text tables or supplementary documents.

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Appendix A. Supplementary data

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References

Aagaard, P., Simonsen, E.B., Andersen, J.L., Magnusson, S.P., Dyhre-Poulsen, P., 2003. Changes in maximal unloaded knee extension velocity induced by resistance training. Med. Sci. Sports Exerc. 35, S369. https://doi.org/10.1097/00005768-200305001-02053.

Acosta, L., Roy, R.R., 1987. Fiber-type composition of selected hindlimb muscles of a primate (cynomolgus monkey). Anat. Rec. 218, 136–141. https://doi.org/10.1002/ar.1092180207.

Adams, G.R., Hather, B.M., Baldwin, K.M., Dudley, G.A., 1993. Skeletal muscle myosin heavy chain composition and resistance training. J. Appl. Physiol. 74, 911–915. https://doi.org/10.1152/jappl.1993.74.2.911.

Aigner, S., Gohlsch, B., Hämäläinen, N., Staron, R.S., Uber, A., Wehrle, U., Pette, D., 1993. Fast myosin heavy chain diversity in skeletal muscles of the rabbit: heavy chain IId, not IIb predominates. Eur. J. Biochem. 211, 367–372. https://doi.org/10.1111/j.1432-1033.1993.tb19906.x.

Aldea, D., Atsuta, Y., Kokalari, B., Schaffner, S.F., Prasasya, R.D., Aharoni, A., Dingwall, H.L., Warder, B., Kamberov, Y.G., 2021. Repeated mutation of a developmental enhancer contributed to human thermoregulatory evolution. Proc. Natl. Acad. Sci. 118, e2021722118 https://doi.org/10.1073/pnas.2021722118.

Allemeier, C.A., Fry, A.C., Johnson, P., Hikida, R.S., Hagerman, F.C., Staron, R.S., 1994. Effects of sprint cycle training on human skeletal muscle. J. Appl. Physiol. 77, 2385–2390. https://doi.org/10.1152/jappl.1994.77.5.2385.

Allen, D.L., Harrison, B.C., Maass, A., Bell, M.L., Byrnes, W.C., Leinwand, L.A., 2001. Cardiac and skeletal muscle adaptations to voluntary wheel running in the mouse. J. Appl. Physiol. 90, 1900–1908. https://doi.org/10.1152/jappl.2001.90.5.1900.

Andersen, J.L., Aagaard, P., 2000. Myosin heavy chain IIX overshoot in human skeletal muscle. Muscle Nerve 23, 1095–1104. https://doi.org/10.1002/1097-4598(200007)23:7<1095::AID-MUS13>3.0.CO;2-O.

Andersen, P., Henriksson, J., 1977a. Training induced changes in the subgroups of human type II skeletal muscle fibres. Acta Physiol. Scand. 99, 123–125. https://doi.org/10.1111/j.1748-1716.1977.tb10361.x.

Andersen, P., Henriksson, J., 1977b. Capillary supply of the quadriceps femoris muscle of man: adaptive response to exercise. J. Physiol. 270, 677–690. https://doi.org/10.1113/jphysiol.1977.sp011975.

Andersen, J.L., Klitgaard, H., Bangsbo, J., Saltin, B., 1994a. Myosin heavy chain isoforms in single fibres from m. vastus lateralis of soccer players: effects of strength-training. Acta Physiol. Scand. 150, 21–26. https://doi.org/10.1111/j.1748-1716.1994.tb09655.x.

Andersen, J.L., Klitgaard, H., Saltin, B., 1994b. Myosin heavy chain isoforms in single fibres from m. vastus lateralis of sprinters: influence of training. Acta Physiol. Scand. 151, 135–142. https://doi.org/10.1111/j.1748-1716.1994.tb09730.x.

Andersen, J.L., Gruschy-Knudsen, T., Sandri, C., Larsson, L., Schiaffino, S., 1999. Bed rest increases the amount of mismatched fibers in human skeletal muscle. J. Appl. Physiol. 86, 455–460. https://doi.org/10.1152/jappl.1999.86.2.455.

Arentson-Lantz, E.J., English, K.L., Paddon-Jones, D., Fry, C.S., 2016. Fourteen days of bed rest induces a decline in satellite cell content and robust atrophy of skeletal muscle fibers in middle-aged adults. J. Appl. Physiol. 120, 965–975. https://doi.org/10.1152/japplphysiol.00799.2015.

Ariano, M.A., Edgerton, V.R., Armstrong, R.B., 1973. Hindlimb muscle fiber populations of five mammals. J. Histochem. Cytochem. 21, 51–55. https://doi.org/10.1177/21.1.51.

Armstrong, R.B., Phelps, R.O., 1984. Muscle fiber type composition of the rat hindlimb. Am. J. Anat. 171, 259–272. https://doi.org/10.1002/aja.1001710303.

Armstrong, R.B., Saubert, C.W., Seeherman, H.J., Taylor, C.R., 1982. Distribution of fiber types in locomotory muscles of dogs. Am. J. Anat. 163, 87–98. https://doi.org/10.1002/aja.1001630107.

Arnaud, N., Lawrenson, T., Østergaard, L., Sablowski, R., 2011. The same regulatory point mutation changed seed-dispersal structures in evolution and domestication. Curr. Biol. 21, 1215–1219. https://doi.org/10.1016/j.cub.2011.06.008.

Ball, M.E., Green, H.J., Houston, M.E., 1983. Alterations in human muscle fibre type distribution induced by acute exercise. Histochemistry 79, 53–57. https://doi.org/10.1007/BF00494341.

Bamman, M.M., Clarke, M.S.F., Feeback, D.L., Talmadge, R.J., Stevens, B.R., Lieberman, S.A., Greenisen, M.C., 1998. Impact of resistance exercise during bed rest on skeletal muscle sarcopenia and myosin isoform distribution. J. Appl. Physiol. 84, 157–163. https://doi.org/10.1152/jappl.1998.84.1.157.

Bamman, M.M., Petrella, J.K., Kim, J., Mayhew, D.L., Cross, J.M., 2007. Cluster analysis tests the importance of myogenic gene expression during myofiber hypertrophy in humans. J. Appl. Physiol. 102, 2232–2239. https://doi.org/10.1152/japplphysiol.00024.2007.

Bauman, J.E., 1923. The strength of the chimpanzee and orang. Sci. Mon. 16, 432–439.

Bauman, J.E., 1926. Observations on the strength of the chimpanzee and its implications. J. Mammal. 7, 1. https://doi.org/10.2307/1373587.

Baumann, H., Jäggi, M., Soland, F., Howald, H., Schaub, M.C., 1987. Exercise training induces transitions of myosin isoform subunits within histochemically typed human muscle fibres. Pflugers Arch. - Eur. J. Physiol. 409, 349–360. https://doi.org/10.1007/BF00583788.

Berg, H.E., Dudley, G.A., Hather, B., Tesch, P.A., 1993. Work capacity and metabolic and morphologic characteristics of the human quadriceps muscle in response to unloading. Clin. Physiol. 13, 337–347. https://doi.org/10.1111/j.1475-097X.1993.tb00334.x.

Berg, H.E., Larsson, L., Tesch, P.A., 1997. Lower limb skeletal muscle function after 6 wk of bed rest. J. Appl. Physiol. 82, 182–188. https://doi.org/10.1152/jappl.1997.82.1.182.

Bickel, C.S., Cross, J.M., Bamman, M.M., 2011. Exercise dosing to retain resistance training adaptations in young and older adults. Med. Sci. Sports Exerc. 43, 1177–1187. https://doi.org/10.1249/MSS.0b013e318207c15d.

Bishop, D., Jenkins, D.G., Mackinnon, L.T., McEniery, M., Carey, M.F., 1999. The effects of strength training on endurance performance and muscle characteristics. Med. Sci. Sports Exerc. 31, 886–891. https://doi.org/10.1097/00005768-199906000-00018.

Blekhman, R., Oshlack, A., Chabot, A.E., Smyth, G.K., Gilad, Y., 2008. Gene regulation in primates evolves under tissue-specific selection pressures. PLoS Genet. 4 https://doi.org/10.1371/journal.pgen.1000271.

Blottner, D., Hastermann, M., Weber, R., Lenz, R., Gambara, G., Limper, U., Rittweger, J., Bosutti, A., Degens, H., Salanova, M., 2020. Reactive jumps preserve skeletal muscle structure, phenotype, and myofiber oxidative capacity in bed rest. Front. Physiol. 10 https://doi.org/10.3389/fphys.2019.01527.

Borina, E., Pellegrino, M.A., D'Antona, G., Bottinelli, R., 2010. Myosin and actin content of human skeletal muscle fibers following 35 days bed rest. Scand. J. Med. Sci. Sports 20, 65–73. https://doi.org/10.1111/j.1600-0838.2009.01029.x.

Bosutti, A., Salanova, M., Blottner, D., Buehlmeier, J., Mulder, E., Rittweger, J., Hoon Yap, M., Ganse, B., Degens, H., 2016. Whey protein with potassium bicarbonate supplement attenuates the reduction in muscle oxidative capacity during 19 days of bed rest. J. Appl. Physiol. 121, 838–848. https://doi.org/10.1152/japplphysiol.00936.2015.-The.

Boyd, J.L., Skove, S.L., Rouanet, J.P., Pilaz, L.-J., Bepler, T., Gordân, R., Wray, G.A., Silver, D.L., 2015. Human-chimpanzee differences in a FZD8 enhancer alter cell-cycle dynamics in the developing neocortex. Curr. Biol. 25, 772–779. https://doi.org/10.1016/j.cub.2015.01.041.

Bozek, K., Wei, Y., Yan, Z., Liu, X., Xiong, J., Sugimoto, M., Tomita, M., Pääbo, S., Pieszek, R., Sherwood, C.C., Hof, P.R., Ely, J.J., Steinhauser, D., Willmitzer, L., Bangsbo, J., Hansson, O., Call, J., Giavalisco, P., Khaitovich, P., 2014. Exceptional evolutionary divergence of human muscle and brain metabolomes parallels human cognitive and physical uniqueness. PLoS Biol. 12 https://doi.org/10.1371/journal.pbio.1001871.

Burgess, M.L., McFarlin, S.C., Mudakikwa, A., Cranfield, M.R., Ruff, C.B., 2018. Body mass estimation in hominoids: age and locomotor effects. J. Hum. Evol. 115, 36–46. https://doi.org/10.1016/j.jhevol.2017.07.004.

Burkholder, T.J., Fingado, B., Baron, S., Lieber, R.L., 1994. Relationship between muscle fiber types and sizes and muscle architectural properties in the mouse hindlimb. J. Morphol. 221, 177–190. https://doi.org/10.1002/jmor.1052210207.

Burnham, R., Martin, T., Stein, R., Bell, G., MacLean, I., Steadward, R., 1997. Skeletal muscle fibre type transformation following spinal cord injury. Spinal Cord 35, 86–91. https://doi.org/10.1038/sj.sc.3100364.

Cadefau, J., Casademont, J., Grau, J.M., Fernández, J., Balaguer, A., Vernet, M., Cussó, R., Urbano-Márquez, A., 1990. Biochemical and histochemical adaptation to sprint training in young athletes. Acta Physiol. Scand. 140, 341–351. https://doi.org/10.1111/j.1748-1716.1990.tb09008.x.

Campbell, C.J., Bonen, A., Kirby, R.L., Belcastro, A.N., 1979. Muscle fiber composition and performance capacities of women. Med. Sci. Sports 11, 260–265.

Campos, G.E.R., Luecke, T.J., Wendeln, H.K., Toma, K., Hagerman, F.C., Murray, T.F., Ragg, K.E., Ratamess, N.A., Kraemer, W.J., Staron, R.S., 2002. Muscular adaptations in response to three different resistance-training regimens: specificity of repetition maximum training zones. Eur. J. Appl. Physiol. 88, 50–60. https://doi.org/10.1007/s00421-002-0681-6.

Cappellini, G., Ivanenko, Y.P., Poppele, R.E., Lacquaniti, F., 2006. Motor patterns in human walking and running. J. Neurophysiol. 95, 3426–3437. https://doi.org/10.1152/jn.00081.2006.

Carroll, T.J., Abernethy, P.J., Logan, P.A., Barber, M., McEniery, M.T., 1998. Resistance training frequency: strength and myosin heavy chain responses to two and three bouts per week. Eur. J. Appl. Physiol. 78, 270–275. https://doi.org/10.1007/s004210050419.

Chopard, A., Arrighi, N., Carnino, A., Marini, J.F., 2005. Changes in dysferlin, proteins from dystrophin glycoprotein complex, costameres, and cytoskeleton in human soleus and vastus lateralis muscles after a long-term bedrest with or without exercise. FASEB J. 19, 1722–1724. https://doi.org/10.1096/fj.04-3336fje.

Christensen, P.M., Krustrup, P., Gunnarsson, T.P., Kiilerich, K., Nybo, L., Bangsbo, J., 2011. VO2 kinetics and performance in soccer players after intense training and inactivity. Med. Sci. Sports Exerc. 43, 1716–1724. https://doi.org/10.1249/MSS.0b013e318211c01a.

Clarke, A., Rothery, P., Isaac, N.J.B., 2010. Scaling of basal metabolic rate with body mass and temperature in mammals. J. Anim. Ecol. 79, 610–619. https://doi.org/10.1111/j.1365-2656.2010.01672.x.

Colegrave, M., Peckham, M., 2014. Structural implications of β-cardiac myosin heavy chain mutations in human disease. Anat. Rec. 297, 1670–1680. https://doi.org/10.1002/ar.22973.

Costill, D.L., Coyle, E.F., Fink, W.F., Lesmes, G.R., Witzmann, F.A., 1979. Adaptations in skeletal muscle following strength training. J. Appl. Physiol. 46, 96–99. https://doi.org/10.1152/jappl.1979.46.1.96.

Dahlström, M., Esbjörnsson, M., Jansson, E., Kaijser, L., 1987. Muscle fiber characteristics in female dancers during an active and an inactive period. Int. J. Sports Med. 08, 84–87. https://doi.org/10.1055/s-2008-1025646.

Dalla Libera, L., Ravara, B., Gobbo, V., Tarricone, E., Vitadello, M., Biolo, G., Vescovo, G., Gorza, L., 2009. A transient antioxidant stress response accompanies the onset of disuse atrophy in human skeletal muscle. J. Appl. Physiol. 107, 549–557. https://doi.org/10.1152/japplphysiol.00280.2009.

D'Antona, G., Lanfranconi, F., Pellegrino, M.A., Brocca, L., Adami, R., Rossi, R., Moro, G., Miotti, D., Canepari, M., Bottinelli, R., 2006. Skeletal muscle hypertrophy and structure and function of skeletal muscle fibres in male body builders. J. Physiol. 570, 611–627. https://doi.org/10.1113/jphysiol.2005.101642.

Daugaard, J.R., Nielsen, J.N., Kristiansen, S., Andersen, J.L., Hargreaves, M., Richter, E. A., 2000. Fiber type-specific expression of GLUT4 in human skeletal muscle: influence of exercise training. Diabetes 49, 1092–1095. https://doi.org/10.2337/diabetes.49.7.1092.

Debevec, T., Ganse, B., Mittag, U., Eiken, O., Mekjavic, I.B., Rittweger, J., 2018. Hypoxia aggravates inactivity-related muscle wasting. Front. Physiol. 9 https://doi.org/10.3389/fphys.2018.00494.

Delp, M.D., Duan, C., 1996. Composition and size of type I, IIA, IID/X, and IIB fibers and citrate synthase activity of rat muscle. J. Appl. Physiol. 80, 261–270. https://doi.org/10.1152/jappl.1996.80.1.261.

Denis, C., Dormois, D., Lacour, J., 1984. Endurance training, VO $_2$ max, and OBLA: a longitudinal study of two different age groups*. Int. J. Sports Med. 05, 167–173. https://doi.org/10.1055/s-2008-1025899.

Deschenes, M.R., Giles, J.A., McCoy, R.W., Volek, J.S., Gomez, A.L., Kraemer, W.J., 2002. Neural factors account for strength decrements observed after short-term muscle unloading. Am. J. Phys. Regul. Integr. Comp. Phys. 282, R578–R583. https://doi.org/10.1152/ajpregu.00386.2001.

Dons, B., Bollerup, K., Bonde-Petersen, F., Hancke, S., 1979. The effect of weight-lifting exercise related to muscle fiber composition and muscle cross-sectional area in humans. Eur. J. Appl. Physiol. Occup. Physiol. 40, 95–106. https://doi.org/10.1007/BF00421155.

dos Santos, M., Backer, S., Auradé, F., Wong, M.M.-K., Wurmser, M., Pierre, R., Langa, F., do Cruzeiro, M., Schmitt, A., Concordet, J.-P., Sotiropoulos, A., Jeffrey Dilworth, F., Noordermeer, D., Relaix, F., Sakakibara, I., Maire, P., 2022. A fast myosin super enhancer dictates muscle fiber phenotype through competitive interactions with myosin genes. Nat. Commun. 13, 1039. https://doi.org/10.1038/s41467-022-28666-1.

Dudley, G.A., Gollnick, P.D., Convertino, V.A., Buchanan, P., 1989. Changes of muscle function and size with bedrest. Physiologist 32, S65–S66.

Edgerton, V.R., Barnard, R.J., Peter, J.B., Maier, A., Simpson, D.R., 1975. Properties of immobilized hind-limb muscles of the Galago senegalensis. Exp. Neurol. 46, 115–131. https://doi.org/10.1016/0014-4886(75)90036-9.

Edgerton, V.R., Zhou, M.Y., Ohira, Y., Klitgaard, H., Jiang, B., Bell, G., Harris, B., Saltin, B., Gollnick, P.D., Roy, R.R., et al., 1995. Human fiber size and enzymatic properties after 5 and 11 days of spaceflight. J. Appl. Physiol. 78, 1733–1739. https://doi.org/10.1152/jappl.1995.78.5.1733.

Edwards, W.E., Clarke, T.E., 1965. Study of monkey, ape, and human morphology and physiology relating to strength and endurance, phase IX: The strength testing of five chimpanzee and seven human subjects. Holloman Air Force Base, Holloman, New Mexico. N. M. 6571st Aeromedical Research Laboratory.

Eng, C.M., Smallwood, L.H., Rainiero, M.P., Lahey, M., Ward, S.R., Lieber, R.L., 2008. Scaling of muscle architecture and fiber types in the rat hindlimb. J. Exp. Biol. 211, 2336–2345. https://doi.org/10.1242/jeb.017640.

Eriksson, B.O., Gollnick, P.D., Saltin, B., 1973. Muscle metabolism and enzyme activities after training in boys 11-13 years old. Acta Physiol. Scand. 87, 485–497. https://doi.org/10.1111/j.1748-1716.1973.tb05415.x.

Esbjörnsson, M., Hellsten-Westing, Y., Balsom, P.D., Sjödin, B., Jansson, E., 1993a. Muscle fibre type changes with sprint training: effect of training pattern. Acta Physiol. Scand. 149, 245–246. https://doi.org/10.1111/j.1748-1716.1993.tb09618.x.

Esbjörnsson, M., Jansson, E., Sundberg, C.J., Sylvén, C., Eiken, O., Nygren, A., Kaijser, L., 1993b. Muscle fibre types and enzyme activities after training with local leg ischaemia in man. Acta Physiol. Scand. 148, 233–242. https://doi.org/10.1111/j.1748-1716.1993.tb09554.x.

Ferretti, G., Antonutto, G., Denis, C., Hoppeler, H., Minetti, A.E., Narici, M.V., Desplanches, D., 1997. The interplay of central and peripheral factors in limiting maximal O2 consumption in man after prolonged bed rest. J. Physiol. 501, 677–686. https://doi.org/10.1111/j.1469-7793.1997.677bm.x.

Ferring, R., Oms, O., Augsti, J., Berna, F., Nioradza, M., Shelia, T., Tappen, M., Vekua, A., Zhvania, D., Lordkipanidze, D., 2011. Earliest human occupations at Dmanisi (Georgian Caucasus) dated to 1.85-1.78 Ma. Proc. Natl. Acad. Sci. U. S. A. 108, 10432–10436.

Finch, G., 1943. The bodily strength of chimpanzees. J. Mammal. 24, 224. https://doi.org/10.2307/1374806.

Fry, A.C., Allemeier, C.A., Staron, R.S., 1994. Correlation between percentage fiber type area and myosin heavy chain content in human skeletal muscle. Eur. J. Appl. Physiol. Occup. Physiol. 68, 246–251. https://doi.org/10.1007/BF00376773.

Gallagher, P., Trappe, S., Harber, M., Creer, A., Mazzetti, S., Trappe, T., Alkner, B., Tesch, P., 2005. Effects of 84-days of bedrest and resistance training on single muscle fibre myosin heavy chain distribution in human vastus lateralis and soleus muscles. Acta Physiol. Scand. 185, 61–69. https://doi.org/10.1111/j.1365-201X.2005.01457.x.

Gehlert, S., Weber, S., Weidmann, B., Gutsche, K., Platen, P., Graf, C., Kappes-Horn, K., Bloch, W., 2012. Cycling exercise-induced myofiber transitions in skeletal muscle depend on basal fiber type distribution. Eur. J. Appl. Physiol. 112, 2393–2402. https://doi.org/10.1007/s00421-011-2209-4.

Genoud, M., Isler, K., Martin, R.D., 2018. Comparative analyses of basal rate of metabolism in mammals: data selection does matter. Biol. Rev. 93, 404–438. https://doi.org/10.1111/brv.12350.

Gollnick, P.D., Armstrong, R.B., Saltin, B., Saubert, C.W., Sembrowich, W.L., Shepherd, R.E., 1973. Effect of training on enzyme activity and fiber composition of human skeletal muscle. J. Appl. Physiol. 34, 107–111. https://doi.org/10.1152/jappl.1973.34.1.107.

Goto, M., Itamoto, K., Tani, Y., Miyata, H., Kihara, I., Mori, F., Tajima, T., Wada, N., 2013a. Distribution of muscle Fibers in skeletal muscles of the African elephant (Loxodonta africana africana). Mammal. Study 38, 135. https://doi.org/10.3106/041.038.0210.

Goto, M., Kawai, M., Nakata, M., Itamoto, K., Miyata, H., Ikebe, Y., Tajima, T., Wada, N., 2013b. Distribution of muscle fibers in skeletal muscles of the cheetah (Acinonyx jubatus). Mamm. Biol. 78, 127–133. https://doi.org/10.1016/j.mambio.2012.07.001.

Grabowski, M., Jungers, W.L., 2017. Evidence of a chimpanzee-sized ancestor of humans but a gibbon-sized ancestor of apes. Nat. Commun. 8, 880. https://doi.org/10.1038/s41467-017-00997-4.

Grabowski, M., Hatala, K.G., Jungers, W.L., Richmond, B.G., 2015. Body mass estimates of hominin fossils and the evolution of human body size. J. Hum. Evol. 85, 75–93. https://doi.org/10.1016/j.jhevol.2015.05.005.

Grabowski, M., Hatala, K.G., Jungers, W.L., 2018. Body mass estimates of the earliest possible hominins and implications for the last common ancestor. J. Hum. Evol. 122, 84–92. https://doi.org/10.1016/j.jhevol.2018.05.001.

Granatosky, M.C., Karantanis, N.E., Rychlik, L., Youlatos, D., 2018. A suspensory way of life: integrating locomotion, postures, limb movements and forces in two-toed sloths Choloepus didactylus (Megalonychidae, Folivora, Pilosa). J. Exp. Zool. 329, 570–588.

Green, H.J., Thomson, J.A., Daub, W.D., Houston, M.E., Ranney, D.A., 1979. Fiber composition, fiber size and enzyme activities in vastus lateralis of elite athletes involved in high intensity exercise. Eur. J. Appl. Physiol. Occup. Physiol. 41, 109–117. https://doi.org/10.1007/BF00421658.

Green, H.J., Thomson, J.A., Daub, B.D., Ranney, A., 1980. Biochemical and histochemical alterations in skeletal muscle in man during a period of reduced activity. Can. J. Physiol. Pharmacol. 58, 1311–1316. https://doi.org/10.1139/y80-199.

Green, H.J., Sutton, J.R., Cymerman, A., Young, P.M., Houston, C.S., 1989. Operation Everest II: adaptations in human skeletal muscle. J. Appl. Physiol. 66, 2454–2461.

Green, H.J., Jones, S., Ball-Burnett, M.E., Smith, D., Livesey, J., Farrance, B.W., 1991. Early muscular and metabolic adaptations to prolonged exercise training in humans. J. Appl. Physiol. 70, 2032–2038. https://doi.org/10.1152/jappl.1991.70.5.2032.

Green, H., Goreham, C., Ouyang, J., Ball-Burnett, M., Ranney, D., 1999. Regulation of fiber size, oxidative potential, and capillarization in human muscle by resistance exercise. Am. J. Phys. Regul. Integr. Comp. Phys. 276, R591–R596. https://doi.org/10.1152/ajpregu.1999.276.2.R591.

Guerreiro, I., Nunes, A., Woltering, J.M., Casaca, A., Nóvoa, A., Vinagre, T., Hunter, M.E., Duboule, D., Mallo, M., 2013. Role of a polymorphism in a Hox/Pax-responsive enhancer in the evolution of the vertebrate spine. Proc. Natl. Acad. Sci. 110, 10682–10686. https://doi.org/10.1073/pnas.1300592110.

Hagiwara, N., Yeh, M., Liu, A., 2007. Sox6 is required for normal fiber type differentiation of fetal skeletal muscle in mice. Dev. Dyn. 236, 2062–2076. https://doi.org/10.1002/dvdy.21223.

Haile-Selassie, Y., 2001. Late Miocene hominids from the middle awash, Ethiopia. Nature 412, 178–181. https://doi.org/10.1038/35084063.

Häkkinen, K., Komi, P.V., Tesch, P.A., 1981. Effect of combined concentric and eccentric strength training and detraining on force-time, muscle fiber and metabolic characteristics of leg extensor muscles. Scand. J. Med. Sci. Sports 3, 50–58.

Häkkinen, K., Pakarinen, A., Kyröläinen, H., Cheng, S., Kim, D., Komi, P., 1990. Neuromuscular adaptations and serum hormones in females during prolonged power training. Int. J. Sports Med. 11, 91–98. https://doi.org/10.1055/s-2007-1024769.

Häkkinen, K., Kraemer, W.J., Newton, R.U., Alen, M., 2001. Changes in electromyographic activity, muscle fibre and force production characteristics during heavy resistance/power strength training in middle-aged and older men and women. Acta Physiol. Scand. 171, 51–62. https://doi.org/10.1046/j.1365-201X.2001.00781.x.

Häkkinen, K., Kraemer, W.J., Pakarinen, A., Tripleltt-Mcbride, T., Mcbride, J.M., Häkkinen, A., Alen, M., Mcguigan, M.R., Bronks, R., Newton, R.U., 2002. Effects of heavy resistance/power training on maximal strength, muscle morphology, and hormonal response patterns in 60-75-year-old men and women. Can. J. Appl. Physiol. 27, 213–231. https://doi.org/10.1139/h02-013.

Hammond, A.S., Mavuso, S.S., Biernat, M., Braun, D.R., Jinnah, Z., Kuo, S., Melaku, S., Wemanya, S.N., Ndiema, E.K., Patterson, D.B., Uno, K.T., Palcu, D.V., 2021. New hominin remains and revised context from the earliest Homo erectus locality in East Turkana, Kenya. Nat. Comm. 12, 1939.

Handsfield, G.G., Knaus, K.R., Fiorentino, N.M., Meyer, C.H., Hart, J.M., Blemker, S.S., 2017. Adding muscle where you need it: non-uniform hypertrophy patterns in elite sprinters. Scand. J. Sports Med. 27, 1050–1060. https://doi.org/10.1111/sms.12723.

Hansen, S., Cutts, J.H., Krause, W.J., Cutts, J.H., 1987. Distribution of fibre types in thirty-seven muscles of Didelphis virginiana. Anat. Anz. 164, 153–158.

Harber, M.P., Fry, A.C., Rubin, M.R., Smith, J.C., Weiss, L.W., 2004. Skeletal muscle and hormonal adaptations to circuit weight training in untrained men. Scand. J. Med. Sci. Sports 14, 176–185. https://doi.org/10.1111/j.1600-0838.2003.371.x.

Harber, M.P., Konopka, A.R., Undem, M.K., Hinkley, J.M., Minchev, K., Kaminsky, L.A., Trappe, T.A., Trappe, S., 2012. Aerobic exercise training induces skeletal muscle hypertrophy and age-dependent adaptations in myofiber function in young and older men. J. Appl. Physiol. 113, 1495–1504. https://doi.org/10.1152/japplphysiol.00786.2012.

Hardin, D.S., Azzarelli, B., Edwards, J., Wigglesworth, J., Maianu, L., Brechtel, G., Johnson, A., Baron, A., Garvey, W.T., 1995. Mechanisms of enhanced insulin sensitivity in endurance-trained athletes: effects on blood flow and differential expression of GLUT 4 in skeletal muscles. J. Clin. Endocrinol. Metab. 80, 2437–2446. https://doi.org/10.1210/jcem.80.8.7629239.

Harridge, S.D.R., Bottinelli, R., Canepari, M., Pellegrino, M.A., Reggiani, C., Esbjörnsson, M., Saltin, B., 1996. Whole-muscle and single-fibre contractile properties and myosin heavy chain isoforms in humans. Pflugers Arch. - Eur. J. Physiol. 432, 913–920. https://doi.org/10.1007/s004240050215.

Harrison, B.C., Allen, D.L., Leinwand, L.A., 2011. IIb or not IIb? Regulation of myosin heavy chain gene expression in mice and men. Skelet. Muscle 1, 5. https://doi.org/10.1186/2044-5040-1-5.

Hather, B.M., Tesch, P.A., Buchanan, P., Dudley, G.A., 1991. Influence of eccentric actions on skeletal muscle adaptations to resistance training. Acta Physiol. Scand. 143, 177–185. https://doi.org/10.1111/j.1748-1716.1991.tb09219.x.

Hather, B.M., Adams, G.R., Tesch, P.A., Dudley, G.A., 1992. Skeletal muscle responses to lower limb suspension in humans. J. Appl. Physiol. 72, 1493–1498. https://doi.org/10.1152/jappl.1992.72.4.1493.

Haygood, R., Fedrigo, O., Hanson, B., Yokoyama, K.-D., Wray, G., 2007. Promoter regions of many neural- and nutrition-related genes have experienced positive selection during human evolution. Nat. Prec. https://doi.org/10.1038/npre.2007.69.1.

Hennebry, A., Berry, C., Siriett, V., O'Callaghan, P., Chau, L., Watson, T., Sharma, M., Kambadur, R., 2009. Myostatin regulates fiber-type composition of skeletal muscle by regulating MEF2 and MyoD gene expression. Am. J. Phys. Cell Phys. 296, C525–C534. https://doi.org/10.1152/ajpcell.00259.2007.

Hepple, R.T., Mackinnon, S.L.M., Thomas, S.G., Goodman, J.M., Plyley, M.J., 1996. Quantitating the capillary supply and the response to resistance training in older men. Pflugers Arch. - Eur. J. Physiol. 433, 238–244. https://doi.org/10.1007/s004240050273.

Herries, A.I.R., Martin, J.M., Leece, A.B., et al., 2020. Contemporaneity of Australopithecus, Paranthropus, and early Homo erecuts in South Africa. Science. 368, eaaw7293.

Hickson, R.C., Dvorak, B.A., Gorostiaga, E.M., Kurowski, T.T., Foster, C., 1988. Potential for strength and endurance training to amplify endurance performance. J. Appl. Physiol. 65, 2285–2290. https://doi.org/10.1152/jappl.1988.65.5.2285.

Hickson, R.C., Hidaka, K., Foster, C., 1994. Skeletal muscle fiber type, resistance training, and strength-related performance. Med. Sci. Sports Exerc. 26, 593–598.

Hikida, R.S., Staron, R.S., Hagerman, F.C., Walsh, S., Kaiser, E., Shell, S., Hervey, S., 2000. Effects of high-intensity resistance training on untrained older men. II. Muscle fiber characteristics and nucleo-cytoplasmic relationships. J. Gerontol. A Biol. Sci. Med. Sci. 55, B347–B354. https://doi.org/10.1093/gerona/55.7.B347.

Hill, M.S., van de Zande, P., Wittkopp, P.J., 2021. Molecular and evolutionary processes generating variation in gene expression. Nat. Rev. Genet. 22, 203–215. https://doi.org/10.1038/s41576-020-00304-w.

Holm, L., Reitelseder, S., Pedersen, T.G., Doessing, S., Petersen, S.G., Flyvbjerg, A., Andersen, J.L., Aagaard, P., Kjaer, M., 2008. Changes in muscle size and MHC composition in response to resistance exercise with heavy and light loading intensity. J. Appl. Physiol. 105, 1454–1461. https://doi.org/10.1152/japplphysiol.90538.2008.

Hortobágyi, T., Houmard, J.A., Stevenson, J.R., Fraser, D.D., Johns, R.A., Israel, R.G., 1993. The effects of detraining on power athletes. Med. Sci. Sports Exerc. 25, 929–935.

Hortobágyi, T., Dempsey, L., Fraser, D., Zheng, D., Hamilton, G., Lambert, J., Dohm, L., 2000. Changes in muscle strength, muscle fibre size and myofibrillar gene expression after immobilization and retraining in humans. J. Physiol. 524, 293–304. https://doi.org/10.1111/j.1469-7793.2000.00293.x.

Hostler, D., Schwirian, C., Campos, G., Toma, K., Crill, M., Hagerman, G., Hagerman, F., Staron, R., 2001. Skeletal muscle adaptations in elastic resistance-trained young men and women. Eur. J. Appl. Physiol. 86, 112–118. https://doi.org/10.1007/s004210100495.

Houston, M.E., Bentzen, H., Larsen, H., 1979. Interrelationships between skeletal muscle adaptations and performance as studied by detraining and retraining. Acta Physiol. Scand. 105, 163–170. https://doi.org/10.1111/j.1748-1716.1979.tb06328.x.

Houston, M.E., Froese, E.A., Valeriote, St P., Green, H.J., Ranney, D.A., 1983. Muscle performance, morphology and metabolic capacity during strength training and detraining: a one leg model. Eur. J. Appl. Physiol. Occup. Physiol. 51, 25–35. https://doi.org/10.1007/BF00952534.

Howald, H., 1982. Training-induced morphological and functional changes in skeletal muscle. Int. J. Sports Med. 03, 1–12. https://doi.org/10.1055/s-2008-1026053.

Hvid, L., Aagaard, P., Justesen, L., Bayer, M.L., Andersen, J.L., Ørtenblad, N., Kjaer, M., Suetta, C., 2010. Effects of aging on muscle mechanical function and muscle fiber morphology during short-term immobilization and subsequent retraining. J. Appl. Physiol. 109, 1628–1634. https://doi.org/10.1152/japplphysiol.00637.2010.

Ichikawa, H., Matsuo, T., Higurashi, Y., Nagahisa, H., Miyata, H., Sugiura, T., Wada, N., 2019. Characteristics of muscle fiber-type distribution in moles. Anat. Rec. 302, 1010–1023. https://doi.org/10.1002/ar.24008.

Indjeian, V.B., Kingman, G.A., Jones, F.C., Guenther, C.A., Grimwood, J., Schmutz, J., Myers, R.M., Kingsley, D.M., 2016. Evolving new skeletal traits by cis -regulatory changes in bone morphogenetic proteins. Cell 164, 45–56. https://doi.org/10.1016/j.cell.2015.12.007.

Ingjer, F., 1979. Effects of endurance training on muscle fibre ATP-ase activity, capillary supply and mitochondrial content in man. J. Physiol. 294, 419–432. https://doi.org/10.1113/jphysiol.1979.sp012938.

James, R.S., Altringham, J.D., Goldspink, D.F., 1995. The mechanical properties of fast and slow skeletal muscles of the mouse in relation to their locomotory function. J. Exp. Biol. 198, 491–502. https://doi.org/10.1242/jeb.198.2.491.

Jansson, E., Sjödin, B., Tesch, P., 1978. Changes in muscle fibre type distribution in man after physical training: a sign of fibre type transformation? Acta Physiol. Scand. 104, 235–237. https://doi.org/10.1111/j.1748-1716.1978.tb06272.x.

Jansson, E., Esbjornsson, M., Holm, I., Jacobs, I., 1990. Increase in the proportion of fast-twitch muscle fibres by sprint training in males. Acta Physiol. Scand. 140, 359–363.

Johansson, P.A., Brattås, P.L., Douse, C.H., Hsieh, P., Adami, A., Pontis, J., Grassi, D., Garza, R., Sozzi, E., Cataldo, R., Jönsson, M.E., Atacho, D.A.M., Pircs, K., Eren, F., Sharma, Y., Johansson, J., Fiorenzano, A., Parmar, M., Fex, M., Trono, D., Eichler, E. E., Jakobsson, J., 2022. A cis-acting structural variation at the ZNF558 locus controls a gene regulatory network in human brain development. Cell Stem Cell 29, 52–69. e8. https://doi.org/10.1016/j.stem.2021.09.008.

Johnson, M.A., Polgar, J., Weightman, D., Appleton, D., 1973. Data on the distribution of fibre types in thirty-six human muscles. An autopsy study. J. Neurol. Sci. 18, 111–129. https://doi.org/10.1016/0022-510X(73)90023-3.

Jones, K.E., Purvis, A., 1997. An optimum body size for mammals? Comparative evidence from bats. Funct. Ecol. 11, 751–756. https://doi.org/10.1046/j.1365-2435.1997.00149.x.

Jouffroy, F.K., Medina, M.F., Renous, S., Gasc, J.-P., 2003. Immunocytochemical characteristics of elbow, knee and ankle muscles of the five-toed jerboa (Allactaga elater). J. Anat. 202, 373–386. https://doi.org/10.1046/j.1469-7580.2003.00167.x.

Kamm, G.B., López-Leal, R., Lorenzo, J.R., Franchini, L.F., 2013. A fast-evolving human NPAS3 enhancer gained reporter expression in the developing forebrain of transgenic mice. Philos. Trans. Royal Soc. B Biol. Sci. 368, 20130019. https://doi.org/10.1098/rstb.2013.0019.

Karavirta, L., Häkkinen, A., Sillanpää, E., García-López, D., Kauhanen, A., Haapasaari, A., Alen, M., Pakarinen, A., Kraemer, W.J., Izquierdo, M., Gorostiaga, E., Häkkinen, K., 2011. Effects of combined endurance and strength training on muscle strength, power and hypertrophy in 40-67-year-old men. Scand. J. Med. Sci. Sports 21, 402–411. https://doi.org/10.1111/j.1600-0838.2009.01059.x.

Kawai, M., Minami, Y., Sayama, Y., Kuwano, A., Hiraga, A., Miyata, H., 2009. Muscle fiber population and biochemical properties of whole body muscles in thoroughbred horses. Anat. Rec. Adv. Integr. Anat. Evol. Biol. 292, 1663–1669. https://doi.org/10.1002/ar.20961.

King, M.-C., Wilson, A.C., 1975. Evolution at two levels in humans and chimpanzees. Science 1979 (188), 107–116. https://doi.org/10.1126/science.1090005.

Klausen, K., Andersen, L.B., Pelle, I., 1981. Adaptive changes in work capacity, skeletal muscle capillarization and enzyme levels during training and detraining. Acta Physiol. Scand. 113, 9–16. https://doi.org/10.1111/j.1748-1716.1981.tb06854.x.

Kojić, F., Mandić, D., Ilić, V., 2021. Resistance training induces similar adaptations of upper and lower-body muscles between sexes. Sci. Rep. 11 https://doi.org/10.1038/s41598-021-02867-y.

Konno, T., Watanabe, K., 2012. Distribution of myofiber types in the crural musculature of sheep. Okajimas Folia Anat. Jpn. 89, 39–45. https://doi.org/10.2535/ofaj.89.39.

Konopka, A.R., Trappe, T.A., Jemiolo, B., Trappe, S.W., Harber, M.P., 2011. Myosin heavy chain plasticity in aging skeletal muscle with aerobic exercise training. J. Gerontol. Ser. A Biol. Sci. Med. Sci. 66 A, 835–841. https://doi.org/10.1093/gerona/glr088.

Kosek, D.J., Kim, J., Petrella, J.K., Cross, J.M., Bamman, M.M., 2006. Efficacy of 3 days/wk resistance training on myofiber hypertrophy and myogenic mechanisms in young vs. older adults. J. Appl. Physiol. 101, 531–544. https://doi.org/10.1152/japplphysiol.01474.2005.

Koshikawa, S., Giorgianni, M.W., Vaccaro, K., Kassner, V.A., Yoder, J.H., Werner, T., Carroll, S.B., 2015. Gain of cis-regulatory activities underlies novel domains of wingless gene expression in *Drosophila*. Proc. Natl. Acad. Sci. 112, 7524–7529. https://doi.org/10.1073/pnas.1509022112.

Kostka, D., Holloway, A.K., Pollard, K.S., 2018. Developmental Loci harbor clusters of accelerated regions that evolved independently in ape lineages. Mol. Biol. Evol. 35, 2034–2045. https://doi.org/10.1093/molbev/msy109.

Kraemer, W.J., Patton, J.F., Gordon, S.E., Harman, E.A., Deschenes, M.R., Reynolds, K., Newton, R.U., Triplett, N.T., Dziados, J.E., 1995. Compatibility of high-intensity strength and endurance training on hormonal and skeletal muscle adaptations. J. Appl. Physiol. 78, 976–989. https://doi.org/10.1152/jappl.1995.78.3.976.

Krainski, F., Hastings, J.L., Heinicke, K., Romain, N., Pacini, E.L., Snell, P.G., Wyrick, P., Palmer, M.D., Haller, R.G., Levine, B.D., 2014. The effect of rowing ergometry and resistive exercise on skeletal muscle structure and function during bed rest. J. Appl. Physiol. 116, 1569–1581. https://doi.org/10.1152/japplphysiol.00803.2013.

Krotkiewski, M., Bylund-Fallenius, A.-C., Holm, J., Björntorp, P., Grimby, G., Mandroukas, K., 1983. Relationship between muscle morphology and metabolism in obese women: the effects of long-term physical training. Eur. J. Clin. Investig. 13, 5–12. https://doi.org/10.1111/j.1365-2362.1983.tb00057.x.

Kryger, A.I., Andersen, J.L., 2007. Resistance training in the oldest old: consequences for muscle strength, fiber types, fiber size, and MHC isoforms. Scand. J. Med. Sci. Sports 17, 422–430. https://doi.org/10.1111/j.1600-0838.2006.00575.x.

Kvon, E.Z., Kamneva, O.K., Melo, U.S., Barozzi, I., Osterwalder, M., Mannion, B.J., Tissières, V., Pickle, C.S., Plajzer-Frick, I., Lee, E.A., Kato, M., Garvin, T.H., Akiyama, J.A., Afzal, V., Lopez-Rios, J., Rubin, E.M., Dickel, D.E., Pennacchio, L.A., Visel, A., 2016. Progressive loss of function in a limb enhancer during snake evolution. Cell 167, 633–642.e11. https://doi.org/10.1016/j.cell.2016.09.028.

Labarque, V., Op’ t Eijnde, B., van Leemputte, M., 2002. Effect of immobilization and retraining on torque-velocity relationship of human knee flexor and extensor muscles. Eur. J. Appl. Physiol. 86, 251–257. https://doi.org/10.1007/s00421-001-0530-z.

Langergraber, K.E., Prüfer, K., Rowney, C., Boesch, C., Crockford, C., Fawcett, K., Inoue, E., Inoue-Muruyama, M., Mitani, J.C., Muller, M.N., Robbins, M.M., Schubert, G., Stoinski, T.S., Viola, B., Watts, D., Wittig, R.M., Wrangham, R.W., Zuberbühler, K., Pääbo, S., Vigilant, L., 2012. Generation times in wild chimpanzees and gorillas suggest earlier divergence times in great ape and human evolution. Proc. Natl. Acad. Sci. 109, 15716–15721. https://doi.org/10.1073/pnas.1211740109.

LaPotin, S., Swartz, M.E., Luecke, D.M., Constantinou, S.J., Gallant, J.R., Eberhart, J.K., Zakon, H.H., 2022. Divergent cis-regulatory evolution underlies the convergent loss of sodium channel expression in electric fish. Sci. Adv. 8 https://doi.org/10.1126/sciadv.abm2970.

Larsson, L., 1982. Physical training effects on muscle morphology in sedentary males at different ages. Med. Sci. Sports Exerc. 14, 203–206.

Larsson, L., Ansved, T., 1985. Effects of long-term physical training and detraining on enzyme histochemical and functional skeletal muscle characteristics in man. Muscle Nerve 8, 714–722. https://doi.org/10.1002/mus.880080815.

Larsson, L., Li, X., Berg, H.E., Frontera, W.R., 1996. Effects of removal of weight-bearing function on contractility and myosin isoform composition in single human skeletal muscle cells. Pflugers Arch. - Eur. J. Physiol. 432, 320–328. https://doi.org/10.1007/s004240050139.

Lee, L.A., Karabina, A., Broadwell, L.J., Leinwand, L.A., 2019. The ancient sarcomeric myosins found in specialized muscles. Skelet. Muscle 9, 7. https://doi.org/10.1186/s13395-019-0192-3.

Letelier, J., de la Calle-Mustienes, E., Pieretti, J., Naranjo, S., Maeso, I., Nakamura, T., Pascual-Anaya, J., Shubin, N.H., Schneider, I., Martinez-Morales, J.R., Gómez-Skarmeta, J.L., 2018. A conserved Shh cis-regulatory module highlights a common developmental origin of unpaired and paired fins. Nat. Genet. 50, 504–509. https://doi.org/10.1038/s41588-018-0080-5.

Lexell, J., Downham, D., 1992. What is the effect of ageing on type 2 muscle fibres? J. Neurol. Sci. 107, 250–251. https://doi.org/10.1016/0022-510X(92)90297-X.

Lexell, J., Taylor, C.C., Sjostrom, M., 1988. What is the cause of the aging atrophy? Total number, size and proportion of different fibre types studies in whole vastus lateralis muscle from 15- to 83-year old men. J. Neurol. Sci. 84, 275–294.

Lexell, J., Downham, D.Y., Larsson, Y., Bruhn, E., Morsing, B., 1995. Heavy-resistance training in older Scandinavian men and women: short- and long-term effects on arm and leg muscles. Scand. J. Med. Sci. Sports 5, 329–341. https://doi.org/10.1111/j.1600-0838.1995.tb00055.x.

Linossier, M.-T., Dormois, D., Geyssant, A., Denis, C., 1997. Performance and fibre characteristics of human skeletal muscle during short sprint training and detraining on a cycle ergometer. Eur. J. Appl. Physiol. 75, 491–498. https://doi.org/10.1007/s004210050194.

Long, K., Su, D., Li, Xiaokai, Li, H., Zeng, S., Zhang, Y., Zhong, Z., Lin, Y., Li, Xuemin, Lu, L., Jin, L., Ma, J., Tang, Q., Li, M., 2022. Identification of enhancers responsible for the coordinated expression of myosin heavy chain isoforms in skeletal muscle. BMC Genomics 23, 519. https://doi.org/10.1186/s12864-022-08737-9.

Lotta, S., Scelsi, R., Alfonsi, E., Saitta, A., Nicolotti, D., Epifani, P., Carraro, U., 1991. Morphometric and neurophysiological analysis of skeletal muscle in paraplegic patients with traumatic cord lesion. Spinal Cord 29, 247–252. https://doi.org/10.1038/sc.1991.35.

Lovejoy, C.O., Suwa, G., Spurlock, L., Asfaw, B., White, T.D., 2009. The pelvis and femur of Ardipithecus ramidus: the emergence of upright walking. Science 1979 (326), 71. https://doi.org/10.1126/science.1175831.

Luden, N., Hayes, E., Minchev, K., Louis, E., Raue, U., Conley, T., Trappe, S., 2012. Skeletal muscle plasticity with marathon training in novice runners. Scand. J. Med. Sci. Sports 22, 662–670. https://doi.org/10.1111/j.1600-0838.2011.01305.x.

Madsen, K., Pedersen, P.K., Djurhuus, M.S., Klitgaard, N.A., 1993. Effects of detraining on endurance capacity and metabolic changes during prolonged exhaustive exercise. J. Appl. Physiol. 75, 1444–1451. https://doi.org/10.1152/jappl.1993.75.4.1444.

Malisoux, L., Francaux, M., Nielens, H., Theisen, D., 2006. Stretch-shortening cycle exercises: an effective training paradigm to enhance power output of human single muscle fibers. J. Appl. Physiol. 100, 771–779. https://doi.org/10.1152/japplphysiol.01027.2005.

Martel, G.F., Roth, S.M., Ivey, F.M., Lemmer, J.T., Tracy, B.L., Hurlbut, D.E., Metter, E.J., Hurley, B.F., Rogers, M.A., 2006. Age and sex affect human muscle fibre adaptations to heavy-resistance strength training. Exp. Physiol. 91, 457–464. https://doi.org/10.1113/expphysiol.2005.032771.

Mashima, D., Oka, Y., Gotoh, T., Tomonaga, S., Sawano, S., Nakamura, M., Tatsumi, R., Mizunoya, W., 2019. Correlation between skeletal muscle fiber type and free amino acid levels in Japanese Black steers. Anim. Sci. J. 90, 604–609. https://doi.org/10.1111/asj.13185.

Mattson, J.P., Miller, T.A., Poole, D.C., Delp, M.D., 2002. Fiber composition and oxidative capacity of hamster skeletal muscle. J. Histochem. Cytochem. 50, 1685–1692. https://doi.org/10.1177/002215540205001214.

Mayfield, D.L., Cronin, N.J., Lichtwark, G.A., 2022. Understanding altered contractile properties in advanced age: insights from a systematic muscle modelling approach. Biomech. Model. Mechanobiol. https://doi.org/10.1007/s10237-022-01651-9.

McLean, C.Y., Reno, P.L., Pollen, A.A., Bassan, A.I., Capellini, T.D., Guenther, C., Indjeian, V.B., Lim, X., Menke, D.B., Schaar, B.T., Wenger, A.M., Bejerano, G., Kingsley, D.M., 2011. Human-specific loss of regulatory DNA and the evolution of human-specific traits. Nature 471, 216–219. https://doi.org/10.1038/nature09774.

Moher, D., 2009. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Ann. Intern. Med. 151, 264. https://doi.org/10.7326/0003-4819-151-4-200908180-00135.

Nekaris, K.A.I., 2001. Activity budget and position behavior of the Mysore slender Loris (Loris tardigradus lydekkereianus): implications for slow climbing locomotion. Folia Primatol. 72, 228–241.

Nekaris, K.A.I., 2014. Extreme primates: ecology and evolution of Asian lorises. Evol. Anthropol. 23, 177–187.

O'Neill, M.C., Umberger, B.R., Holowka, N.B., Larson, S.G., Reiser, P.J., Slade, J.M., 2017. Chimpanzee super strength and human skeletal muscle evolution. Proc. Natl. Acad. Sci. U. S. A. 114, 7343–7348. https://doi.org/10.1073/pnas.1619071114.

O'Neill, M.C., Demes, B., Thompson, N.E., Larson, S.G., Stern Jr., J.T., Umberger, B.R., 2022. Adaptations for bipedal walking: musculoskeletal structure and three-dimensional joint mechanics of humans and bipedal chimpanzees (Pan troglodytes). J. Hum. Evol. 168, 103195.

Ordway, A.J., Hancuch, K.N., Johnson, W., Wiliams, T.M., Rebeiz, M., 2014. The expansion of body coloration involves coordinated evolution in cis and trans within the pigmentation regulatory network of Drosophila prostipennis. Dev. Biol. 392, 431–440. https://doi.org/10.1016/j.ydbio.2014.05.023.

Orme, D., Freckleton, R., Thomas, G., Petzoldt, T., Fritz, S., Isaac, N., Pearse, W., 2013. The caper package: comparative analysis of phylogenetics and evolution in R. In: R Package Version 5, pp. 1–36.

Pagel, M., 1999. Inferring the historical patterns of biological evolution. Nature 401, 877–884. https://doi.org/10.1038/44766.

Parcell, A.C., Sawyer, R.D., Drummond, M.J., O'Neil, B., Miller, N., Woolstenhulme, M. T., 2005. Single-fiber MHC polymorphic expression is unaffected by sprint cycle training. Med. Sci. Sports Exerc. 37, 1133–1137. https://doi.org/10.1249/01.mss.0000170123.27209.e1.

Pareja-Blanco, F., Rodríguez-Rosell, D., Sánchez-Medina, L., Sanchis-Moysi, J., Dorado, C., Mora-Custodio, R., Yáñez-García, J.M., Morales-Alamo, D., Pérez-Suárez, I., Calbet, J.A.L., González-Badillo, J.J., 2017. Effects of velocity loss during resistance training on athletic performance, strength gains and muscle adaptations. Scand. J. Med. Sci. Sports 27, 724–735. https://doi.org/10.1111/sms.12678.

Parente, V., D'Antona, G., Adami, R., Miotti, D., Capodaglio, P., de Vito, G., Bottinelli, R., 2008. Long-term resistance training improves force and unloaded shortening velocity of single muscle fibres of elderly women. Eur. J. Appl. Physiol. 104, 885–893. https://doi.org/10.1007/s00421-008-0845-0.

Pellegrino, J., Ruby, B.C., Dumke, C.L., 2016. Effect of plyometrics on the energy cost of running and MHC and titin isoforms. Med. Sci. Sports Exerc. 48, 49–56. https://doi.org/10.1249/MSS.0000000000000747.

Pereira, A.G., Grizante, M.B., Kohlsdorf, T., 2022. What snakes and caecilians have in common? Molecular interaction units and the independent origins of similar morphotypes in Tetrapoda. Proc. R. Soc. B Biol. Sci. 289 https://doi.org/10.1098/rspb.2022.0841.

Pereira Sant'Ana, Ennion, S., Sargeant, A.J., Moorman, A.F., Goldspink, G., 1997. Comparison of the molecular, antigenic and ATPase determinants of fast myosin heavy chains in rat and human: a single-fibre study. Pflug. Arch. Eur. J. Physiol. 435 (1), 151–163. https://doi.org/10.1007/s004240050495.

Petter, A., Jouffroy, F.K., 1993. Fiber type population in limb muscles of Microcebus murinus. Primates 34, 181–196. https://doi.org/10.1007/BF02381389.

Pilbeam, D.R., Lieberman, D.E., 2017. Reconstructing the last common ancestor of chimpanzees and humans. In: Muller, M.N., Wrangham, R.W., Pilbeam, D.R. (Eds.), Chimpanzees and Human Evolution. Harvard University Press, Cambridge, pp. 22–141.

Prabhakar, S., Visel, A., Akiyama, J.A., Shoukry, M., Lewis, K.D., Holt, A., Plajzer-Frick, I., Morrison, H., Fitzpatrick, D.R., Afzal, V., Pennacchio, L.A., Rubin, E.M., Noonan, J.P., 2008. Human-specific gain of function in a developmental enhancer. Science 1979 (321), 1346–1350. https://doi.org/10.1126/science.1159974.

Prescott, S.L., Srinivasan, R., Marchetto, M.C., Grishina, I., Narvaiza, I., Selleri, L., Gage, F.H., Swigut, T., Wysocka, J., 2015. Enhancer divergence and cis-regulatory evolution in the human and chimp neural crest. Cell 163, 68–83. https://doi.org/10.1016/j.cell.2015.08.036.

Putman, CharlesT, Xu, X., Gillies, E., MacLean, IanM, Bell, GordonJ, 2004. Effects of strength, endurance and combined training on myosin heavy chain content and fibre-type distribution in humans. Eur. J. Appl. Physiol. 92, 376–384. https://doi.org/10.1007/s00421-004-1104-7.

Rassmusen, D.T., Nekaris, K.A., 1998. The evolutionary history of the lorisiform primates. Folia Primatol. 69, 250–285.

Richard, D., Liu, Z., Cao, J., Kiapour, A.M., Willen, J., Yarlagadda, S., Jagoda, E., Kolachalama, V.B., Sieker, J.T., Chang, G.H., Muthuirulan, P., Young, M., Masson, A., Konrad, J., Hosseinzadeh, S., Maridas, D.E., Rosen, V., Krawetz, R., Roach, N., Capellini, T.D., 2020. Evolutionary selection and constraint on human knee chondrocyte regulation impacts osteoarthritis risk. Cell 181, 362–381.e28. https://doi.org/10.1016/j.cell.2020.02.057.

Rivero, J.L., Serrano, A.L., Barrey, E., Valette, J.P., Jouglin, M., 1999. Analysis of myosin heavy chains at the protein level in horse skeletal muscle. J. Muscle Res. Cell Motil. 20, 211–221. https://doi.org/10.1023/A:1005461214800.

Ruff, C.B., Holt, B., Trinkaus, E., 2006. Who's afraid of the big bad Wolff?: "Wolff's Law" and bone functional adaptation. Am. J. Phys. Anthropol. 129, 484–498.

Ruff, C.B., Burgess, M.L., Squyres, N., Junno, J.-A., Trinkaus, E., 2018. Lower limb articular scaling and body mass estimation in Pliocene and Pleistocene hominins. J. Hum. Evol. 115, 85–111. https://doi.org/10.1016/j.jhevol.2017.10.014.

Sackton, T.B., Grayson, P., Cloutier, A., Hu, Z., Liu, J.S., Wheeler, N.E., Gardner, P.P., Clarke, J.A., Baker, A.J., Clamp, M., Edwards, S.V., 2019. Convergent regulatory evolution and loss of flight in paleognathous birds. Science 1979 (364), 74–78. https://doi.org/10.1126/science.aat7244.

Sahd, L., Doubell, N., Bennett, N.C., Kotzé, S.H., 2022. Hind foot drumming: myosin heavy chain muscle fiber distribution in the hind limb muscles of three African mole-rat species (Bathyergidae). Anat. Rec. 305, 170–183. https://doi.org/10.1002/ar.24712.

Salanova, M., Gelfi, C., Moriggi, M., Vasso, M., Viganò, A., Minafra, L., Bonifacio, G., Schiffl, G., Gutsmann, M., Felsenberg, D., Cerretelli, P., Blottner, D., 2014. Disuse deterioration of human skeletal muscle challenged by resistive exercise superimposed with vibration: evidence from structural and proteomic analysis. FASEB J. 28, 4748–4763. https://doi.org/10.1096/fj.14-252825.

Schiaffino, S., Reggiani, C., 2011. Fiber types in mammalian skeletal muscles. Physiol. Rev. 91, 1447–1531. https://doi.org/10.1152/physrev.00031.2010.

Schiaffino, S., Rossi, A.C., Smerdu, V., Leinwand, L.A., Reggiani, C., 2015. Developmental myosins: expression patterns and functional significance. Skelet. Muscle 5, 22. https://doi.org/10.1186/s13395-015-0046-6.

Schoch, C.L., Ciufo, S., Domrachev, M., Hotton, C.L., Kannan, S., Khovanskaya, R., Leipe, D., Mcveigh, R., O'Neill, K., Robbertse, B., Sharma, S., Soussov, V., Sullivan, J. P., Sun, L., Turner, S., Karsch-Mizrachi, I., 2020. NCBI taxonomy: a comprehensive update on curation, resources and tools. Database 2020. https://doi.org/10.1093/database/baaa062.

Scholz, M.N., D'Août, K., Bobbert, M.F., Aerts, P., 2006. Vertical jumping performance of bonobo (Pan paniscus) suggests superior muscle properties. Proc. R. Soc. B Biol. Sci. 273, 2177–2184. https://doi.org/10.1098/rspb.2006.3568.

Schuenke, M.D., Herman, J.R., Gliders, R.M., Hagerman, F.C., Hikida, R.S., Rana, S.R., Ragg, K.E., Staron, R.S., 2012. Early-phase muscular adaptations in response to slow-speed versus traditional resistance-training regimens. Eur. J. Appl. Physiol. 112, 3585–3595. https://doi.org/10.1007/s00421-012-2339-3.

Short, K.R., Vittone, J.L., Bigelow, M.L., Proctor, D.N., Coenen-Schimke, J.M., Rys, P., Nair, K.S., 2005. Changes in myosin heavy chain mRNA and protein expression in human skeletal muscle with age and endurance exercise training. J. Appl. Physiol. 99, 95–102. https://doi.org/10.1152/japplphysiol.00129.2005.

Sickles, D.W., Pinkstaff, C.A., 1981. Comparative histochemical study of prosimian primate hindlimb muscles. II. Populations of fiber types. Am. J. Anat. 160, 187–194. https://doi.org/10.1002/aja.1001600205.

Signor, S.A., Liu, Y., Rebeiz, M., Kopp, A., 2016. Genetic convergence in the evolution of male-specific color patterns in drosophila. Curr. Biol. 26, 2423–2433. https://doi.org/10.1016/j.cub.2016.07.034.

Simoneau, J.-A., Lortie, G., Boulay, M.R., Marcotte, M., Thibault, M.-C., Bouchard, C., 1985. Human skeletal muscle fiber type alteration with high-intensity intermittent training. Eur. J. Appl. Physiol. Occup. Physiol. 54, 250–253. https://doi.org/10.1007/BF00426141.

Simpson, S.W., Levin, N., Quade, J., Rogers, M.J., Semaw, S., 2019. Ardipithecus ramidus postcrania from the Gona Project area, Afar regional state, Ethipoia. J. Hum. Evol. 129, 1–45.

Sipila, S., Elorinne, M., Alen, M., Suominen, H., Kovanen, V., 1997. Effects of strength and endurance training on muscle fibre characteristics in elderly women. Clin. Physiol. 17, 459–474. https://doi.org/10.1046/j.1365-2281.1997.05050.x.

Slivka, D., Raue, U., Hollon, C., Minchev, K., Trappe, S., 2008. Single muscle fiber adaptations to resistance training in old (80 yr) men: evidence for limited skeletal muscle plasticity. Am. J. Phys. Regul. Integr. Comp. Phys. 295, R273–R280. https://doi.org/10.1152/ajpregu.00093.2008.

Smerdu, V., Cvetko, E., 2013. Myosin heavy chain-2b transcripts and isoform are expressed in human laryngeal muscles. Cells Tissues Organs 198, 75–86. https://doi.org/10.1159/000351293.

Smith, R.J., Jungers, W.L., 1997. Body mass in comparative primatology. J. Hum. Evol. 32, 523–559. https://doi.org/10.1006/jhev.1996.0122.

Snijders, T., Leenders, M., de Groot, L.C.P.G.M., van Loon, L.J.C., Verdijk, L.B., 2019. Muscle mass and strength gains following 6 months of resistance type exercise training are only partly preserved within one year with autonomous exercise continuation in older adults. Exp. Gerontol. 121, 71–78. https://doi.org/10.1016/j.exger.2019.04.002.

Sockol, M.D., Raichlen, D.A., Pontzer, H., 2007. Chimpanzee locomotor energetics and the origin of human bipedalism. Proc. Natl. Acad. Sci. 104, 12265–12269. https://doi.org/10.1073/pnas.0703267104.

Spainhower, K.B., Metz, A.K., Yusuf, A.-R.S., Johnson, L.E., Avey-Arroyo, J.A., Butcher, M.T., 2021. Coming to grips with life upside down: how myosin fiber type and metabolic properties of sloth hindlimb muscles contribute to suspensory function. J. Comp. Physiol. B. 191, 207–224. https://doi.org/10.1007/s00360-020-01325-x.

Staron, R.S., Malicky, E.S., Leonardi, M.J., Falkel, J.E., Hagerman, F.C., Dudley, G.A., 1990. Muscle hypertrophy and fast fiber type conversions in heavy resistance-trained women. Eur. J. Appl. Physiol. Occup. Physiol. 60, 71–79. https://doi.org/10.1007/BF00572189.

Staron, R.S., Leonardi, M.J., Karapondo, D.L., Malicky, E.S., Falkel, J.E., Hagerman, F.C., Hikida, R.S., 1991. Strength and skeletal muscle adaptations in heavy-resistance-trained women after detraining and retraining. J. Appl. Physiol. 70, 631–640. https://doi.org/10.1152/jappl.1991.70.2.631.

Staron, R.S., Karapondo, D.L., Kraemer, W.J., Fry, A.C., Gordon, S.E., Falkel, J.E., Hagerman, F.C., Hikida, R.S., 1994. Skeletal muscle adaptations during early phase of heavy-resistance training in men and women. J. Appl. Physiol. 76, 1247–1255. https://doi.org/10.1152/jappl.1994.76.3.1247.

Staron, R.S., Herman, J.R., Schuenke, M.D., 2012. Misclassification of hybrid fast fibers in resistance-trained human skeletal muscle using histochemical and immunohistochemical methods. J. Strength Cond. Res. 26, 2616–2622. https://doi.org/10.1519/JSC.0b013e3182667095.

Sumiyama, K., Saitou, N., 2011. Loss-of-function mutation in a repressor module of human-specifically activated enhancer HACNS1. Mol. Biol. Evol. 28, 3005–3007. https://doi.org/10.1093/molbev/msr231.

Summerbell, D., Ashby, P.R., Coutelle, O., Cox, D., Yee, S., Rigby, P.W., 2000. The expression of Myf5 in the developing mouse embryo is controlled by discrete and dispersed enhancers specific for particular populations of skeletal muscle precursors. Development 127, 3745–3757. https://doi.org/10.1242/dev.127.17.3745.

Suzuki, A., 1990. Composition of myofiber types in limb muscles of the house shrew (Suncus murinus): lack of type I myofibers. Anat. Rec. 228, 23–30. https://doi.org/10.1002/ar.1092280105.

Suzuki, A., Tamate, H., 1988. Distribution of myofiber types in the hip and thigh musculature of sheep. Anat. Rec. 221, 494–502. https://doi.org/10.1002/ar.1092210106.

Suzuki, A., Watanabe, K., Konno, T., Ohwada, S., 1999. Distribution of myofiber types in the hip and thigh musculature of pigs. Anim. Sci. J. 70, 519–525.

Tajsharghi, H., Hilton-Jones, D., Raheem, O., Saukkonen, A.M., Oldfors, A., Udd, B., 2010. Human disease caused by loss of fast IIa myosin heavy chain due to recessive MYH2 mutations. Brain 133, 1451–1459. https://doi.org/10.1093/brain/awq083.

Talmadge, R.J., Grossman, E.J., Roy, R.R., 1996. Myosin heavy chain composition of adult feline (Felis catus) limb and diaphragm muscles. J. Exp. Zool. 275, 413–420. https://doi.org/10.1002/(SICI)1097-010X(19960815)275:6<413::AID-JEZ3>3.0.CO;2-R.

Terzis, G., Stratakos, G., Manta, P., Georgiadis, G., 2008. Throwing performance after resistance training and detraining. J. Strength Cond. Res. 22, 1198–1204. https://doi.org/10.1519/JSC.0b013e31816d5c97.

Thorpe, S.K., Crompton, R.H., Günther, M.M., Ker, R.F., McNeill Alexander, R., 1999. Dimensions and moment arms of the hind- and forelimb muscles of common chimpanzees (Pan troglodytes). Am. J. Phys. Anthropol. 110, 179–199. https://doi.org/10.1002/(SICI)1096-8644(199910)110:2<179::AID-AJPA5>3.0.CO;2-Z.

Thorstensson, A., Hultén, B., von Döbeln, W., Karlsson, J., 1976. Effect of strength training on enzyme activities and fibre characteristics in human skeletal muscle. Acta Physiol. Scand. 96, 392–398. https://doi.org/10.1111/j.1748-1716.1976.tb10207.x.

Tirrell, T.F., Cook, M.S., Carr, J.A., Lin, E., Ward, S.R., Lieber, R.L., 2012. Human skeletal muscle biochemical diversity. J. Exp. Biol. 215, 2551–2559. https://doi.org/10.1242/jeb.069385.

Trappe, S., Williamson, D., Godard, M., Porter, D., Rowden, G., Costill, D., 2000. Effect of resistance training on single muscle fiber contractile function in older men. J. Appl. Physiol. 89, 143–152. https://doi.org/10.1152/jappl.2000.89.1.143.

Trappe, S.W., Trappe, T.A., Lee, G.A., Widrick, J.J., Costill, D.L., Fitts, R.H., 2001. Comparison of a space shuttle flight (STS-78) and bed rest on human muscle function. J. Appl. Physiol. 91, 57–64. https://doi.org/10.1152/jappl.2001.91.1.57.

Trappe, S., Trappe, T., Gallagher, P., Harber, M., Alkner, B., Tesch, P., 2004. Human single muscle fibre function with 84 day bed-rest and resistance exercise. J. Physiol. 557, 501–513. https://doi.org/10.1113/jphysiol.2004.062166.

Trappe, S., Harber, M., Creer, A., Gallagher, P., Slivka, D., Minchev, K., Whitsett, D., 2006. Single muscle fiber adaptations with marathon training. J. Appl. Physiol. 101, 721–727. https://doi.org/10.1152/japplphysiol.01595.2005.

Trappe, S., Creer, A., Slivka, D., Minchev, K., Trappe, T., 2007. Single muscle fiber function with concurrent exercise or nutrition countermeasures during 60 days of bed rest in women. J. Appl. Physiol. 103, 1242–1250. https://doi.org/10.1152/japplphysiol.00560.2007.

Trappe, S., Creer, A., Minchev, K., Slivka, D., Louis, E., Luden, N., Trappe, T., 2008. Human soleus single muscle fiber function with exercise or nutrition countermeasures during 60 days of bed rest. Am. J. Phys. Regul. Integr. Comp. Phys. 294, 939–947. https://doi.org/10.1152/ajpregu.00761.2007.-The.

Trappe, S., Costill, D., Gallagher, P., Creer, A., Peters, J.R., Evans, H., Riley, D.A., Fitts, R.H., 2009. Exercise in space: human skeletal muscle after 6 months aboard the international Space Station. J. Appl. Physiol. 106, 1159–1168. https://doi.org/10.1152/japplphysiol.91578.2008.-The.

Upham, N.S., Esselstyn, J.A., Jetz, W., 2019. Inferring the mammal tree: species-level sets of phylogenies for questions in ecology, evolution, and conservation. PLoS Biol. 17, e3000494 https://doi.org/10.1371/journal.pbio.3000494.

Urbani, B., Bosque, C., 2007. Feeding ecology and postural behavior of the three-toed sloth (Bradypus variegatus flaccidus) in northern Venezeula. Mamm. Biol. 72, 321–329.

Veldhuizen, J., Verstappen, F., Vroemen, J., Kuipers, H., Greep, J., 1993. Functional and morphological adaptations following four weeks of knee immobilization. Int. J. Sports Med. 14, 283–287. https://doi.org/10.1055/s-2007-1021178.

Vigelsø, A., Gram, M., Wiuff, C., Andersen, J., Helge, J., Dela, F., 2015. Six weeks' aerobic retraining after two weeks' immobilization restores leg lean mass and aerobic capacity but does not fully rehabilitate leg strength in young and older men. J. Rehabil. Med. 47, 552–560. https://doi.org/10.2340/16501977-1961.

Vikne, H., Strøm, V., Pripp, A.H., Gjøvaag, T., 2020. Human skeletal muscle fiber type percentage and area after reduced muscle use: a systematic review and meta-analysis. Scand. J. Med. Sci. Sports 30, 1298–1317. https://doi.org/10.1111/sms.13675.

Walsh, R., Rutland, C., Thomas, R., Loughna, S., 2010. Cardiomyopathy: a systematic review of disease-causing mutations in myosin heavy chain 7 and their phenotypic manifestations. Cardiology 115, 49–60. https://doi.org/10.1159/000252808.

Ward, C.V., Walker, A., Leakey, M.G., 1999. The new hominid species Australopithecus anamensis. Evol. Anthropol. 7, 197–205.

Widrick, J.J., Stelzer, J.E., Shoepe, T.C., Garner, D.P., 2002. Functional properties of human muscle fibers after short-term resistance exercise training. Am. J. Phys. Regul. Integr. Comp. Phys. 283, R408–R416. https://doi.org/10.1152/ajpregu.00120.2002.

Williamson, D.L., Godard, M.P., Porter, D.A., Costill, D.L., Trappe, S.W., 2000. Progressive resistance training reduces myosin heavy chain coexpression in single muscle fibers from older men. J. Appl. Physiol. 88, 627–633. https://doi.org/10.1152/jappl.2000.88.2.627.

Williamson, D.L., Gallagher, P.M., Carroll, C.C., Raue, U., Trappe, S.W., 2001. Reduction in hybrid single muscle fiber proportions with resistance training in humans. J. Appl. Physiol. 91, 1955–1961. https://doi.org/10.1152/jappl.2001.91.5.1955.

Winchester, J.B., McBride, J.M., Maher, M.A., Mikat, R.P., Allen, B.K., Kline, D.E., McGuigan, M.R., 2008. Eight weeks of ballistic exercise improves power independently of changes in strength and muscle Fiber type expression. J. Strength Cond. Res. 22, 1728–1734. https://doi.org/10.1519/JSC.0b013e3181821abb.

Yamashita-Goto, K., Okuyama, R., Honda, M., Kawasaki, K., Fujita, K., Yamada, T., Nonaka, I., Ohira, Y., Yoshioka, T., 2001. Maximal and submaximal forces of slow fibers in human soleus after bed rest. J. Appl. Physiol. 91, 417–424. https://doi.org/10.1152/jappl.2001.91.1.417.

Yasuda, N., Glover, E.I., Phillips, S.M., Isfort, R.J., Tarnopolsky, M.A., 2005. Sex-based differences in skeletal muscle function and morphology with short-term limb immobilization. J. Appl. Physiol. 99, 1085–1092. https://doi.org/10.1152/japplphysiol.00247.2005.

Young, M., Richard, D., Grabowski, M., Auerbach, B.M., de Bakker, B.S., Hagoort, J., Muthuirulan, P., Kharkar, V., Kurki, H.K., Betti, L., Birkenstock, L., Lewton, K.L., Capellini, T.D., 2022. The developmental impacts of natural selection on human pelvic morphology. Sci. Adv. 8 https://doi.org/10.1126/sciadv.abq4884.

Zhong, W.W.H., Lucas, C.A., Hoh, J.F.Y., 2008. Myosin isoforms and fibre types in limb muscles of Australian marsupials: adaptations to hopping and non-hopping locomotion. J. Comp. Physiol. B. 178, 47–55. https://doi.org/10.1007/s00360-007-0198-8.

Zhu, R.X., Potts, R., Pan, Y.X., Yao, H.T., Lu, L.Q., Zhao, X., Gao, X., Chen, L.W., Gao, F., Deng, C.L., 2008. Early evidence of the genus Homo in East Asia. J. Hum. Evol. 55, 1075–1085.

Zhu, Z., Dennell, R., Huang, W., Wu, Y., Qiu, S., Yang, S., Rao, Z., Hou, Y., Xie, J., Ouyang, T., 2018. Hominin occupation of the Chinese Loess Plateau since about 2.1 million years ago. Nature. 559, 608–612.

Zihlman, A.L., Bolter, D.R., 2015. Body composition in Pan paniscus compared with Homo sapiens has implications for changes during human evolution. Proc. Natl. Acad. Sci. 112, 7466–7471. https://doi.org/10.1073/pnas.1505071112.