Evolution of the patellar sesamoid bone in mammals

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The patella is a sesamoid bone located in the major extensor tendon of the knee joint, in the hindlimb of many tetrapods. Although numerous aspects of knee morphology are ancient and conserved among most tetrapods, the evolutionary occurrence of the patella is highly variable. Among extant (crown clade) groups it is found in most birds, most lizards, the monotreme mammals and almost all placental mammals, but it is absent in most marsupial mammals as well as many reptiles. Here we integrate data from the literature and first-hand studies of fossil and recent skeletal remains to reconstruct the evolution of the mammalian patella. We infer that patellae most likely evolved between four to six times in crown group Mammalia: in monotremes, in the extinct multituberculates, in one or more stem-mammal genera outside of therian or eutherian mammals, and up to three times in therian mammals. Furthermore, a patella was lost several times in mammals, not including those with absent hindlimbs: once or more in marsupials (with some re-acquisition), and at least once in bats. Our inferences about patellar evolution in mammals are reciprocally informed by the existence of several human genetic conditions in which the patella is either absent or severely reduced. Clearly, development of the patella is under close genomic control, although its responsiveness to its mechanical environment is also important (and perhaps variable among taxa). Where a patella is present it plays an important role in hindlimb function; especially in resisting gravity by providing an enhanced lever system for the knee joint. Yet the evolutionary origins, persistence and modifications of a patella in diverse groups with widely varying habits and habitats -- from digging to running to aquatic, small or large body sizes, bipeds or quadrupeds -- remain complex and perplexing, impeding a conclusive synthesis of form, function, development and genetics across mammalian evolution. This meta-analysis takes an initial step toward such a synthesis by collating available data and elucidating areas of promising future inquiry.

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13   Running head: Patellar evolution in mammals

15   INTRODUCTION

17   This meta-analysis addresses the evolution of the ossified patella (tibial sesamoid or "kneecap"

18   bone) in mammals. We compiled voluminous literature and firsthand observational data on the

19   presence or absence of the patella in extinct and extant mammals, then conducted phylogenetic

20   analysis of patellar evolution by mapping these data onto a composite phylogeny of mammals

21   (Kielan-Jaworowska et al. 2004; Luo 2007a; Luo 2007b) using multiple phylogenetic

22   optimization methods. We used the results to address patterns of acquisition and loss of this

23   structure within Mammaliaformes. In particular, we investigated whether an ossified patella was

24   ancestrally present in all crown group Mammalia, and lost in particular groups especially

25   marsupials (Metatheria), or whether it evolved multiple times in separate crown clades.

26   Furthermore, if the patella had multiple origins, how many times was it gained or lost, and what

27   did it become if it was lost (such as a vestigial fibrocartilage versus complete loss)? These were

28   our study's key questions. We provide some broader context here first.

30   Some aspects of the morphology of the knee in tetrapods (four-legged vertebrates bearing limbs

31   with digits) are evolutionarily ancient. Tetrapods had their ancestry amongst lobe-finned

32   sarcopterygian fish, in which jointed, muscular fins transitioned into limbs. Early stages of

33   distinct bony articulations between the femur and tibia-fibula are evident in the hind fins/limbs of

34   Devonian (~370 million years ago; Mya) animals such as *Eusthenopteron*, *Panderichthys*, and

35   *Ichthyostega* (Ahlberg et al. 2005; Andrews & Westoll 1970; Boisvert 2005; Dye 1987; Dye

36   2003; Haines 1942). These fossil sarcopterygians also have subtle differences between the

37   homologous joints in the pectoral fin/forelimb and the pelvic fin/hindlimb, indicating that

38   specification of forelimb/hindlimb identity was already in place (Boisvert 2005; Daeschler et al.

39   2006; Shubin et al. 2006). Furthermore, the morphology of the forelimb and hindlimb joints

40   indicates divergent functions of these limbs, with the forelimb evolving into a more

41   "terrestrialized" capacity earlier than the hindlimb (Pierce et al. 2012). Developmental and

42   morphological modifications to the hindlimb and particularly the mid-limb joint between the

43   stylopod and zeugopod continued, until a recognizable knee articulation of almost modern,

44   derived aspect arose in tetrapods of the Carboniferous period, ~350 Mya (Dye 2003).

46   Sesamoids are best defined as "skeletal elements that develop within a continuous band of

47   regular dense connective tissue (tendon or ligament) adjacent to an articulation or joint"

48   (Vickaryous & Olson 2007). The tibial patella is a sesamoid bone that arises during development

49   within the main extensor tendon of the knee, subsequently 'dividing' it (though there remains

50   some continuity) into the quadriceps and patellar tendons (the latter is sometimes inappropriately

51   called the patellar ligament) (Bland & Ashhurst 1997; Fox et al. 2012; Pearson & Davin 1921a;

52   Tecklenburg et al. 2006; Tria & Alicea 1995; Vickaryous & Olson 2007). These tendons span

53   from the quadriceps muscle group to the tibia (Fig. 1). The patella itself tends to be incorporated

54   mainly into the vastus muscles of the quadriceps in mammals, with the tendon of M. rectus

55   femoris lying more superficial to them (Tria & Alicea 1995), with variable degrees of attachment

56   to it (Jungers et al. 1980). Hereafter, the term patella implies ossification and hindlimb

57   localization unless otherwise specified (some literature inconsistently and confusingly refers to

58   non-ossified cartilaginous structures in this location as patellae), and implicitly refers to either a

59   single patella or the left and right patellae normally present in an individual. There is an "ulnar

60   patella" in the forelimbs of some taxa (notably lizards, but also some frogs, birds and mammals

61   (Barnett & Lewis 1958; Haines 1940; Maisano 2002a; Maisano 2002b; Pearson & Davin 1921a;

62   Pearson & Davin 1921b; Romer 1976; Vanden Berge & Storer 1995; Vickaryous & Olson 2007)

63   but a full discussion of this enigmatic structure is beyond the scope of this study. Figure 2 depicts

64   the anatomical orientations used throughout this study to refer to tetrapod limbs.

65

66   The patella appears broadly similar amongst mammals possessing it, as far as has been studied,

67   although it varies greatly in size, generally in accordance with body size. It ossifies

68   endochondrally; from a cartilaginous precursor (*i.e.* anlage (Vickaryous & Olson 2007));

69   relatively late in gestation (*e.g.* sheep, goats (Harris 1937; Parmar et al. 2009)) or sometime after

70   birth (*e.g.* rabbits, rats, mice, humans (Bland & Ashhurst 1997; Clark & Stechschulte 1998;

71   Patton & Kaufman 1995; Spark & Dawson 1928; Tria & Alicea 1995; Walmsley 1940)). Very

72   recently, the development of the patella in mouse embryos was re-examined and the claim made

73   that the patella develops as a process that branches off the femur, strongly influenced by

74   mechanical loading in that region (Eyal et al. 2015). Whether this truly happens as described in

75   mice, let alone other mammals, and whether it can be accepted as unexpected support for the

76   "traction epiphysis" origin of patellar sesamoids (*e.g.* Pearson & Davin, 1921a; Pearson &

77   Davin, 1921b), remains to be determined, but the surprising results deserve attention. The

78   general form of the mature osseous patella in mammals is a hemispherical structure, with a

79   superficial surface (covered by fibrocartilage (Clark & Stechschulte 1998) and quadriceps tendon

80   fibres (Bland & Ashhurst 1997)) and a deep surface which articulates with the femur, gliding

81   along the patellar sulcus or groove in this bone. In maturity, the patella is composed of an outer

82   lamellar cortex enclosing an inner cancellous bone structure with marrow spaces, and has an

83   articular hyaline cartilage lining on the deep surface for articulation with the patellar sulcus

84   (groove) of the femur (Benjamin et al. 2006; Clark & Stechschulte 1998; Vickaryous & Olson

85   2007).

86

87   The vastus muscles' tendons (especially M. vastus intermedialis) may have a fibrocartilaginous

88   region at the approximate position of the patella, called the "suprapatella" or "patelloid" (Fig. 1).

89   the latter two terms are sometimes used synonymously, though "suprapatella" is more usual

90   when an osseous patella is also present, and "patelloid" when it is not. The suprapatella is

91   described as proximal to the patella, occasionally with a fat pad interposed between it and the

92   ossified patella (Fig. 1), whilst the patelloid is described as occupying the same approximate

93   region that a bony patella would (though absence of a patella makes this difficult to objectively

94   assess) (Bland & Ashhurst 1997; Jungers et al. 1980; Ralphs et al. 1991; Ralphs et al. 1998;

95   Ralphs et al. 1992; Reese et al. 2001; Walji & Fasana 1983). It is not clear whether the fibrous

96   patelloid in some marsupials (and perhaps some bats (Smith et al. 1995)) is homologous to the

97   suprapatella, equivalent to an evolutionarily reduced patella, or an independently occurring

98   structure.

99

100   The human patellar anlage is first visible at O'Rahilly stage 19, and chondrifies at stage 22.

101   Ossification begins 14 weeks after birth (Merida-Velasco et al. 1997a; Merida-Velasco et al.

102   1997b; Tria & Alicea 1995), but is not grossly visible until 4-6 years of age (when multiple,

103   eventually-coalescing centres of ossification can be seen radiographically (Ogden 1984)) and

104   sometimes not in its fully ossified form until adolescence. The patella is the only sesamoid bone

105   counted regularly among the major bones of the human body (Vickaryous & Olson 2007),

106   although there are other, much smaller sesamoids in the hands and feet (and in some cases even

107   the spine (Scapinelli 1963)). Other small sesamoids, such as the lunula, fabella, cyamella and

108   parafibula, also occur in the knee joint in many tetrapod species including some mammals (Fig.

109   1); these occur sporadically in humans (Pearson & Davin 1921a; Sarin et al. 1999).

110

111   The patella is covered by the thickest layer of articular cartilage in the human body (Palastanga

112   et al. 2006). The patella may thus also play a protective role for the underlying joint architecture

113   (Haines 1974), in addition to protecting the patellar tendon from excessive compressive stresses

114   (Giori et al. 1993; Sarin & Carter 2000a; Wren et al. 2000). The patellar tendon itself, to the

115   extent that its properties are known for some species (e.g. humans), is stiff and strong, able to

116   withstand about twice as much stress as typical knee joint ligaments and enduring strains (i.e.

117   lengthening) of up to 11-14% (Butler et al. 1986). Regional variations in the microscopic

118   anatomy of the human patella have also been recognised, for example in tissue thickness and

119   nerve arrangement), which may reflect load distribution (Barton et al. 2007; Eckstein et al. 1992;

120   Toumi et al. 2006; Toumi et al. 2012). There is convincing evidence from numerous species that

121   excessive loads on the patella can lead to degeneration of the articular cartilages and damage to

122   the underlying bone, leading to osteoarthritis (Aglietti & Menchetti 1995; Hargrave-Thomas et

123   al. 2013; Tria & Alicea 1995), so those regional variations of patellar structure are likely

124   important. Similarly, the tissues involved in anchoring the patellar tendon to the proximal and

125   distal surfaces of the patella as well as to the proximal tibia (tuberosity/tubercle) vary in their

126   composition and presumably are adapted, and exhibit phenotypic plasticity, to reduce the risk of

127   tendon avulsion from the bone (Evans et al. 1991).

128

129   Functions of the patella notwithstanding, there was once some enthusiasm for its outright

130   removal for treatment of certain joint problems. Patellectomy was first performed in 1860 and

131   for some time was an established treatment option for several conditions (Pailthorpe et al. 1991;

132   Sweetnam 1964). However, partial and complete patellectomies are now considered as last resort

133   salvage procedures; this is also the mainstream view of the veterinary profession (Langley-

134   Hobbs 2009). The historical lack of clarity on the pros and cons of patellectomy was summarised

135   eloquently by *The Lancet*, stating, "Sadly, most of our interventions on the patella are empirical,

136   and are supported more by the enthusiasm of proponents than by a very deep knowledge of the

137   biology or biomechanics of this unusual joint. The knee cap could do with more scientific

138   attention" (Editors 1992).

139

140   The latter complaint regarding lack of scientific attention to form, development, function and

141   clinical treatment of the patella applies even more so to non-human tetrapods. One exception is a

142   study that measured the inter- and intra-specific variability of the patellae and other bones

143   (Raymond & Prothero 2012). They found generally greater variation in patellae (and other

144   sesamoids) vs. "normal" long bones. Their inference was that this greater variability might

145   pertain to the "intermembranous" [*sic*- intramembranous] development of sesamoids, vs. an

146   endochondral location in long bones. However, the patella and most other major limb sesamoids

147   of mammals are pre-formed in cartilage and thus clearly are endochondral bones (Farnum 2007).

148   Yet the latter study reinforces that sesamoids are more variable than most other bones, in part

149   due to their mechanical environment, in part due to their embedding in soft tissues (themselves

150   quite variable) such as tendons and ligaments (Bland & Ashhurst 1997; Clark & Stechschulte

151   1998), and perhaps due to other factors not yet understood. This uncertainty about the causes of

152   variability in the patella may also relate to incomplete understanding of its mechanical loading

153   and function *in vivo*, as follows.

154

155   Where a patella is present in its typical form, its primary function is to modify the mechanical

156   advantage (ratio of output force to muscle force) at the knee joint, by increasing the moment arm

157   of the tendon in which it is embedded and thereby altering the amount of force needed from the

158   quadriceps muscles in order to generate a particular moment (torque; rotational force) about the

159   knee joint (Alexander & Dimery 1985; Fox et al. 2012; Haines 1974; Heegaard et al. 1995;

160   Herzmark 1938; Howale & Patel 2013; Tecklenburg et al. 2006). In humans, the patella causes

161   the quadriceps muscle group's moment arm about the knee to increase as the knee becomes more

162   extended, causing the amount of quadriceps muscle force required per unit of patellar tendon

163   force (i.e. at the insertion onto the tibial tubercle) to vary significantly across knee joint flexion-

164   extension (Aglietti & Menchetti 1995; Fellows et al. 2005). By articulating with the femur, the

165   patella also transmits some forces of the quadriceps muscle group directly onto the femur (the

166   patellofemoral joint reaction force); forces which can reach a maximum of 20-25 times body

167   weight (Aglietti & Menchetti 1995).

168

169   The mobility of the patella is an important aspect of its function. While, in humans, the patella

170   mostly flexes and extends relative to the femur as the knee is flexed and extended, it also

171   translates and pitches (tilts) and rolls (Aglietti & Menchetti 1995; Fellows et al. 2005), leading to

172   variable contact between the patella and femur that is reflected in the angled facets of the human

173   patella (Lovejoy 2007). In contrast to the situation in humans (as well as in early hominins such

174   as *Australopithecus*), in chimpanzees and presumably many other primates (as well as other taxa

175   such as sheep (Bertollo et al. 2012; Bertollo et al. 2013)), the patella remains in tight articulation

176   with the femur throughout the knee's range of motion, reducing patellofemoral stresses

177   especially when the knee is strongly flexed, as it habitually is in those non-human primates

178   (Lovejoy 2007). Other primates show varying degrees of specialization of patellar morphology

179   that alter the moment arm of the patellar tendon, with great apes apparently having a patella most

180   specialized for widely varying knee joint postures (Pina et al. 2014). It has been claimed that in

181   hominids and ursids (bears) alike, there is an association between plantigrady (flat-footedness),

182   increased knee range of motion, and patellar mechanics (Lovejoy 2007); this is an interesting

183   hypothesis that deserves further consideration.

184

185   In the elbow of humans and other mammals, there is an extension of the ulnar bone called the

186   olecranon (process), which serves a lever-like function analogous to that of the patella

187   (Herzmark 1938). However, a mobile sesamoid bone like the patella has a more flexible

188   ("dynamic gearing") function in improving mechanical advantage compared with an immobile

189   retroarticular process like the olecranon (Alexander & Dimery 1985). There tends to be an

190   inverse relationship between mechanical advantage and speed of joint motion (Hildebrand 1998),

191   thus a high mechanical advantage is not necessarily useful in all cases, which may in part explain

192   the variable occurrence, size and shape of the patella in animals with different lifestyles and

193   modes of locomotion. Biomechanical studies of primates (Lovejoy 2007; Pina et al. 2014) and

194   domesticated mammalian species (*e.g.* dogs (Griffith et al. 2007; Kaiser et al. 2001), sheep

195   (Bertollo et al. 2012; Bertollo et al. 2013), horses (Schuurman et al. 2003; Wentink 1978)) have

196   contributed some knowledge of how the patella functions in these groups, or in individual

197   species, but a general "functional synthesis" for the patella is still lacking.

198

199   De Vriese performed pioneering comparative analyses and attempted syntheses of patellar size

200   and morphology in comparison to other leg bones, between species and among multiple

201   individuals in some species (De Vriese 1909). No clear correlations were observed between the

202   size of the patella and other major hindlimb bones (femur, tibia, and fibula). A correlation was

203   claimed between the sizes of the patella and the talus (or intermedium) in the ankle, although no

204   clear, plausible mechanistic/functional justification was suggested and no statistical analyses

205   were performed. Somewhat oddly, no relationship was evident between the size and shape of the

206   patella and the femoral patellar groove (De Vriese 1909). The more restricted but quantitative

207   analysis of Valois (Valois 1917) focused mainly on primates and challenged many of De

208   Vriese's claims that mechanical or physiological explanations of patellar morphology have "no

209   scientific merit". Haxton also criticised De Vriese for focusing on relative length of bones; his

210   own "patellar index" based on relative width found no correlation with animal speed or size, but

211   he inferred that the patella confers functional advantages in knee extension (Haxton 1944). There

212   has been little examination of these questions in a modern comparative, rigorously statistical

213   context since these studies. A notable exception is a study of the distal femur and patellar groove

214   in bovid mammals, indicating increased mechanical advantage of the knee in larger species

215   (Kappelman 1988).

216

217   The occurrence of an ossified patella in the knee joint is not universal among tetrapods (Fig. 3).

218   It is absent in extinct early Tetrapoda and crown clade Lissamphibia (Dye 1987; Haines 1942;

219   Herzmark 1938; Vickaryous & Olson 2007), all non-avian dinosaurs, Crocodylia, and Testudines

220   (turtles), and all other extinct tetrapods. In contrast, an ossified patella is present in many or most

221   Squamata (lizards and kin) with limbs (Camp 1923; Carrano 2000; De Vriese 1909; Dye 1987;

222   Dye 2003; Gauthier et al. 2012; Haines 1940; Haines 1942; Hutchinson 2002; Hutchinson 2004;

223   Jerez & Tarazona 2009; Maisano 2002a; Regnault et al. 2016; Vickaryous & Olson 2007).

224   Patellar status (used throughout our study to refer to presence/absence) is unknown for the

225   (mostly extinct) Rhynchocephalia (sister group to Squamata), although a patella is at least

226   sometimes present in the tuatara *Sphenodon* – the only extant rhynchocephalian (Regnault et al.

227   2016). An apparent sesamoid bone was noted in the knee joint region of a specimen of

228   *Macrocnemus*, a mid-Triassic (~235 Mya) reptile, which may be the earliest identified

229   occurrence of a patella in any animal group (Rieppel 1989), although this structure may have

230 been a different sesamoid bone or ossicle. There have been anecdotal accounts of

231 fibrocartilaginous or "fibrovesicular" patelloids in some reptiles such as turtles and crocodiles

232 (Haines 1940; Haines 1942; Pearson & Davin 1921a; Pearson & Davin 1921b)), but these are not

233 well-explored. Thus, although such fibrous tissues seem to be excellent candidates for

234 intermediate character states between "absence of ossified patella (normal extensor tendon)" and

235 "presence of ossified patella", empirical grounding for this transformational sequence within

236 Sauropsida is weak.

237

238 No patella has been observed in early, stem-group birds throughout the Jurassic and Cretaceous

239 periods, except in the well-documented Cretaceous Hesperornithes, diving birds with vestigial

240 wings and an extremely large and unusually shaped patella, resembling that in some extant

241 diving birds (Lucas 1903; Marsh 1875; Martin 1984; Martin & Tate 1976; Shufeldt 1884;

242 Thompson 1890). A patella is found in some Cenozoic fossil bird specimens, most notably

243 archaic penguins, and commonly among many crown clade birds (Dye 1987; Dye 2003;

244 Hutchinson 2001; Hutchinson 2002; Ksepka et al. 2012; Shufeldt 1884; Vickaryous & Olson

245 2007; Walsh & Suarez 2006). A recent study by Regnault *et al.* inferred that a patella was

246 probably ancestrally present in the common ancestor of Hesperornithes and living birds over 70

247 Mya (Regnault et al. 2014). However, the patella was lost (and in some cases replaced by fatty

248 cartilaginous tissue) in some large flightless birds such as emus, cassowaries and the extinct moa,

249 yet unexpectedly is present as a double ossification in the knee joints of ostriches (Chadwick et

250 al. 2014).

251

252 A patella is generally found in two of the three crown groups of Mammalia: Eutheria (Fig. 3) and

253 Monotremata (see Fig. 4A-D), but not in most Metatheria (see Fig. 4E, F) (Dye 1987; Dye 2003;

254 Vickaryous & Olson 2007). This raises the question whether this patella represents independent,

255 convergent evolutionary origins in the Eutheria and Monotremata, or an ancestral origin for all

256 three groups, with loss of the ossified patella amongst most Metatheria. To address this question,

257 we conducted phylogenetic character mapping with Mesquite software (Maddison & Maddison

258 2014) that reconstructed patellar evolution in Mammalia. Using likelihood methods, we also

259 traced the most likely pattern of evolution over existing phylogenies, and considered alternate

260 proposed topologies to test how they affected our reconstructions. Based on the predicted

261   evolutionary patterns and individual morphologies, we propose suggestions as to the lifestyle of

262   particular taxa, and consider where general correlations between lifestyle and patellar

263   presence/absence might exist (or not).

264

265   Mottershead called the patella "that prince among sesamoids" but questioned whether it is "not

266   typical of its kind" (Mottershead 1988). But is there even a "typical" patella? Our synthesis of

267   key data from morphology and function to phylogeny, development and genetics allows us to

268   evaluate just how "typical" any patella is, even for a mammalian patella.

269

270

271   MATERIALS AND METHODS

272

273   We surveyed the literature and additional specimens (see Supplementary Table S1) and coded

274   the patella as absent (score = 0), fibrocartilaginous (i.e., "patelloid"; score = 1), or ossified (score

275   = 2) for each taxon in our analysis, with "?" denoting an ambiguous character coding. We used

276   two phylogenetic optimization methods in Mesquite software to reconstruct possible

277   evolutionary polarity of the patella in the clade Mammaliamorpha (with a focus on

278   Mammaliaformes), as follows. First, for broad reconstruction across Tetrapoda, we used a

279   phylogeny based on Shedlock and Edwards (2009) and Gauthier et al. (1988), with average

280   branch lengths they derived from several studies. Some aspects of the phylogeny remain

281   controversial, such as the position of Testudines (turtles; Hedges 2012). Reconstruction was

282   performed using Mesquite's parsimony algorithm and unordered character states and results are

283   illustrated in Figure 3. As this analysis only involved major clades and not any stem lineages, it

284   was intended as purely illustrative of general patterns and the current state of knowledge, given

285   that patellar evolution across Tetrapoda had not been analyzed phylogenetically before.

286   We adopted composite phylogenetic trees for our study taxa (Archibald 1998; Beck 2012; Bi et

287   al. 2014; Cardillo et al. 2004; Forasiepi et al. 2006; Gatesy et al. 2013; Goloboff et al. 2009;

288   Kielan-Jaworowska et al. 2004; Luo et al. 2003; Luo 2007a; Luo et al. 2002; Luo 2007b; May-

289   Collado et al. 2015; Meredith et al. 2009; Meredith et al. 2011; Mitchell et al. 2014; O'Leary et

290   al. 2013; O'Leary & Gatesy 2008; dos Reis et al. 2012; Rose 2006; Sánchez-Villagra et al. 2007;

291   Song et al. 2012; Spaulding et al. 2009; Springer et al. 2003; Springer et al. 2007; Springer et al.

292 2009; Thewissen 1990; Thewissen et al. 2007; Wible et al. 2007; Zack et al. 2005). As defined

293 by several authors, the clade Mammaliaformes includes crown group Mammalia plus closely

294 related extinct stem-mammals such as the iconic *Morganucodon* and the more recently

295 discovered *Sinoconodon*, and is characterised by diagnostic features involving the teeth, jaw and

296 inner ear (Kielan-Jaworowska et al. 2004; Rose 2006). Extant mammals (crown group

297 Mammalia) include three main clades: Placentalia, Marsupialia and Monotremata. Placentalia lie

298 within the Eutheria; Marsupialia lie within the Metatheria, and Monotremata lie within the

299 Australosphenida, all of which diverged during the Mesozoic, pre-dating the K-Pg extinction

300 event ~66 Mya.

301

302 We reconstructed patellar evolution amongst Mesozoic Mammaliaformes, including key fossils

303 with hindlimb material. The main topology used was based on Bi et al. (2014), congruent with

304 other sources (e.g. Rose 2006; Luo 2007b; O'Leary et al. 2013). We used parsimony

305 optimisation, with both unordered and ordered states, and maximum likelihood optimisation. We

306 also reconstructed ancestral states over an alternative topology with †*Eomaia* placed on the

307 therian stem (after O'Leary et al., 2013) using parsimony optimisation and unordered states.

308 Results are illustrated in Figures 5 and S4.

309

310 To examine these evolutionary patterns in more detail, we performed further reconstructions of

311 ancestral states within both Metatheria and Eutheria. For Metatheria, we used topology and

312 approximate divergence times based on (Cardillo et al. 2004, Forasiepi et al., 2006, Forasiepi,

313 2006, Sánchez-Villagra et al., 2007, Luo et al., 2003, Meredith et al., 2009, Springer et al., 2009,

314 Beck, 2012, Mitchell et al., 2014), and ran reconstructions with parsimony optimisation for

315 unordered and ordered states and maximum likelihood. An alternative topology with

316 Microbiotheriidae nested slightly further within Marsupialia (after May-Collado et al., 2015) was

317 also explored using parsimony optimisation and unordered character states. Results for

318 Metatheria are illustrated in Figures 6 and S5.

319

320 For Eutheria, our topology is based on O'Leary et al. (2013) with minor modifications and

321 reconstructed with parsimony optimisation and unordered states. Results are illustrated in Figure

322 7. For the four major crown placental groups, *per* O'Leary *et al.* (2013), the first divergence was

323   Xenarthra, followed by Afrotheria, and finally the branching of Boreoeutheria into

324   Laurasiatheria and Euarchontaglires. Other studies have suggested Afrotheria as the first group

325   to diverge, followed either by Xenarthra (Springer et al. 2003; Springer et al. 2007) or

326   Laurasiatheria (Goloboff et al. 2009) or alternatively a basal branching between Boreoeutheria

327   and Atlantogenata (comprised of Afrotheria+Xenarthra; dos Reis et al. 2012; Meredith et al.

328   2011; Song et al. 2012). These alternative topologies did not change our fundamental results.

329   Divergence order within Laurasiatheria was (see Figure 7 for subgroupings): Eulipotyphla

330   (called Lipotyphla by O'Leary *et al.* (2013); Pholidota+Palaenodonta;

331   Carnivora+Miacidae+Creodonta (Spaulding et al. 2009); Chiroptera; Condylarthra (see below);

332   Mesonychia; Perissodactyla; Cetartiodactyla. Within Euarchontoglires, the order of divergence

333   was (see figure for subgroupings): (Scandentia+Dermoptera)+Primates; (Glires+Rodentia).

334   Regarding individual species, *Leptictidium* was placed with Macroscelidea based on its relation

335   to the mapped *Leptictis*; *Carodnia* was placed within Afrotheria; Mesonychia (*Mesonyx et al.*)

336   were placed between Euungulata (Perissodactyla and Cerartiodactyla) and Chiroptera;

337   *Protungulatum* was placed between Mesonychia and Chiroptera. Among species broadly

338   described as "condylarths", *Phenacodus* (albeit a likely perissodactyl), *Hyopsodus, Tetraclaenus*

339   and *Copecion* were grouped together (Thewissen 1990); *Mioclaenus* was grouped with

340   *Hyopsodus* (Zack et al. 2005); *Meniscotherium* was grouped with *Phenacodus* (Wible et al.

341   2007); *Arctocyon* and *Chriacus* were grouped together and with other condylarths (Archibald

342   1998). O'Leary *et al.* (2013) placed *Notharctus* just outside Primates, but noted that this was

343   possibly incorrect as they did not include other notharctids, therefore Notharctidae were here

344   placed within Primates. *Plesiadapis* was placed as the sister taxon to Primates. O'Leary *et al.*

345   (2013) placed *Rodhocetus* basal to Cetartiodactyla, but *Artiocetus* and *Basilosaurus* as basal

346   Cetacea. For consistency with other studies including additional archaic Cetacea (O'Leary &

347   Gatesy 2008; Thewissen et al. 2007), *Rodhocetus* was retained within the stem cetaceans (Gatesy

348   et al. 2013). Additional archaic Perissodactyla and Artiodactyla not included in O'Leary *et al.*

349   (2013) were here grouped with included group members. Additional stem placentals, including

350   Taeniodonta, Pantodonta, Dinocerata and selected individual species, were not included in the

351   study of O'Leary *et al.* (2013) and here were placed equally as stem groups. O'Leary *et al.*

352   (2013) placed *Protolipterna* basal to Euungulata, but do not incorporate other archaic South

353   American ungulates, whereas this study did not include Litopterna. Pending more analysis,

354   Notoungulata were here placed as stem placentals. Tillodontia, another stem placental group,

355   was not included in this study due to lack of identified specimens with sufficient hindlimb

356   material.

357

358   Our analysis involved numerous challenges and caveats. Many anatomical studies of extant or

359   extinct species omit any mention of the patella, leaving its provenance in these taxa as uncertain.

360   Interpretation of patellar status is especially challenging in fossils due to the rarity of finds with

361   extensive, articulated postcranial material, the potential occurrence of other small non-patellar

362   bones in the knee joint, and the uncertain age of the animal at time of death versus the

363   developmental timing of sesamoid ossification (usually unknown; often relatively late in

364   ontogeny). For the present analysis, statements in the primary literature regarding patellar status

365   were generally accepted at face value except when superseded by more recent observations.

366   From some publications with high quality photographs, patellar status was tentatively interpreted

367   even if not discussed in the original text. In some cases, patellar status was confirmed by direct

368   observation (e.g. Fig. 4; Figs. S1-S3; Table S1). Drawings found in secondary citations were

369   mostly not been taken as definitive evidence, as we noticed examples of discrepancies between

370   primary references and such drawings found in review articles or even textbooks, which may

371   simply assume patellar status in mammals. Also, many mammalian groups are found over long

372   temporal and geological spans, thus we were cautious about using the presence of a patella in

373   one or a few individual extant or fossil specimens to infer presence throughout the group,

374   although in some cases there was clearly enough conservatism within a clade to score it for all

375   members.

376

377   An important knee structure related to the patella is the femoral patellar or intercondylar sulcus

378   (groove) (Norell & Clarke 2001; Polly 2007). This sulcus is anatomically associated with a true

379   patella (Figs. 1,4) in terms of its direct role in guiding the patellar sesamoid and tendon's path of

380   movement during leg flexion/extension, and in mediolaterally confining the patellar tendon,

381   which may enhance osteogenic stresses favouring the formation of a patella (Sarin & Carter

382   2000b; Wren et al. 2000). In the absence of an observed patella in fossil specimens, this sulcus at

383   the distal end of the femur is sometimes treated as evidence of a patella even in the absence of

384   the observed bone itself. We deemed this conclusion to be unwarranted. For example, the

385 evolution of a patellar sulcus in early pygostylian birds substantially predated the evolution of an
386 ossified patella in later ornithurine birds; moreover the sulcus was retained in some avian taxa
387 that lost the patella (Clarke & Norell 2002; Hutchinson 2002; Livezey & Zusi 2006; Regnault et
388 al. 2014). In contrast, a prominent sulcus is absent in many Squamata despite the presence of a
389 patella (S.R. and J.R.H., pers. obs.). Together these observations indicate that these two
390 anatomical features are not obligatorily coupled, so reliance on the observed presence of an
391 ossified patella in fossil specimens was warranted. Nonetheless, at least among mammals the
392 complete absence of a femoral patellar sulcus might be indicative of the absence of an ossified
393 patella (Chester et al. 2012).
394
395
396 RESULTS AND DISCUSSION
397
398 Our overall evolutionary reconstruction of the patella for Mesozoic mammals is shown in Fig. 5,
399 for Metatheria/Marsupialia in Fig. 6, and for Cenozoic Eutheria/Placentalia in Fig. 7, with details
400 for specific taxa in Table S1 and alternative phylogenetic analyses in Figs. S4 and S5. Here we
401 sequentially summarize and discuss our findings for five subgroups of Mammaliamorpha
402 (especially Mammaliaformes): (1) Mesozoic pre-therians and stem-therians; (2) Mesozoic
403 Metatheria and Eutheria; (3) Cenozoic Monotremata; (4) Cenozoic Metatheria, and (5) Cenozoic
404 Eutheria. We then conclude with a general synthesis of our study's insights (as well as
405 uncertainties) and a consideration of how available and emerging data on developmental genetics
406 of the patella might help shed light on the "evo-devo" of the patella, augmenting the
407 phylogenetic and anatomical insights that this study focuses on.
408
409 *1. Mesozoic pre-therian and stem-therian mammals*
410 The earliest mammals as widely construed include *Sinoconodon*, the Morganucodonta and
411 Docodonta. These were mostly small, probably insectivorous animals, that appear to have lacked
412 a patella, although it is unclear whether the known specimens contain sufficient postcranial
413 material or are from verified adults, to allow for definitive conclusions. The absence of a clear
414 patella in two stunningly preserved docodonts (the scansorial [climbing-adapted] *Agilodocodon*
415 and fossorial [digging-adapted] *Docofossor*) lends credence to the conclusion that it was

416   generally absent in early mammalians (Luo et al. 2015b; Meng et al. 2015). There is

417   convincingly strong evidence of absence of a patella in earlier pre-mammals in lineages dating

418   from the divergence of Synapsida and Sauropsida/Reptilia (~320 Mya), including the ancestral

419   "pelycosaurs", therapsids and cynodonts (Kemp 2005).

420

421   *Australosphenida,* the clade containing and thus ancestral to extant Monotremata, diverged from

422   other mammals extremely early, possibly in the mid-Jurassic (Kielan-Jaworowska et al. 2004).

423   There is little postcranial material for any extinct members of this lineage however, and no

424   hindlimbs (Kemp 2005). The patella in crown clade monotremes will be discussed below.

425

426   *Fruitafossor,* from the late Jurassic (150 Mya), diverged after the Australosphenida (Luo &

427   Wible 2005). Its relationship to other early mammals is complicated by its mixture of characters

428   in the molar teeth, middle ear and elsewhere. *Fruitafossor* is described as lacking a patella, and it

429   is proposed to have had a fossorial lifestyle.

430

431   The Eutriconodonta were found abundantly across the world from the middle Jurassic to early

432   Cretaceous periods (Kielan-Jaworowska et al. 2004). Among eutriconodonts, a poorly developed

433   distal femoral patellar groove is found but a patella is absent.

434

435   The Allotheria were an extremely successful and widely dispersed group of mammals, among

436   which the best understood are the multituberculates (Kielan-Jaworowska et al. 2004; Wilson et

437   al. 2012). Generally Allotheria are found from the late Triassic to the Eocene periods, thus this

438   group spans much of the heyday of the (classic) dinosaurs, and survived the K-Pg extinction

439   (Kielan-Jaworowska et al. 2004). Multituberculates were predominantly small animals, either

440   herbivorous or omnivorous (Kielan-Jaworowska et al. 2004). A patella is noted for the nearly

441   complete multituberculate *Ptilodus*, a proposed scansorial animal from the early Cenozoic. A

442   patella is also present in the Cretaceous multituberculate *Chulsanbaatar*. It is unclear whether a

443   patella is typical of all members of the multituberculate group and is under-reported due to lack

444   of hindlimb material for most group members, or whether it occurs only among selected species,

445   although the former seems more plausible. A patella is not reported, however, for the early

446   Jurassic basal *Rugosodon*, a proposed multituberculate specimen with one relatively intact knee

447   joint (Yuan et al. 2013), so it is conceivable that an ossified patella evolved later within the

448   Allotheria (Fig. 5).

449

450   Specimens of the diverse group "Haramiyida" are mostly restricted to cranial material, and the

451   relationship of this ancient group to other Allotheria and Mammaliaformes has been

452   controversial (Butler 2000; Kielan-Jaworowska et al. 2004; Rose 2006). However, several

453   recently described more complete haramiyid specimens from the Jurassic with at least one

454   preserved knee joint lack a patella (Bi et al. 2014; Zheng et al. 2013; Zhou et al. 2013). These

455   new specimens have been interpreted to support an Allotheria clade including a paraphyletic

456   "Haramiyida" (but a valid clade Euharamiyida including many "haramiyid" taxa) and

457   Multituberculata (Fig. 5), although new analyses of a key specimen of *Haramiyavia* concluded

458   that the haramiyids and multituberculates are not closely related (Luo et al. 2015a). The inclusion

459   of the "Euharamiyida" in Allotheria pushes the divergence date of the group significantly earlier

460   into the late Triassic, whereas multituberculates themselves appear only in the middle to late

461   Jurassic. Final resolution of this controversy will undoubtedly require additional fossil material.

462

463   Symmetrodonta were a group of diverse, small mammals widely distributed in time from the late

464   Triassic to the late Cretaceous (Kielan-Jaworowska et al. 2004). In the subgroup of

465   spalacotheroids, a patella is reported for one fairly complete specimen (*Zhangheotherium*) but

466   not for another (*Akidolestes*) (Chen & Luo 2012; Luo & Ji 2005) (these two specimens are coded

467   oppositely in character matrices in some subsequent publications, probably in error (Bi et al.

468   2014; Zhou et al. 2013)); a patella was absent in *Maotherium*.

469

470   Eupantotheria was a diverse group found commonly from the mid-Jurassic to the early

471   Cretaceous (Kielan-Jaworowska et al. 2004). The patella is reported as absent in both an early

472   European specimen (*Henkelotherium*, late Jurassic) and a later South American specimen

473   (*Vincelestes*, early Cretaceous) (Fig. 5). Of the large group of dryolestid Eupantotheria, which

474   possibly survived past the K-Pg boundary, patellar status is unknown.

475

476   The tribotherians were the earliest-diverging group to share key molar features with the therians.

477   However, no postcranial specimens have been reported; thus nothing is known of their patellar

478   morphology (Kielan-Jaworowska et al. 2004).

479

480   The single specimen of *Juramaia* from the Jurassic (~160 Mya) unfortunately lacks hindlimb

481   material; therefore its patellar status is unknown. Based on its forelimb, *Juramaia* is proposed to

482   have been scansorial or possibly arboreal (Luo et al. 2011). The later specimen of *Eomaia* from

483   the early Cretaceous includes all limb elements, and is described with a patella (Ji et al. 2002).

484   Based on limb and foot features, *Eomaia* was probably scansorial or arboreal. In the original

485   publication, *Eomaia* was described as the earliest eutherian mammal (Fig. 5), however a more

486   recent and much more extensive analysis confidently placed *Eomaia* prior to the

487   eutherian/metatherian divergence (O'Leary et al. 2013) and thus at least as a stem member of the

488   clade Theria (see Figure S4). *Eomaia* (and presumably *Juramaia*) postdate the divergence of the

489   Symmetrodonta, but their positions relative to the Eupantotheria remain to be determined, as

490   does any close relationship between these two key taxa. Lacking a better alternative, here we

491   refer to these taxa as "Theria", and in Fig. 5 vs. Fig. S4, consider the consequences of *Eomaia*'s

492   phylogenetic position on our conclusions.

493

494   In surveying the available data mapped onto our composite phylogeny (Figs. 5, S4), it becomes

495   evident that an ossified patella evolved multiple times (at least four) along the mammalian stem

496   lineages during the Mesozoic era, whether using parsimony or maximum likelihood optimisation

497   methods: at some highly uncertain time in the long mammalian lineage that led to Monotremata,

498   in multituberculates/Allotheria, in *Zhangheotherium* or a direct ancestor, and likely twice (or

499   between one to three times, depending on the placement of *Eomaia*; See Figs. 5 and S4) in the

500   clade containing *Eomaia* and Theria (Metatheria and Eutheria). This remains the same if the

501   Euharamiyida are not included with multituberculates but pre-dated crown Mammalia, as

502   suggested by some recent studies (e.g. Luo et al. 2015a).

503

504   *2. Mesozoic Metatheria and Eutheria*

505   The two major extant mammalian groups, the Metatheria and Eutheria (together forming the

506   clade Theria), diverged as early as the Jurassic (Fig. 5). The earliest fossil defined as

507   metatherian, *Sinodelphys*, dates from the early Cretaceous of China (125 Mya, approximately

508   contemporary to *Eomaia*), and lacks a patella (Luo et al. 2003). A patella also seems absent in

509   the less complete Cretaceous metatherian *Asiatherium* (Szalay & Trofimov 1996).

510

511   The earliest occurrences of the patella in definitive eutherians (Figs. 5,7) are in the late

512   Cretaceous *Ukhaatherium* (Horovitz 2003), a relatively unspecialized form, and in

513   *Zalambdalestes* (Wible et al. 2005), a more specialized taxon sometimes described as resembling

514   later lagomorphs (Rose 2006). Patellar status at the crown group node for Theria (plus *Eomaia*)

515   remains ambiguous (Figs. 5,6,S4), as we consider below.

516

517   *3. Cenozoic Monotremata*

518   The origins of the Monotremata (egg-laying mammals) are poorly understood. They are

519   considered extant members of the clade Australosphenida (the alternative term Prototheria has

520   been superseded), and hence with early roots in the Mesozoic. Molecular studies based on the

521   sequenced genome of the platypus corroborate the long held interpretation that the monotremes

522   diverged prior to the metatherian/eutherian split, consistent with proposed fossil-based

523   phylogenies (Warren et al. 2008). Unfortunately, there are almost no reported hindlimb

524   specimens of any extinct monotreme (including probable early monotreme fossils found in South

525   America; (Musser 2003)), with the exception of the Pleistocene *Zaglossus* (echidna) from

526   Australia and New Guinea (which may be the same as the extant species of that name).

527   Unfortunately, although fossil *Zaglossus* hindlimb elements exist, including an articulated knee,

528   neither presence nor absence of the patella has been reported (Murray 1984). The extant

529   monotremes, the platypus (*Ornithorhynchus anatinus*) and the echidnas (Tachyglossidae, two

530   genera *Zaglossus* and *Tachyglossus*; four known species) all have substantial patellae (see Fig.

531   4A, B, C, D) (Herzmark 1938; Rowe 1988). It is unclear when the two extant monotreme genera

532   diverged although a date early in the Cretaceous has been proposed (Rowe et al. 2008), and it is

533   impossible for now to date the appearance of the patella in the monotreme lineage. Regardless,

534   an ossified patella is homologous for this crown clade (Fig. 5), and alternative phylogenetic

535   topologies do not change the general pattern of patellar evolution (Fig. S4).

536

537   *4. Cenozoic Metatheria*

538   All extant Metatheria are within the subgroup of Marsupialia, however non-marsupials did exist

539   earlier during the Cenozoic. As documented in the pioneering study of sesamoids in Marsupialia

540   by Reese et al. (2001), the patella is absent in the great majority of extant marsupial species, both

541   from Australia and the Americas (Flores 2009; Herzmark 1938; Holladay et al. 1990; Reese et al.

542   2001; Rose 2006; Rowe 1988), including the sole surviving North American marsupial, the

543   North American opossum (*Didelphis virginiana,* see Fig. 4E, F showing tendon lacking a true

544   patella. Many marsupials have other sesamoids in the knee region (e.g. the parafibula, lateral

545   sesamoid, or "sesamoid bone of Vesalli"), as well as a fibrocartilaginous "patelloid", which may

546   to some degree serve the mechanical function of a bony patella (Reese et al. 2001). However, the

547   mechanics of a fibrous or bony patella remain essentially unstudied (to our knowledge) in non-

548   placental mammals, so this is simply speculation. Studies have claimed some association

549   between reduction of the patella in many marsupials and locomotor style or ecology (Holladay et

550   al. 1990; Reese et al. 2001), but these deserve testing with more detailed sampling across

551   phylogeny and ontogeny.

552

553   Nonetheless, a true, ossified patella is found in a small number of extant marsupial species

554   among otherwise divergent clades, both from Australia: at least several Peramelidae or

555   bandicoots, and the two marsupial mole species of *Notoryctes*); and from South America:

556   *Tarsipes*, an opossum; and several, and possibly all, Caenolestidae or shrew opossums (see Fig.

557   6: note collapse of several large clades in terms of total number of species, in which no species

558   have been shown to possess a patella; Table S1).

559

560   Possibly uniquely among crown clade marsupials, bandicoots also possess a chorioallantois

561   fused to the uterine epithelium (i.e. a true placenta) (Freyer et al. 2003; Padykula & Taylor

562   1976), which combined with a patella led to the initial suggestion that they might actually be

563   eutherians (Reese et al. 2001). However, more recent molecular and fossil-based phylogenetic

564   studies provide no support for that hypothesis of eutherian bandicoots (Asher et al. 2004;

565   Meredith et al. 2008b; Sanchez-Villagra et al. 2007; Westerman et al. 2012). Bandicoots clearly

566   are metatherians, and their chorioallantois is thus a convergently evolved trait rather than

567   plesiomorphic. It remains to be determined whether a patella is present in all or only some

568   bandicoots, as so far it is only reported in the Peramelinae of dry or temperature forests of

569   Australia, not yet in the Peroryctinae of tropical rainforests of New Guinea, or the more distantly

570   related bilbies (Groves & Flannery 1990; Meredith et al. 2008a; Westerman et al. 2012).

571   Similarly, a comprehensive study of the Caenolestidae remains to be performed, much as a more

572   thorough study of the major marsupial clade Diprotodontia (wombats, kangaroos and kin) is

573   needed.

574

575   Not surprisingly given the absence of a patella in most extant marsupials, the patella is absent in

576   the early Cenozoic Metatheria *Pucadelphys, Mayulestes,* and the later *Herpetotherium.*

577   Unexpectedly, a patella is reliably reported in the Borhyaenoidea, an unusual group of dog-like

578   carnivorous South American marsupials found from the Paleocene through the Miocene (Argot

579   2002; Argot 2003a; Argot 2003b; Argot 2003c; Argot 2004; Argot & Babot 2011; de Muizon et

580   al. 1997). Patellar status in some members of Borhyaenoidea (*e.g. Borhyaena* itself and *Lycopsis*

581   *(Argot 2004)*), and in the more inclusive group Sparassodonta, is uncertain due to the incomplete

582   state of specimens (C. Argot, pers. comm.) Szalay and Sargis (2001) noted other enigmatic

583   fossils from the Palaeocene of Brazil that they assigned to Metatheria, but the phylogenetic

584   relationships of those fragmentary remains are unclear and no patellae were shown (Szalay &

585   Sargis 2001). However, no patella is reported in extant or recent carnivorous marsupials such as

586   *Thylacinus*, thus it is not obligatorily correlated with that particular ecological adaptation.

587

588   Two related, pernicious problems remain for interpreting the evolution of the patella in

589   Metatheria that may have ramifications for all of Mammalia/Mammaliaformes. First, Szalay and

590   Sargis (2001:pp.164-5) reported the presence of an ossified patella in older individuals of

591   *Didelphis virginiana* in their study of an ontogenetic series from this species. They stated (p.165)

592   "In older individuals there is occasionally an elongated and small sesamoid ossification within

593   the tendon of the quadriceps femoris where it crosses the knee joint when the knee is flexed."

594   However, this observation was not documented with illustrations or photographs (especially

595   tissue histology or x-rays) and hence remains simply tantalizing. Similarly, Owen (Owen 1866)

596   commented that some marsupials had no ossifications in their patellar tendon but others had

597   "only a few irregular specks of ossification" and a "distinct but small bony patella in the

598   *Macropus Bennettii*." In contrast, Reese et al. (2001) and Holladay et al. (1990) respectively

599   sampled 61 specimens (~39 adults) from 30 species of marsupials and 3 macropodid specimens

600   (of unknown maturity), documenting no ossified patellae except as noted in bandicoots

601   (Holladay et al. 1990; Reese et al. 2001). It remains possible that patellar ossification occurs

602   variably in older individuals among Metatheria, which would help explain its patchy description

603   in known taxa.

604

605   If the latter situation is the case (i.e., the literature is unclear about patellar ossification in

606   marsupials because they have more inherent variability), then it relates to a second problem, a

607   cladistic one of character coding and transformational homology (*sensu* (Brower & Schawaroch

608   1996; Pinna 1991). Should character states of the patella in metatherians, or even all mammals

609   and their kin, be coded as an ordered transformational series such as absent (0),

610   fibrocartilaginous (1) or ossified (2), or as an unordered series (i.e. should evolutionary steps be

611   required to go from 0-1-2 as 2 steps, or unordered allowing 0-2 transformations as 1 step)? We

612   chose the unordered character option by default for all crown group mammals, but the legends

613   for Figs. 5-7 explain how an ordered option changes (or does not change) our results. An

614   endochondral ossification of the patella is certain, but a fibrocartilaginous or otherwise soft tissue

615   composition of the patella (coded as state 1) is not unambiguously the necessary (i.e. ordered)

616   precursor character state to state 2 (ossified patella in adults). The solution to both of these

617   problems lies in more developmental data for the patella in diverse mammalian species, in

618   addition to more scrutiny of the adult morphology in extant and fossil Mammalia (especially

619   Metatheria).

620

621   As noted briefly in the Introduction, many marsupials have a primarily fibrocartilaginous

622   patelloid in place of an ossified patella and some other mammals may have a "suprapatella". The

623   developmental and evolutionary relationships of these structures remain somewhat unclear,

624   particularly as some marsupials with an ossified patella (*e.g.* bandicoots) also possess a patelloid

625   (Reese et al., 2001), suggesting that the patelloid is not developmentally equivalent to the patella

626   in marsupials (Vickaryous & Olson 2007). If so, this would suggest independent evolutionary

627   histories of these two structures. Further work is required to clarify the relationships of the

628   patelloid and suprapatella at least in extant taxa, before definitive evolutionary trajectories can be

629   inferred.

630

631   A non-osseous patelloid/suprapatella is also found in several closely related modern placental

632   clades that lie far from the base of Eutheria (Fig. 7), suggesting that these represent independent

633   acquisitions. We have not attempted to explicitly reconstruct the evolution of the patelloid in

634   Eutheria. Lewis (1958) and Broome and Houghton (1989) speculated that the mammalian

635   patelloid might be a precursor to the tibial epiphysis (Broome & Houghton 1989; Lewis 1958) --

636   a so-called "traction epiphysis" (Vickaryous & Olson 2007) -- but considering that the patelloid

637   evolved after the tibial tuberosity (and proximal epiphysis) of mammals, not before it, and lies

638   proximal rather than distal to the patella, we reject this hypothesis. Furthermore, this same

639   phylogenetic evidence indicates that the patelloid in Euarchontoglires, some Carnivora and

640   bandicoots is not ancestrally associated with leaping or other behaviours (e.g. Jungers et al.,

641   1980)-- as Walji & Fasana (1983) caution, its ancestral mechanical environment and roles in

642   different behaviours remain unclear, although it does seem to be associated with knee

643   hyperflexion like a typical fibrocartilaginous "wrap-around" tendon (e.g. Ralphs et al. 1991;

644   Alexander & Dimery, 1985).

645

646   Our unordered parsimony reconstruction indicated that an ossified patella was absent in the

647   ancestor of Metatheria, then evolved in the ancestor of Borhyaenoidea and Marsupialia. The

648   most likely pattern shows loss of the patella in the basal lineages of Marsupialia, with subsequent

649   re-acquisition in certain groups (Notoryctidae, possibly with Thylacomyidae + Peramelidae, and

650   Tarsipedidae) (Fig. 6). Ordered parsimony reconstruction resulted in subtle differences; making

651   some nodes less ambiguous (i.e. state 1 within basal Marsupialia) and others more ambiguous

652   (such as the ancestor of Borhyaenoidea and Marsupialia, which becomes equally parsimonious

653   between states 1 and 2). In contrast, Maximum likelihood reconstruction suggested multiple

654   evolutions of the osseous patella in Metatheria, perhaps preceded in some taxa by a patelloid, but

655   this is unclear. Because presence of a patelloid has not been clearly excluded in some extant

656   marsupials (e.g. Petauridae, Acrobatidae) and is unlikely to be fossilised, its reconstruction must

657   be treated carefully. Finally, alternative placement of Microbiotheriidae did not drastically alter

658   the reconstructions (Fig. S5).

659

660   *5. Cenozoic Eutheria*

661   The Placentalia include all extant Eutheria as well as some fossil stem taxa (Fig. 7). Although

662   there is some fossil evidence for placentals pre-dating the K-Pg event (Archibald et al. 2011), as

663   well as substantial molecular dating consistent with an older placental radiation, the timing of the

664   placental radiation remains highly controversial. However, our major conclusions about patellar

665   evolution in placentals are not dependent on how this controversy is ultimately resolved, as a

666   recent large-scale phylogenetic analysis convincingly established the presence of a patella as a

667   derived character state in the ancestral placental irrespective of its true date of divergence

668   (O'Leary et al. 2013).

669

670   Fossil evidence supports the presence of the patella in essentially all Cenozoic placental groups

671   (Fig. 7; also see Table S1 and Figs. S1-S3, with citations therein). Specimens with sufficient

672   hindlimb material to make a determination of the patella are rare in the early Cenozoic Paleogene

673   period (~66-23 Mya), but Paleocene groups in which a patella has been reported include the

674   Taeniodonta (small to medium sized fossorial animals), Pantodonta (early herbivores),

675   Palaeanodonta (small, possible insectivores; perhaps related to pangolins), "Condylarthra" (a

676   diverse assemblage of putatively related taxa, probably polyphyletic, including both herbivores

677   and carnivores, many of which may be stem members of subclades within the placental crown

678   group), and the important Plesiadapiformes, a sister group to crown clade primates (and possibly

679   members of the clade Primates as well) (Bloch & Boyer 2007; Silcox 2007). In general, the

680   evolutionary relationships between Paleocene taxa and more recent placentals remain enigmatic.

681

682   Eocene placentals include examples whose close relationships to modern groups are well

683   accepted. Among Eocene groups (Fig. 7, Table S1), a patella has been reported in older, extinct

684   groups such as "Condylarthra", Creodonta (carnivores), Mesonychia (carnivorous/omnivorous

685   artiodactyls or cetartiodactyls), Dinocerata (large rhinoceros-like herbivores), Brontotheriidae

686   (large equid-like herbivores), and Notoungulata (fairly diverse South American hoofed

687   herbivores; probably related to Afrotheria) (O'Leary et al. 2013), as well as in extinct species (in

688   parentheses, see Table S1 for citations) recognized as stem members of several extant groups:

689   Glires (*Rhombomylus*), Perissodactyla (*Propalaotherium*), early Sirenia retaining hindlimbs

690   (*Pesoziren, Protosiren*), Proboscidea (*Numidotherium, Moeritherium, Barytherium*), Rodentia

691   (the horse-sized *Pseudotomus, Paramys*), Pholidota (*Eomanis*), Artiodactyla (*Gervachoerus*),

692   early Cetacea retaining hindlimbs (*Maiacetus*) and Chiroptera (*Icaronycteris, Tachypteron*). A

693   patella is also reported for several Eocene primates, including the lemur-like Notharctidae

694   (*Northarctus*) and the tarsier-like *Omomys* and *Archicebus*, in addition to the enigmatic primate

695   *Darwinius*.

696

697   Despite an extensive literature search, we found no reports attesting to the presence of the patella

698   in certain important and widely cited Paleocene and Eocene species, including: *Protungulatum*,

699   frequently cited as the earliest true placental; *Miacis*, *Vulpavus, Viverravus* and *Didymictis*,

700   which are stem Carnivora (Gregory 1920; Heinrich & Houde 2006; Heinrich & Rose 1995;

701   Heinrich & Rose 1997; Samuels et al. 2013); *Pakicetus*, a fully quadrupedal early cetacean

702   (though sometimes reconstructed with a patella as in Fig. 7 and Fig. S1 M, N) (Thewissen et al.

703   2001); *Leptictis*, possibly related to crown clade lagomorphs (Rose 1999); *Sinopa*, a creodont

704   (Matthew 1906); and the early primates *Adapis*, *Leptadapis*, *Teilhardina*, and *Cantius* (Dagosto

705   1983; Gebo et al. 2012a; Gebo et al. 2012b; Rose & Walker 1985; Schlosser 1887; Szalay et al.

706   1975). There is no reason to expect that the patella is missing in these species. These absences

707   are more likely due to incompleteness of the fossil record and/or literature descriptions and

708   images. Moreover, the massive collections of Eocene specimens from the Messel and Green

709   River lagerstätten in Germany and Wyoming have not yet been fully described (Grande 1984;

710   Schaal & Ziegler 1992). There are many examples of the patella in specimens from extant

711   placental groups across the more recent Miocene, Oligocene, Pliocene and Pleistocene, but a

712   comprehensive search of the literature for those geologic epochs was deemed redundant for our

713   major conclusions.

714

715   Based on fossil evidence plus extensive genomic DNA sequencing, there is a consensus that

716   crown clade placentals can be historically and geographically defined by four major groups:

717   Xenarthra, Afrotheria, Euarchontoglires (further divided into Euarchonta; featuring Primates;

718   and Glires) and Laurasiatheria (Rose 2006). These in turn may be resolved, with somewhat less

719   consensus, into 19 crown clade "orders" (Fig. 7) (O'Leary et al. 2013). In two of these orders, the

720   afrotherian clade Sirenia and the cetacean branch of (Cet)artiodactyla (laurasiatherian clade),

721   extant members have extensively reduced or absent hindlimbs and thus lack skeletal knee

722   structures, including a patella. In contrast, the patella is retained among the aquatic seals and sea

723   lions in Carnivora, although unlike Sirenia and Cetacea these animals still display some

724   terrestrial habits and thus presumably still employ the antigravity mechanism that the patella is

725   involved in at the knee. A patella is documented as present in at least some members of all other

726   17 placental "orders" (e.g. Figs. 7,S1-S3,4G,H; Table S1) (de Panafieu & Gries 2007; De Vriese

727   1909; Dye 1987; Herzmark 1938; Lessertisseur & Saban 1867; Rose 2006).

728

729   The evolution of the Cetacea presents an interesting scenario regarding patellar evolution (Fig.

730   7). Cetaceans evolved from a common ancestor with other (cet)artiodactyls (Spaulding et al.

731   2009; Thewissen et al. 2007). Early members, *Diacodexis* and *Indohyus*, shared morphological

732   similarities with both extant groups of Cetacea (toothed and baleen whales) and yet retained a

733   patella (Rose 1982; Thewissen et al. 2007), much as stem Sirenia did (Domning 2001; Zalmout

734   2008). Patellar status in *Pakicetus*, a presumptive early cetacean with full hindlimbs, remains

735   uncertain based on the primary literature, but presence is likely considering the presence of a

736   patella in its closest relatives. *Rodhocetus* and *Ambulocetus*, probably semi-aquatic early

737   cetaceans, still had large hindlimbs and patellae (Madar et al. 2002). The pelvis and hindlimbs

738   are greatly reduced in the later cetaceans *Dorudon* and *Basilosaurus*, but a patella is still present

739   in these animals (Gingerich et al. 1990; Uhen 2004). It is not clear exactly when the patella was

740   lost in later cetaceans with increasingly reduced hindlimbs.

741

742   Bats present another interesting case of patellar evolution (Fig. 7; Table S1). The patella is

743   generally present in bats (Pearson & Davin 1921b). A patella is also reported in a well-preserved

744   hindlimb of an early Eocene bat, *Icaronycteris*, of intermediate form but proposed to be a

745   microchiropteran (Jepsen 1966). However, in studies of multiple genera of modern bats

746   including members from both of the major subgroups Megachiroptera and Microchiroptera

747   (which is possibly paraphyletic), a patella was noted as absent in four species of the

748   megachiropteran *Pteropus* (flying foxes of various sizes), and a few individual species of

749   *Cephalotes, Epomophorus and Vespertilio* (De Vriese 1909; Lessertisseur & Saban 1867; Smith

750   et al. 1995). No obvious lifestyle distinction was noted for the *Pteropus* genus as compared to

751   many other bats, hence the loss of the patella in members of this particular subgroup (and others)

752   remains mysterious. In general, bat hindlimbs are highly derived, adapted to hanging and pulling

753   rather than pushing. A few bats such as the vampire bats are actively quadrupedal (Adams &

754   Thibault 2000; Riskin & Hermanson 2005). Bat hindlimbs are articulated in abduction, so that

755   the knee faces dorsally; as in the original ancestral orientation for Tetrapoda (Fig. 2) (Neuweiler

756   2000; Schutt & Simmons 2006). There remains a need for a comprehensive study of the patella

757   in bats (Smith *et al.* only studied 31 specimens of 13 species), but this is challenging due to the

758   existence of >900 extant bat species (Jones et al. 2002). The microstructure of the "patelloid" in

759   *Pteropus* is generally similar to that in many marsupials (e.g. deep layer of fibrocartilage;

760   superficial layer of dense connective tissue contiguous with the quadriceps/patellar tendon)

761   (Smith et al. 1995). This also raises the question of whether the patella only ossifies later in

762   adulthood in *Pteropus*, rather than not ossifying at all.

763

764   *General evolutionary patterns and ambiguities*

765   Considering the above distributions of patellar presence/absence in Mammalia (Figs. 5-7; Figs.

766   S4,S5) and our data matrix (Table S1), the simplest interpretation of the evolutionary record of

767   the patella in mammals (by parsimony-based mapping of presence/absence) is that this structure

768   arose independently at least four times (but possibly up to six), mostly during the Mesozoic era:

769   1, in Australosphenida ancestral to modern monotremes; 2, in Multituberculata (later than

770   *Rugosodon*); 3, in Symmetrodonta (specifically in Spalacotheroidea that were ancestral to

771   *Zhangheotherium* but not *Akidolestes*); 4-6, in early Theria (including Eutheria, Metatheria,

772   *Eomaia* and related stem groups; depending on topology between one and three times this clade);

773   Conceivably, a single common patelloid precursor may pre-date the evolutions of the bony

774   patellae, or the patella may have arisen fewer times and undergone loss (and re-gain) in some

775   lineages, similarly to the pattern in Metatheria. Each of these scenarios remain difficult to test

776   purely with fossil evidence, however, due to the typical lack of preservation of cartilaginous

777   structures.

778

779   Once the bony patella evolved in Eutheria, it was highly conservative in its presence. There are

780   very few examples of fossil or extant Eutheria in which the hindlimb remains intact but the

781   patella is absent. A caveat is that many fossil specimens are not sufficiently complete for a

782   definitive rejection of patellar occurrence in those taxa. Still, the evolutionary stability of the

783   patella in Eutheria stands in contrast to its general variability across mammals, and suggests

784   some conserved functional requirement and/or ontogenetic mechanism that remains to be

785   determined.

786

787   Although an ossified patella is absent in the majority of Metatheria, it is reported in several

788   groups (Figs. 6, S5). This likely represents loss and regain(s) of the early metatherian patella.

789   Importantly, in this case the presence of a fibrocartilaginous "patelloid" in most marsupials

790   shows a clear evolutionary polarity from an ossified patella to a non-ossified patelloid, and back

791   again in the case of the secondary gain of ossification, in each case within Metatheria (Reese et

792   al. 2001). This "patella to patelloid" transition suggests the reverse may also be possible – that a

793   soft tissue patelloid may represent the evolutionary precursor to an ossified patella – but it has

794   yet to be clearly documented. There is no obvious lifestyle or biomechanical correlate among all

795   four groups of patella-bearing Metatheria: the notoryctid moles are underground burrowers, and

796   bandicoots may dig for insects, but *Tarsipes* is a nectar feeder and the borhyaenoids were largely

797   terrestrial carnivores. In contrast, other Australasian carnivorous marsupials including the

798   recently extinct thylacine, and the extant quoll, numbat and Tasmanian devil are not reported to

799   have a patella.

800

801   The large size of the patella in the monotreme platypus might be related to its aquatic (and partly

802   fossorial; burrowing of dens) lifestyle. Reduction of the patella in the Cetacea and Sirenia is not

803   intrinsically correlated with their aquatic lifestyle, but with the reduction of the hindlimbs as part

804   of their particular adaptations. Elsewhere in groups with aquatic adaptations, for example in

805   various diving birds, an unusually large patella is found. The other monotremes, the echidnas,

806   also burrow and the long-beaked species (*Zaglossus*) lives in underground dens-- further

807   suggesting an association between fossorial habits and the presence or enlargement of a patella in

808   Monotremata, as well as in some fossil Mammaliaformes (multituberculates?) but curiously not

809   in other fossorial stem taxa (*e.g.* the docodont *Docofossor*). It seems premature to weave detailed

810   scenarios around the high degree of convergent evolution of the patella in mammals until the

811   function and genomic control of the patella are better understood, and improved phylogenetic

812   sampling improves resolution of when it evolved in particular lineages.

813

814   *Patellar developmental genetics*

815   Molecular phylogenomics provides a potential independent or synergistic approach to resolving

816   issues of patellar evolution. If specific genomic sequence signatures could be associated with

817   patellar status, then comparison of the genomes of the various extant but widely separated groups

818   with a patella might indicate whether these represent convergence events or a common ancestral

819   event (*i.e.* identified via shared evolutionarily transmitted genetic markers required for patellar

820   development). For example, it has recently been shown that the ability to taste sweet

821   carbohydrates in hummingbirds represents a trait convergence. Hummingbirds diverged from the

822   insectivorous swifts, in which the sweet taste receptor is inactivated by mutations in the receptor

823   coding gene. In hummingbirds, the ability to taste sweet has been re-acquired, apparently

824   through molecular adaptation of the umami receptor to detect sweet molecules (Baldwin et al.

825   2014). It would be helpful to understand the (developmental) genetics of the patella as a step

826   toward the identification of such sequence signatures. Developmental genetic studies in two

827   mammals, humans and mice, have identified genes required for correct patellar specification.

828   The known functions of some of these genes are informative regarding their requirements.

829

830   There are currently approximately 12 human genetic disorders with identified molecular bases

831   that regularly include abnormal, reduced or absent patellae (hypoplasia or aplasia) as an

832   important aspect of the phenotype (reviewed by Bongers *et al*. (2005), see also Warman *et al*.

833   (2011) and Supplementary Table S2 for details). There are also several genes whose genetics in

834   mice indicates relevance to patellar development at least in rodents. A detailed discussion of all

835   these syndromes and genes is beyond the scope of this study. However, the known patellar genes

836   can be broadly organized according to three major developmental processes: limb specification

837   and pattern formation (transcription factors such as *LMX1B, TBX4*, *PITX1* and mouse

838   *Hoxaaccdd-11, OSR1, OSR2*, *SOX11*, and signalling factor *WNT7A*); bone development,

839   biochemistry and regulation (*GDF5*, *CHRNG*, *SLC26A2*, *COL9A2*, *AKT1*); and genes involved

840   in DNA replication and chromatin (*ORC1*, *ORC4*, *ORC6*, *CDT1*, *CDC6*, *GMNN*, *CDC45*,

841   *RECQL4, KAT6B, ESCO2*). Of these, the genes of replication and chromatin are the most

842   unexpected, and potentially of the most interest for evolutionary studies. Patellar ossification

843   may be dependent on the timing of DNA replication in particular cells, or else may be affected

844   by aberrant gene regulation resulting from mutations in replication and chromatin factors. In

845   either case, the target genes mis-regulated in these syndromes, if they can be identified, may

846   provide useful evolutionary markers to distinguish convergent from homologous patellar status.

847

848   Developmental studies in mouse or chick embryos, sometimes with induced paralysis, document

849   the additional importance of local environmental factors in patellar ontogenesis (Hosseini &

850   Hogg 1991; Mikic et al. 2000; Nowlan et al. 2010a; Nowlan et al. 2010b; Osborne et al. 2002;

851   Rot-Nikcevic et al. 2006). Similarly, embryonic development and hindlimb activity in the case of

852   particular marsupials may be important in understanding the diversity of patellar states in this

853   group. A better understanding of these environmental processes will also be helpful to

854   disentangle genomic versus epigenomic regulation of patellar development, and hence evolution.

855

856

857   CONCLUSIONS

858

859   *How "the mammalian patella" evolved*

860   The widespread, repeated evolution of the patella across evolution argues for an important role in

861   locomotor biomechanics. In animals lacking a patella (*e.g.* Lissamphibia, Testudines,

862   Crocodylia; as well as many extinct lineages of tetrapods), the consequences of this ancestral

863   absence for hindlimb function remain mostly unstudied. This mystery is striking, in particular,

864   within Mammalia where most marsupials lack an ossified patella, as did numerous fossil stem-

865   mammals, despite seeming to share common ecological niches and the associated locomotor

866   requirements. This sporadic occurrence in marsupials and stem mammals contrasts with its near

867   universality and evolutionary stability in the Eutheria as noted above.

868

869   The exact number of independent origins of a patella among mammals remains unclear, but we

870   have estimated at least four convergent episodes inside Mammaliaformes, and several instances

871   of patellar loss (with apparent re-gain in some marsupials). The pattern of acquisition and loss

872   will require revisiting as new fossil material is discovered, as our evolutionary reconstructions

873   are dependent on single specimens for many ancient taxa. Moreover, patellar status has not been

874   verified for all >5,000 eutherian and >330 metatherian species (Wilson & Reeder 2005), so it is

875   possible that additional placental species (other than the fully aquatic forms) may be found

876   lacking, or marsupials having, a patella. A recent evolutionary study documented many

877   apparently independent evolutionary origins of the caecal appendix in mammals; thus the

878   convergent evolution of complex anatomical structures like the patella has precedent (Smith et

879   al. 2013). Similarly, blue coloration among tarantula spiders apparently involves at least eight

880   independent evolutionary acquisitions, among different microscopic anatomical structures

881   affecting spectral reflectance hence general external color (Hsiung et al. 2015). A better

882   understanding of the genomic signatures required for development of such novel structures

883   should be very helpful to deconstruct the observed complex patterns of evolution, distinguishing

884   between convergent evolution (homoplasy) and shared inheritance (synapomorphy/homology).

885

886   Given that the patella evolved, and was also lost, multiple times in mammals and other

887   Tetrapoda (Fig. 3), one thing is clear. Much as we have referred to "the patella" throughout this

888   study, there is no such thing—perhaps not even a single "mammalian patella". The story of

889   patellar evolution is one of many patellae; a story of diverse evolutionary origins as well as

890   forms, functions, ontogenies and perhaps even diverse underlying genetics. Mottershead (1988)

891   wondered if the patella is "not typical of its kind" for a sesamoid bone (Mottershead 1988). Yet

892   even patellae are not necessarily typical for patellae, let alone other sesamoids-- there are double

893   or fatty patellae in some birds (Regnault et al. 2014), proximal suprapatellae and/or

894   fibrocartilaginous patelloids in many marsupials, no patellae at all in many species, and even

895   amongst those animals that have patellae, there are numerous shapes and sizes of patellae (Figs.

896   4, S1-S3), suggesting still-unappreciated lifestyle constraints in patellar (and knee joint)

897   mechanics.

898

899   *Future prospects*

900   Our discussion of patellar evolution in Mammalia has identified several areas where key

901   questions remain unresolved, in addition to uncertainties about the amount of

902   convergence/parallel evolution in origins of the patella and about specific roles of (and

903   interactions between) genetic/developmental factors in patellar formation/loss. Considering that

904   mechanical loads are known to play an important role in the development of sesamoid bones (in

905   particular in early ontogeny), studies linking these loads to genetic/developmental control as well

906   as broad evolutionary patterns could prove very insightful, especially in explaining the

907   seemingly large amount of patellar homoplasy in mammalian evolution. Mammals may be less

908   sensitive (*i.e.* more genetically assimilated (Vickaryous & Olson 2007)) than birds in terms of

909   the relative influence of mechanical loads on bone (including sesamoid) ontogeny (Nowlan et al.

910   2010b) - this idea deserves better testing as insight into load-based influences improves.

911   Furthermore, indications that some bones within an organism may be more responsive to their

912   loading regime (Nowlan et al. 2010a) may be of great relevance to interpreting patellar biology

913   and evolution, but at present strong inferences cannot be drawn about how variable the patella's

914   responsiveness to mechanics is within or among organisms. There is clearly much room for

915   further study of the patellae of mammals and other tetrapods, and here we have noted directions

916   in which these might most beneficially be directed.

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934

935   REFERENCES
936

937   Adams RA, and Thibault KM. 2000. Ontogeny and evolution of the hindlimb and calcar:
938   assessing phylogenetic trends. In: Adams RA, and Pedersen SC, eds. *Ontogeny,*
939   *functional ecology, and evolution of bats*. Cambridge: Cambridge University Press.
940   Aglietti P, and Menchetti PPM. 1995. Biomechanics of the patellofemoral joint. In: Scuderi GR,
941   ed. *The Patella*. New York City: Springer.
942   Ahlberg PE, Clack JA, and Blom H. 2005. The axial skeleton of the Devonian tetrapod
943   Ichthyostega. *Nature* 437:137-140.
944   Alexander RM, and Dimery NJ. 1985. The significance of sesamoids and retro-articular
945   processes for the mechanics of joints. *Journal of Zoology* 205:357-371.
946   Andrews SM, and Westoll TS. 1970. The postcranial skeleton of Eusthenopteron foordi
947   whiteaves. *Transactions of the Royal Society of Edinburgh* 68:207-329.
948   Archibald JD. 1998. Archaic ungulates ("Condylarthra"). In: Janis CM, Scott KM, and Jacobs
949   LL, eds. *Evolution of Tertiary Mammals of North America*. Cambridge: Cambridge
950   University Press.
951   Archibald JD, Zhang Y, Harper T, and Cifelli R. 2011. Protungulatum, confirmed Cretaceous
952   occurrence of an otherwise Paleocene Eutherian (Placental?) mammal. *Journal of*
953   *Mammalian Evolution* 18:153-161.
954   Argot C. 2002. Functional-adaptive analysis of the hindlimb anatomy of extant marsupials and
955   the paleobiology of the Paleocene marsupials Mayulestes ferox and Pucadelphys andinus.
956   *J Morphol* 253:76-108.
957   Argot C. 2003a. Functional-adaptive anatomy of the axial skeleton of some extant marsupials
958   and the paleobiology of the paleocene marsupials Mayulestes ferox and Pucadelphys
959   andinus. *J Morphol* 255:279-300.
960   Argot C. 2003b. Functional adaptations of the postcranial skeleton of two Miocene borhyaenoids
961   (Mammalia, Metatheria), Borhaena and Prothylacinus, from South America.
962   *Palaeontology* 46:1213-1267.
963   Argot C. 2003c. Postcranial functional adaptations in the South American Miocene borhyaenoids
964   (Mammalia, Metatheria): Cladosictis, Pseudonotictis and Sipalocyon. *Alcheringa: An*
965   *Australasian Journal of Palaeontology* 27:303-356.
966   Argot C. 2004. Functional-adaptive analysis of the postcranial skeleton of a Laventan
967   Borhyaenoid, Lycopsis longirostris (Marsupialia, Mammalia)
968   *Journal of Vertebrate Paleontology* 24:689-708.
969   Argot C, and Babot J. 2011. Postcranial morphology, functional adapations and palaeobiology of
970   Callistoe vincei, a predaceous metatherian from the Eocene of Salta, northwestern
971   Argentina. *Palaeontology* 54:447-480.
972   Asher RJ, Horovitz I, and Sanchez-Villagra MR. 2004. First combined cladistic analysis of
973   marsupial mammal interrelationships. *Mol Phylogenet Evol* 33:240-250.
974   Baldwin MW, Toda Y, Nakagita T, O'Connell MJ, Klasing KC, Misaka T, Edwards SV, and
975   Liberles SD. 2014. Sensory biology. Evolution of sweet taste perception in
976   hummingbirds by transformation of the ancestral umami receptor. *Science* 345:929-933.
977   Barnett CH, and Lewis OJ. 1958. The evolution of some traction epiphyses in birds and
978   mammals. *J Anat* 92:593-601.

979   Barton RS, Ostrowski ML, Anderson TD, Ilahi OA, and Heggeness MH. 2007. Intraosseous
980   innervation of the human patella: a histologic study. *Am J Sports Med* 35:307-311.
981   Benjamin M, Toumi H, Ralphs JR, Bydder G, Best TM, and Milz S. 2006. Where tendons and
982   ligaments meet bone: attachment sites ('entheses') in relation to exercise and/or
983   mechanical load. *J Anat* 208:471-490.
984   Bertollo N, Pelletier MH, and Walsh WR. 2012. Simulation of patella alta and the implications
985   for in vitro patellar tracking in the ovine stifle joint. *J Orthop Res* 30:1789-1797.
986   Bertollo N, Pelletier MH, and Walsh WR. 2013. Relationship between patellar tendon shortening
987   and in vitro kinematics in the ovine stifle joint. *Proc Inst Mech Eng H* 227:438-447.
988   Bi S, Wang Y, Guan J, Sheng X, and Meng J. 2014. Three new Jurassic euharamiyidan species
989   reinforce early divergence of mammals. *Nature*.
990   Bland YS, and Ashhurst DE. 1997. Fetal and postnatal development of the patella, patellar
991   tendon and suprapatella in the rabbit; changes in the distribution of the fibrillar collagens.
992   *J Anat* 190 (Pt 3):327-342.
993   Bloch JI, and Boyer DM. 2007. New skeletons of Paleocene-Eocene Plesiadapiformes: A
994   diversity of arboreal positional behaviors in early primates. In: Ravoso MJ, and Dagosto
995   M, eds. *Primate Origins: Adaptations and Evolution*. New York: Springer, 535-581.
996   Boisvert CA. 2005. The pelvic fin and girdle of Panderichthys and the origin of tetrapod
997   locomotion. *Nature* 438:1145-1147.
998   Broome GH, and Houghton GR. 1989. A congenital abnormality of the tibial tuberosity
999   representing the evolution of traction epiphyses. *J Anat* 165:275-278.
1000   Brower AV, and Schawaroch V. 1996. Three steps of homology assessment. *Cladistics* 12:265-
1001   272.
1002   Butler DL, Kay MD, and Stouffer DC. 1986. Comparison of material properties in fascicle-bone
1003   units from human patellar tendon and knee ligaments. *J Biomech* 19:425-432.
1004   Butler PM. 2000. Review of the early Allotherian mammals. *Acta Palaeontologica Polonica*
1005   45:317-342.
1006   Camp CL. 1923. Classification of the lizards. *Bulletin of the American Museum of Natural*
1007   *History* 48:289-480.
1008   Carrano M. 2000. Homoplasy and the evolution of dinosaur locomotion. *Paleobiology* 26:489-
1009   512.
1010   Chadwick KP, Regnault S, Allen V, and Hutchinson JR. 2014. Three-dimensional anatomy of
1011   the ostrich (Struthio camelus) knee joint. *PeerJ* 2:e706.
1012   Chen M, and Luo Z. 2012. Postcranial skeleton of the Cretaceous mammal Akidolestes cifellii
1013   and its locomotor adaptations. *Journal of Mammalian Evolution*.
1014   Chester SGB, Sargis EJ, Szalay FS, Archibald JD, and Averianov AO. 2012. Therian femora
1015   from the Late Cretaceous of Uzbekistan. *Acta Palaeontologica Polonica* 57:53-64.
1016   Clark J, and Stechschulte DJ, Jr. 1998. The interface between bone and tendon at an insertion
1017   site: a study of the quadriceps tendon insertion. *J Anat* 192 (Pt 4):605-616.
1018   Clarke JA, and Norell MA. 2002. The morphology and phylogenetic position of Apsaravis
1019   ukhaana from the late Cretaceous of Mongolia. *American Museum Novitates* 3387:1-47.
1020   Daeschler EB, Shubin NH, and Jenkins FA, Jr. 2006. A Devonian tetrapod-like fish and the
1021   evolution of the tetrapod body plan. *Nature* 440:757-763.
1022   Dagosto M. 1983. Postcranium of Adapis parisiensis and Leptadapis magnus (Adapiformes,
1023   Primates). *Folia Primatological* 41:49-101.

de Muizon C, Cifelli RL, and Paz RC. 1997. The origin of the dog-like borhyaenoid marsupials of South America. *Nature* 389:486-489.

de Panafieu J-B, and Gries P. 2007. *Evolution*. New York: Seven Stories Press.

De Vriese B. 1909. Recherches sur l' anatomie comparée de la rotule. *Bulletin of the Royal Academy of Medicine of Belgium*.

Domning DP. 2001. The earliest known fully quadrupedal sirenian. *Nature* 413:625-627.

dos Reis M, Inoue J, Hasegawa M, Asher RJ, Donoghue PC, and Yang Z. 2012. Phylogenomic datasets provide both precision and accuracy in estimating the timescale of placental mammal phylogeny. *Proc Biol Sci* 279:3491-3500.

Dye SF. 1987. An evolutionary perspective of the knee. *J Bone Joint Surg Am* 69:976-983.

Dye SF. 2003. Functional morphologic features of the human knee: an evolutionary perspective. *Clin Orthop Relat Res*:19-24.

Eckstein F, Muller-Gerbl M, and Putz R. 1992. Distribution of subchondral bone density and cartilage thickness in the human patella. *J Anat* 180 (Pt 3):425-433.

Editors. 1992. The patella. *Lancet* 339:341.

Evans EJ, Benjamin M, and Pemberton DJ. 1991. Variations in the amount of calcified tissue at the attachments of the quadriceps tendon and patellar ligament in man. *J Anat* 174:145-151.

Eyal S, Blitz E, Shwartz Y, Akiyama H, Ronen S, and Zelzer E. 2015. On the development of the patella. *Development*.

Farnum CE. 2007. Postnatal growth of fins and limbs through endochondral ossification. In: Hall BK, ed. *Fins into Limbs*. Chicago: University of Chicago.

Fellows RA, Hill NA, Gill HS, MacIntyre NJ, Harrison MM, Ellis RE, and Wilson DR. 2005. Magnetic resonance imaging for in vivo assessment of three-dimensional patellar tracking. *J Biomech* 38:1643-1652.

Flores DA. 2009. Phylogenetic analyses of postcranial skeletal morphology in Didelphid marsupials. *Bulletin of the American Museum of Natural History* 320:1-81.

Fox AJ, Wanivenhaus F, and Rodeo SA. 2012. The basic science of the patella: structure, composition, and function. *J Knee Surg* 25:127-141.

Freyer C, Zeller U, and Renfree MB. 2003. The marsupial placenta: a phylogenetic analysis. *J Exp Zool A Comp Exp Biol* 299:59-77.

Gatesy J, Geisler JH, Chang J, Buell C, Berta A, Meredith RW, Springer MS, and McGowen MR. 2013. A phylogenetic blueprint for a modern whale. *Mol Phylogenet Evol* 66:479-506.

Gauthier JA, Kearney M, Maisano JA, Rieppel O, and Behlke ADB. 2012. Assembling the squamate tree of life : perspectives from the phenotype and the fossil record. *Gauthier, JA, Kearney, M, Maisano, JA, Rieppel, O and ADB Behlke 2012 Assembling the squamate tree of life : perspectives from the phenotype and the fossil record Bulletin of the Peabody Museum of Natural History 53(1):3-308* 53:3-308.

Gebo DL, Dagosto M, Ni X, and Beard KC. 2012a. Species diversity and postcranial anatomy of eocene primates from Shanghuang, China. *Evol Anthropol* 21:224-238.

Gebo DL, Smith T, and Dagosto M. 2012b. New postcranial elements for the earliest Eocene fossil primate Teilhardina belgica. *J Hum Evol* 63:205-218.

Gingerich PD, Smith BH, and Simons EL. 1990. Hind limbs of eocene basilosaurus: evidence of feet in whales. *Science* 249:154-157.

1069 Giori NJ, Beaupre GS, and Carter DR. 1993. Cellular shape and pressure may mediate
1070   mechanical control of tissue composition in tendons. *J Orthop Res* 11:581-591.
1071 Goloboff PA, Catalano SA, Mirande JM, Szumik CA, Arias JA, Kallersjo M, and Farris JS.
1072   2009. Phylogenetic analysis of 73 060 taxa corroborates major eukaryotic groups.
1073   *Cladistics* 25:211-230.
1074 Grande L. 1984. Paleontology of the Green River Formation, with a review of the fish fauna.
1075   Wyoming: Geological Survey of Wyoming.
1076 Gregory WK. 1920. On the structure and relations of Notharctus, an American Eocene primate.
1077   Memoirs of the American Museum of Natural History. New York: American Museum of
1078   Natural HIstory. p 1-243.
1079 Griffith CJ, Laprade RF, Coobs BR, and Olson EJ. 2007. Anatomy and biomechanics of the
1080   posterolateral aspect of the canine knee. *J Orthop Res* 25:1231-1242.
1081 Groves CP, and Flannery T. 1990. Revision of the families and genera of bandicoots. In:
1082   Seebeck JH, Brown PR, Wallis RL, and Kemper CM, eds. *Bandicoots and Bilbies*.
1083   Chipping Norton: Surrey Beatty and Sons.
1084 Guernsey DL, Matsuoka M, Jiang H, Evans S, Macgillivray C, Nightingale M, Perry S, Ferguson
1085   M, LeBlanc M, Paquette J, Patry L, Rideout AL, Thomas A, Orr A, McMaster CR,
1086   Michaud JL, Deal C, Langlois S, Superneau DW, Parkash S, Ludman M, Skidmore DL,
1087   and Samuels ME. 2010. Mutations in origin recognition complex gene ORC4 cause
1088   Meier-Gorlin syndrome. *Nat Genet* 43:360-364.
1089 Haines RW. 1940. Note on the independence of sesamoid and epiphysial centres of ossification.
1090   *Journal of Anatomy* 75:101-105.
1091 Haines RW. 1942. The tetrapod knee joint. *Journal of Anatomy* 76:270-301.
1092 Haines RW. 1974. Epiphyses and Sesamoids. In: Gans C, ed. *Biology of the Reptilia*. New York:
1093   Academic Press, 81-115.
1094 Hargrave-Thomas EJ, Thambyah A, McGlashan SR, and Broom ND. 2013. The bovine patella
1095   as a model of early osteoarthritis. *J Anat* 223:651-664.
1096 Harris HA. 1937. The Foetal Growth of the Sheep. *J Anat* 71:516-527.
1097 Haxton H. 1944. The patellar index in mammals. *J Anat* 78:106-107.
1098 Heegaard J, Leyvraz PF, Curnier A, Rakotomanana L, and Huiskes R. 1995. The biomechanics
1099   of the human patella during passive knee flexion. *J Biomech* 28:1265-1279.
1100 Heinrich RE, and Houde P. 2006. Postcranial anatomy of Viverravus (Mammalia, Carnivora)
1101   and implications for substrate use in basal Carnivora. *Journal of Vertebrate Paleontology*
1102   26:422-435.
1103 Heinrich RE, and Rose KD. 1995. Partial skeleton of the primitive Carnivoran Miacis petilus
1104   from the early Eocene of Wyoming. *Journal of Mammalogy* 76:148-162.
1105 Heinrich RE, and Rose KD. 1997. Postcranial morphology and locomotor behaviour of two early
1106   Eocene Miacoid carnivorans, Vulpavus and Didymictis. *Palaeontology* 40:297-305.
1107 Herzmark MH. 1938. Evolution of the Knee Joint. *Journal of Bone and Joint Surgery* 200:77-84.
1108 Hildebrand M. 1998. *Analysis of Vertebrate Structure*: Wiley.
1109 Holladay SD, Smith BJ, Smallwood JE, and Hudson LC. 1990. Absence of an osseous patella
1110   and other observations in Macropodidae stifle. *Anat Rec* 226:112-114.
1111 Horovitz I. 2003. Postcranial Skeleton of Ukhaatherium nessovi (Eutheria, Mammalia) from the
1112   Late Cretaceous of Mongolia. *Journal of Vertebrate Paleontology* 23:857-868.
1113 Hosseini A, and Hogg DA. 1991. The effects of paralysis on skeletal development in the chick
1114   embryo. I. General effects. *Journal of Anatomy* 177:159-168.

1115   Howale DS, and Patel ZK. 2013. Hypothesis: morphology and development of the patella.
1116   *International Journal of Scientific and Research Publications* 3:1-5.
1117   Hsiung BK, Deheyn DD, Shawkey MD, and Blackledge TA. 2015. Blue reflectance in tarantulas
1118   is evolutionarily conserved despite nanostructural diversity. *Sci Adv* 1:e1500709.
1119   Hutchinson JR. 2001. The evolution of femoral osteology and soft tissues on the line to extant
1120   birds (Neornithes). *Zoological Journal of the Linnean Society* 131:169-197.
1121   Hutchinson JR. 2002. The evolution of hindlimb tendons and muscles on the line to crown-group
1122   birds. *Comp Biochem Physiol A Mol Integr Physiol* 133:1051-1086.
1123   Hutchinson JR. 2004. Biomechanical modeling and sensitivity analysis of bipedal running
1124   ability. II. Extinct taxa. *J Morphol* 262:441-461.
1125   Jepsen GL. 1966. Early eocene bat from wyoming. *Science* 154:1333-1339.
1126   Jerez A, and Tarazona OA. 2009. Appendicular skeleton in Bachia bicolor (Squamata:
1127   Gymnophthalmidae): osteology, limb reduction and postnatal skeletal ontogeny. *Acta
1128   Zoologica (Stockholm)* 90:42-50.
1129   Ji Q, Luo ZX, Yuan CX, Wible JR, Zhang JP, and Georgi JA. 2002. The earliest known
1130   eutherian mammal. *Nature* 416:816-822.
1131   Jones KE, Purvis A, MacLarnon A, Bininda-Emonds OR, and Simmons NB. 2002. A
1132   phylogenetic supertree of the bats (Mammalia: Chiroptera). *Biol Rev Camb Philos Soc*
1133   77:223-259.
1134   Jungers WL, Jouffroy FK, and Stern JT, Jr. 1980. Gross structure and function of the quadriceps
1135   femoris in Lemur fulvus: an analysis based on telemetered electromyography. *J Morphol*
1136   164:287-299.
1137   Kaiser S, Cornely D, Golder W, Garner M, Waibl H, and Brunnberg L. 2001. Magnetic
1138   resonance measurements of the deviation of the angle of force generated by contraction
1139   of the quadriceps muscle in dogs with congenital patellar luxation. *Vet Surg* 30:552-558.
1140   Kappelman J. 1988. Morphology and locomotor adaptations of the bovid femur in relation to
1141   habitat. *J Morphol* 198:119-130.
1142   Kemp TS. 2005. *The Origin and Evolution of Mammals*. London: Oxford University Press.
1143   Kielan-Jaworowska Z, Cifelli RL, and Luo Z. 2004. *Mammals from the Age of Dinosaurs*. New
1144   York: Columbia University Press.
1145   Ksepka DT, Fordyce RE, Ando T, and Jones CM. 2012. New fossil penguins (Aves,
1146   Sphenisciformes) from the Oligocene of New Zealand reveal the skeletal plan of stem
1147   penguins. *Journal of Vertebrate Paleontology* 32:235-254.
1148   Langley-Hobbs SJ. 2009. Survey of 52 fractures of the patella in 34 cats. *Vet Rec* 164:80-86.
1149   Lessertisseur J, and Saban R. 1867. Squelette appendiculaire. In: Grasse P, ed. *Traite de
1150   Zoologie, anoatomie, systematique, biologie*. Paris: Masson.
1151   Lewis OJ. 1958. The tubercle of the tibia. *Journal of Anatomy* 92:587.
1152   Livezey BC, and Zusi RL. 2006. Higher-order phylogeny of modern birds (Theropoda, Aves:
1153   Neornithes) based on comparative anatomy: I. – Methods and characters. *Bulletin of the
1154   Carnegie Museum of Natural History* 37:1-556.
1155   Lovejoy CO. 2007. The natural history of human gait and posture. Part 3. The knee. *Gait Posture*
1156   25:325-341.
1157   Lucas FA. 1903. Notes on the osteology and relationships of the fossil birds of the genera
1158   Hesperornis, Hargeria, Baptornis and Diatryma. *Proceedings of the United States
1159   National Museum* 26:546-556.

1160 Luo Z-L. 2007a. Successive Diversifications in Early Mammalian Evolution. In: Anderson JS,
1161   and Sues H-D, eds. *Major Transitions in Vertebrate Evolution*. Bloomington: Indiana
1162   University Press.
1163 Luo Z, and Ji Q. 2005. New Study on Dental and Skeletal Features of the Cretaceous
1164   "Symmetrodontan" Mammal Zhangheotherium. *J Mammal Evol* 12:337-357.
1165 Luo Z, Kielan-Jaworowska Z, and Cifelli RL. 2002. In quest for a phylogeny of Mesozoic
1166   mammals. *Acta Palaeontologica Polonica* 47:1-78.
1167 Luo ZX. 2007b. Transformation and diversification in early mammal evolution. *Nature*
1168   450:1011-1019.
1169 Luo ZX, Gatesy SM, Jenkins FA, Jr., Amaral WW, and Shubin NH. 2015a. Mandibular and
1170   dental characteristics of Late Triassic mammaliaform Haramiyavia and their
1171   ramifications for basal mammal evolution. *Proc Natl Acad Sci U S A* 112:E7101-7109.
1172 Luo ZX, Ji Q, Wible JR, and Yuan CX. 2003. An Early Cretaceous tribosphenic mammal and
1173   metatherian evolution. *Science* 302:1934-1940.
1174 Luo ZX, Meng QJ, Ji Q, Liu D, Zhang YG, and Neander AI. 2015b. Mammalian evolution.
1175   Evolutionary development in basal mammaliaforms as revealed by a docodontan. *Science*
1176   347:760-764.
1177 Luo ZX, and Wible JR. 2005. A Late Jurassic digging mammal and early mammalian
1178   diversification. *Science* 308:103-107.
1179 Luo ZX, Yuan CX, Meng QJ, and Ji Q. 2011. A Jurassic eutherian mammal and divergence of
1180   marsupials and placentals. *Nature* 476:442-445.
1181 Madar SI, Thewissen JGM, and Hussain ST. 2002. Additional holotype remains of Ambulocetus
1182   natans (Cetacea, Ambulocetidae), and their implications for locomotion in early whales.
1183   *Journal of Vertebrate Paleontology* 22:405-422.
1184 Maddison WP, and Maddison DR. 2014. Mesquite: a modular system for evolutionary analysis.
1185   3.01 ed.
1186 Maisano JA. 2002a. Postnatal skeletal ontogeny in Callisaurus draconoides and Uta stansburiana
1187   (Iguania: Phrynosomatidae). *J Morphol* 251:114-139.
1188 Maisano JA. 2002b. Postnatal skeletal ontogeny in five Xantusiids (Squamata: Scleroglossa). *J
1189   Morphol* 254:1-38.
1190 Marsh OC. 1875. Odontornithes, or birds with teeth. *American Naturalist* 9:625-631.
1191 Martin LD. 1984. A new Hesperornithid and the relationships of the Mesozoic birds.
1192   *Transactions of the Kansas Academy of Science* 87:141-150.
1193 Martin LD, and Tate J. 1976. The skeleton of Baptornis avenus. *Smithsonian Contributions to
1194   Paleobiology* 27:35-66.
1195 Matthew WD. 1906. The osteology of Sinopa, a creodont mammal of the middle Eocene.
1196   *Proceedings of the United States National Museum* 30:203-233.
1197 Meng QJ, Ji Q, Zhang YG, Liu D, Grossnickle DM, and Luo ZX. 2015. Mammalian evolution.
1198   An arboreal docodont from the Jurassic and mammaliaform ecological diversification.
1199   *Science* 347:764-768.
1200 Meredith RW, Janecka JE, Gatesy J, Ryder OA, Fisher CA, Teeling EC, Goodbla A, Eizirik E,
1201   Simao TL, Stadler T, Rabosky DL, Honeycutt RL, Flynn JJ, Ingram CM, Steiner C,
1202   Williams TL, Robinson TJ, Burk-Herrick A, Westerman M, Ayoub NA, Springer MS,
1203   and Murphy WJ. 2011. Impacts of the Cretaceous Terrestrial Revolution and KPg
1204   extinction on mammal diversification. *Science* 334:521-524.

1205 Meredith RW, Westerman M, and Springer M. 2008a. A timescale and phylogeny for
1206   "Bandicoots" (Peramelemorphia, Marsupialia) based on sequences for five nuclear genes.
1207   *Molecular Phylogenetics and Evolution* 47:1-20.
1208 Meredith RW, Westerman M, and Springer MS. 2008b. A timescale and phylogeny for
1209   "bandicoots" (Peramelemorphia: Marsupialia) based on sequences for five nuclear genes.
1210   *Mol Phylogenet Evol* 47:1-20.
1211 Merida-Velasco JA, Sanchez-Montesinos I, Espin-Ferra J, Merida-Velasco JR, Rodriguez-
1212   Vazquez JF, and Jimenez-Collado J. 1997a. Development of the human knee joint
1213   ligaments. *Anat Rec* 248:259-268.
1214 Merida-Velasco JA, Sanchez-Montesinos I, Espin-Ferra J, Rodriguez-Vazquez JF, Merida-
1215   Velasco JR, and Jimenez-Collado J. 1997b. Development of the human knee joint. *Anat*
1216   *Rec* 248:269-278.
1217 Mikic B, Johnson TL, Chhabra AB, Schalet BJ, Wong M, and Hunziker EB. 2000. Differential
1218   effects of embryonic immobilization on the development of fibrocartilaginous skeletal
1219   elements. *Journal of Rehabilitation Research and Development* 37:127-133.
1220 Mottershead S. 1988. Sesamoid bones and cartilages: an enquiry into their function. *Clinical*
1221   *Anatomy* 1:59-62.
1222 Murray P. 1984. Furry egg layers: the monotreme radiation. In: Archer M, and Clayton G, eds.
1223   *Vertebrate Zoogeography and Evolution in Australasia*. Carlisle: Hesperian press.
1224 Musser AM. 2003. Review of the monotreme fossil record and comparison of palaeontological
1225   and molecular data. *Comp Biochem Physiol A Mol Integr Physiol* 136:927-942.
1226 Neuweiler G. 2000. *The Biology of Bats*. Oxford: Oxford University Press.
1227 Norell MA, and Clarke JA. 2001. Fossil that fills a critical gap in avian evolution. *Nature*
1228   409:181-184.
1229 Nowlan NC, Bourdon C, Dumas G, Tajbakhsh S, Prendergast PJ, and Murphy P. 2010a.
1230   Developing bones are differentially affected by compromised skeletal muscle formation.
1231   *Bone* 46:1275-1285.
1232 Nowlan NC, Sharpe J, Roddy KA, Prendergast PJ, and Murphy P. 2010b. Mechanobiology of
1233   embryonic skeletal development: Insights from animal models. *Birth Defects Res C*
1234   *Embryo Today* 90:203-213.
1235 O'Leary MA, Bloch JI, Flynn JJ, Gaudin TJ, Giallombardo A, Giannini NP, Goldberg SL, Kraatz
1236   BP, Luo ZX, Meng J, Ni X, Novacek MJ, Perini FA, Randall ZS, Rougier GW, Sargis
1237   EJ, Silcox MT, Simmons NB, Spaulding M, Velazco PM, Weksler M, Wible JR, and
1238   Cirranello AL. 2013. The placental mammal ancestor and the post-K-Pg radiation of
1239   placentals. *Science* 339:662-667.
1240 O'Leary MA, and Gatesy J. 2008. Impact of increased character sampling on the phylogeny of
1241   Cetartiodactyla (Mammalia): combined analysis including fossils. *Cladistics* 24:397-442.
1242 Ogden JA. 1984. Radiology of postnatal skeletal development. X. Patella and tibial tuberosity.
1243   *Skeletal Radiol* 11:246-257.
1244 Osborne AC, Lamb KJ, Lewthwaite JC, Dowthwaite GP, and Pitsillides AA. 2002. Short-term
1245   rigid and flaccid paralyses diminish growth of embryonic chick limbs and abrogate joint
1246   cavity formation but differentially preserve pre-cavitated joints. *J Musculoskelet*
1247   *Neuronal Interact* 2:448-456.
1248 Owen R. 1866. *On the Anatomy of Vertebrates*. Cambridge: Cambridge University Press.

1249 Padykula HA, and Taylor JM. 1976. Ultrastructural evidence for loss of the trophoblastic layer in
1250   the chorioallantoic placenta of Australian bandicoots (Marsupialia: Peramelidae). *Anat*
1251   *Rec* 186:357-385.
1252 Pailthorpe CA, Milner S, and Sims MM. 1991. Is patellectomy compatible with an Army career?
1253   *J R Army Med Corps* 137:76-79.
1254 Palastanga N, Field D, and Soames R. 2006. *Anatomy and Human Movement: Structure and*
1255   *Function*: Butterworth-Heinemann.
1256 Parmar VK, Patel KB, Desai MC, Mistry JN, and Chaudhary SS. 2009. Radiographic study on
1257   the first appearance of ossification centres of bones in the goat fetuses : the pelvic limb.
1258   *Indian Journal of Field Veterinarians* 4:6-10.
1259 Patton JT, and Kaufman MH. 1995. The timing of ossification of the limb bones, and growth
1260   rates of various long bones of the fore and hind limbs of the prenatal and early postnatal
1261   laboratory mouse. *J Anat* 186 (Pt 1):175-185.
1262 Pearson K, and Davin AG. 1921a. On the sesamoids of the knee joint. *Biometrika* 13:133-175.
1263 Pearson K, and Davin AG. 1921b. On the sesamoids of the knee joint. Part II. Evolution of the
1264   sesamoids. *Biometrika* 13:350-400.
1265 Pierce SE, Clack JA, and Hutchinson JR. 2012. Three-dimensional limb joint mobility in the
1266   early tetrapod Ichthyostega. *Nature* 486:523-526.
1267 Pina M, Almecija S, Alba DM, O'Neill MC, and Moya-Sola S. 2014. The Middle Miocene ape
1268   Pierolapithecus catalaunicus exhibits extant great ape-like morphometric affinities on its
1269   patella: inferences on knee function and evolution. *PLoS One* 9:e91944.
1270 Pinna MC. 1991. Concepts and tests of homology in the cladistic paradigm. *Cladistics* 7:367-
1271   394.
1272 Polly PD. 2007. Limbs in Mammalian Evolution. In: Hall BK, ed. *Fins into Limbs*. Chicago:
1273   University of Chicago.
1274 Ralphs JR, Benjamin M, and Thornett A. 1991. Cell and matrix biology of the suprapatella in the
1275   rat: a structural and immunocytochemical study of fibrocartilage in a tendon subject to
1276   compression. *Anat Rec* 231:167-177.
1277 Ralphs JR, Benjamin M, Waggett AD, Russell DC, Messner K, and Gao J. 1998. Regional
1278   differences in cell shape and gap junction expression in rat Achilles tendon: relation to
1279   fibrocartilage differentiation. *Journal of Anatomy* 193:215-222.
1280 Ralphs JR, Tyers RN, and Benjamin M. 1992. Development of functionally distinct
1281   fibrocartilages at two sites in the quadriceps tendon of the rat: the suprapatella and the
1282   attachment to the patella. *Anat Embryol (Berl)* 185:181-187.
1283 Raymond KR, and Prothero DR. 2012. Comparative variability of intermembranous and
1284   endochondral bones in Pleistocene mammals. Palaeontologia Electronica.
1285 Reese S, Pfuderer UR, Bragulla H, Loeffler K, and Budras KD. 2001. Topography, structure and
1286   function of the patella and the patelloid in marsupials. *Anat Histol Embryol* 30:289-294.
1287 Regnault S, Jones ME, Pitsillides AA, and Hutchinson JR. 2016. Anatomy, morphology and
1288   evolution of the patella in squamate lizards and tuatara (Sphenodon punctatus). *J Anat*
1289   228:864-876.
1290 Regnault S, Pitsillides AA, and Hutchinson JR. 2014. Structure, ontogeny and evolution of the
1291   patellar tendon in emus (Dromaius novaehollandiae) and other palaeognath birds. *PeerJ*
1292   2:e711.
1293 Rieppel O. 1989. The hindlimb of Macrocnemus bassanii (Nopsca) (Reptilia, Diapsida):
1294   development and functional anatomy. *Journal of Vertebrate Paleontology* 9:373-387.

1295   Riskin DK, and Hermanson JW. 2005. Biomechanics: independent evolution of running in
1296   vampire bats. *Nature* 434:292.
1297   Romer AS. 1976. *Osteology of the Reptiles*. Chicago: University of Chicago.
1298   Rose KD. 1982. Skeleton of diacodexis, oldest known artiodactyl. *Science* 216:621-623.
1299   Rose KD. 1999. Postcranial skeletons of Eocene Leptictidae (Mammalia), and its implications
1300   for behavior and relationships. *Journal of Vertebrate Paleontology* 19:355-372.
1301   Rose KD. 2006. *The Beginning of the Age of Mammals*. Baltimore: Johns Hopkins University
1302   Press.
1303   Rose KD, and Walker A. 1985. The Skeleton of Early Eocene Cantius, Oldest Lemuriform
1304   Primate. *American Journal of Physical Anthropology* 66:73-89.
1305   Rot-Nikcevic I, Reddy T, Downing KJ, Belliveau AC, Hallgrimsson B, Hall BK, and Kablar B.
1306   2006. Myf5-/- :MyoD-/- amyogenic fetuses reveal the importance of early contraction
1307   and static loading by striated muscle in mouse skeletogenesis. *Dev Genes Evol* 216:1-9.
1308   Rowe T. 1988. Definition, diagnosis and origin of Mammalia. *Journal of Vertebrate
1309   Paleontology* 8:241-264.
1310   Rowe T, Rich TH, Vickers-Rich P, Springer M, and Woodburne MO. 2008. The oldest platypus
1311   and its bearing on divergence timing of the platypus and echidna clades. *Proc Natl Acad
1312   Sci U S A* 105:1238-1242.
1313   Samuels JX, Meachen JA, and Sakai SA. 2013. Postcranial morphology and the locomotor habits
1314   of living and extinct Carnivorans *J Morphol* 274:121-146.
1315   Sanchez-Villagra M, Ladeveze S, Horovitz I, Argot C, Hooker JJ, Macrini TE, Martin T, Moore-
1316   Fay S, de Muizon C, Schmelzle T, and Asher RJ. 2007. Exceptionally preserved North
1317   American Paleogene metatherians: adaptations and discovery of a major gap in the
1318   opossum fossil record. *Biol Lett* 3:318-322.
1319   Sarin VK, and Carter DR. 2000a. Mechanobiology and joint conformity regulate endochondral
1320   ossification of sesamoids. *J Orthop Res* 18:706-712.
1321   Sarin VK, and Carter DR. 2000b. Mechanobiology and joint conformity regulate endochondral
1322   ossification of sesamoids. *06-712Journal of Orthopaedic Research* 18:7.
1323   Sarin VK, Erickson GM, Giori NJ, Bergman AG, and Carter DR. 1999. Coincident development
1324   of sesamoid bones and clues to their evolution. *Anat Rec* 257:174-180.
1325   Scapinelli R. 1963. Sesamoid Bones in the Ligamentum Nuchae of Man. *J Anat* 97:417-422.
1326   Schaal S, and Ziegler W. 1992. Messel: An insight into the history of life and of the earth.
1327   London: Clarendon Press.
1328   Schlosser M. 1887. Die Affen, Lemuren, Chiropteren, Insectivoren, Marsupialen, Creodonten
1329   und Carnivoren des europaischen Tertiars und deren Beziehungen zu ihren lebenden und
1330   fossilen aussereuropaischen Verwandten. In: Mojsisovics Ev, and Neumayr M, eds.
1331   *Beitrage zur Palaontologie osterreich-ungarns und des orients*. Wien: Holder, 1-162.
1332   Schutt WA, and Simmons NB. 2006. Quadrupedal Bats: Form, Function and Evolution. In:
1333   Zubaid A, McCracken GF, and Kunz TH, eds. *Functional and Evolutionary Ecology of
1334   Bats*. Oxford: Oxford University Press.
1335   Schuurman SO, Kersten W, and Weijs WA. 2003. The equine hind limb is actively stabilized
1336   during standing. *J Anat* 202:355-362.
1337   Shubin NH, Daeschler EB, and Jenkins FA, Jr. 2006. The pectoral fin of Tiktaalik roseae and the
1338   origin of the tetrapod limb. *Nature* 440:764-771.
1339   Shufeldt RW. 1884. Concerning some of the forms assumed by the patella in birds. *Proceedings
1340   of the United States National Museum* 7:324-331.

1341 Silcox MT. 2007. Primate Taxonomy, Plesiadapiforms, and Approaches to Primate Origins. In:
1342   Ravoso MJ, and Dagosto M, eds. *Primate Origins: Adaptations and Evolution*. New
1343   York: Springer, 143-178.
1344 Smith BJ, Holladay SD, and Smith SA. 1995. Patella of selected bats: patterns of occurrence or
1345   absence and associated modifications of the quadriceps femoris tendon. *Anat Rec*
1346   242:575-580.
1347 Smith HF, Parker W, Kotze SH, and Laurin M. 2013. Multiple independent appearances of the
1348   cecal appendix in mammalian evolution and an investigation of related ecological and
1349   anatomical factors. *Comptes Rendus Palevol*.
1350 Song S, Liu L, Edwards SV, and Wu S. 2012. Resolving conflict in eutherian mammal
1351   phylogeny using phylogenomics and the multispecies coalescent model. *Proc Natl Acad*
1352   *Sci U S A* 109:14942-14947.
1353 Spark C, and Dawson AB. 1928. The order and time of appearance of centers of ossification in
1354   the fore and hind limbs of the albino rat, with special reference to the possible influence
1355   of the sex factor. *Developmental Dynamics* 41:411-445.
1356 Spaulding M, O'Leary MA, and Gatesy J. 2009. Relationships of Cetacea (Artiodactyla) among
1357   mammals: increased taxon sampling alters interpretations of key fossils and character
1358   evolution. *PLoS One* 4:e7062.
1359 Springer MS, Burk-Herrick A, Meredith R, Eizirik E, Teeling E, O'Brien SJ, and Murphy WJ.
1360   2007. The adequacy of morphology for reconstructing the early history of placental
1361   mammals. *Syst Biol* 56:673-684.
1362 Springer MS, Murphy WJ, Eizirik E, and O'Brien SJ. 2003. Placental mammal diversification
1363   and the Cretaceous-Tertiary boundary. *Proc Natl Acad Sci U S A* 100:1056-1061.
1364 Sweetnam R. 1964. Patellectomy. *Postgrad Med J* 40:531-535.
1365 Szalay FS, and Sargis EJ. 2001. Model-based analysis of postcranial osteology of marsupials
1366   from the Palaeocene of Itaboraí (Brazil) and the phylogenetics and biogeography of
1367   Metatheria. *Geodiversitas* 23:139-302.
1368 Szalay FS, Tattersall I, and Decker RL. 1975. Phyogenetic Relationships of Pleasiadapis -
1369   Postcranial Evidence. In: Szalay FS, ed. *Approaches to Primate Paleobiology*. Basel:
1370   Karger.
1371 Szalay FS, and Trofimov BA. 1996. The Mongolian late Cretaceous Asiatherium, and the early
1372   phylogeny and paleobiogeography of metatheria. *Journal of Vertebrate Paleontology*
1373   16:474-509.
1374 Tecklenburg K, Dejour D, Hoser C, and Fink C. 2006. Bony and cartilaginous anatomy of the
1375   patellofemoral joint. *Knee Surg Sports Traumatol Arthrosc* 14:235-240.
1376 Thewissen JG. 1990. Evolution of Paleocene and Eocene Phenacodontidae (Mammalia,
1377   Condylarthra). *Papers on Paleontology University of Michigan* 29:1-107.
1378 Thewissen JG, Cooper LN, Clementz MT, Bajpai S, and Tiwari BN. 2007. Whales originated
1379   from aquatic artiodactyls in the Eocene epoch of India. *Nature* 450:1190-1194.
1380 Thewissen JG, Williams EM, Roe LJ, and Hussain ST. 2001. Skeletons of terrestrial cetaceans
1381   and the relationship of whales to artiodactyls. *Nature* 413:277-281.
1382 Thompson D. 1890. On the systematic position of Hesperornis. *Studies from the Museum of*
1383   *Zoology in University College, Dundee* 1:97-112.
1384 Toumi H, Higashiyama I, Suzuki D, Kumai T, Bydder G, McGonagle D, Emery P, Fairclough J,
1385   and Benjamin M. 2006. Regional variations in human patellar trabecular architecture and
1386   the structure of the proximal patellar tendon enthesis. *J Anat* 208:47-57.

1387   Toumi H, Larguech G, Filaire E, Pinti A, and Lespessailles E. 2012. Regional variations in
1388   human patellar trabecular architecture and the structure of the quadriceps enthesis: a
1389   cadaveric study. *J Anat* 220:632-637.
1390   Tria AJ, Jr., and Alicea JA. 1995. Embryology and Anatomy of the Patella. In: Scuderi GR, ed.
1391   *The Patella*. New York: Springer-Verlag.
1392   Uhen MD. 2004. Form. function and anatomy of Dorudon atrox (Mammalia, Cetacea): an
1393   archaeocete from the middle to late Eocene of Egypt. University of Michigan Papers on
1394   Palaeontology. Ann Arbor: University of Michigan.
1395   Valois H. 1917. La valeur morphologique de la rotule chez les mammifères. *Bulletins et
1396   Mémoires de la Société d'anthropologie de Paris* 8:1-34.
1397   Vanden Berge JL, and Storer RW. 1995. Intratendinous ossification in birds: a review. *J
1398   Morphol* 226:47-77.
1399   Vickaryous MK, and Olson WM. 2007. Sesamoids and Ossicles in the Appendicular Skeleton.
1400   In: Hall BK, ed. *Fins into Limbs*. Chicago: University of Chicago.
1401   Walji AH, and Fasana FV. 1983. Structural and functional organization of the suprapatella in
1402   two cercopithecines. *J Morphol* 176:113-119.
1403   Walmsley R. 1940. Development of the patella. *Journal of Anatomy* 73:360-368.
1404   Walsh SA, and Suarez ME. 2006. New penguin remains from the Pliocene of northern Chile.
1405   *Historical Biology: An International Journal of Paleobiology* 18:119-130.
1406   Warren WC, Hillier LW, Marshall Graves JA, Birney E, Ponting CP, Grutzner F, Belov K,
1407   Miller W, Clarke L, Chinwalla AT, Yang SP, Heger A, Locke DP, Miethke P, Waters
1408   PD, Veyrunes F, Fulton L, Fulton B, Graves T, Wallis J, Puente XS, Lopez-Otin C,
1409   Ordonez GR, Eichler EE, Chen L, Cheng Z, Deakin JE, Alsop A, Thompson K, Kirby P,
1410   Papenfuss AT, Wakefield MJ, Olender T, Lancet D, Huttley GA, Smit AF, Pask A,
1411   Temple-Smith P, Batzer MA, Walker JA, Konkel MK, Harris RS, Whittington CM,
1412   Wong ES, Gemmell NJ, Buschiazzo E, Vargas Jentzsch IM, Merkel A, Schmitz J,
1413   Zemann A, Churakov G, Kriegs JO, Brosius J, Murchison EP, Sachidanandam R, Smith
1414   C, Hannon GJ, Tsend-Ayush E, McMillan D, Attenborough R, Rens W, Ferguson-Smith
1415   M, Lefevre CM, Sharp JA, Nicholas KR, Ray DA, Kube M, Reinhardt R, Pringle TH,
1416   Taylor J, Jones RC, Nixon B, Dacheux JL, Niwa H, Sekita Y, Huang X, Stark A,
1417   Kheradpour P, Kellis M, Flicek P, Chen Y, Webber C, Hardison R, Nelson J, Hallsworth-
1418   Pepin K, Delehaunty K, Markovic C, Minx P, Feng Y, Kremitzki C, Mitreva M,
1419   Glasscock J, Wylie T, Wohldmann P, Thiru P, Nhan MN, Pohl CS, Smith SM, Hou S,
1420   Nefedov M, de Jong PJ, Renfree MB, Mardis ER, and Wilson RK. 2008. Genome
1421   analysis of the platypus reveals unique signatures of evolution. *Nature* 453:175-183.
1422   Wentink GH. 1978. Biokinetical analysis of the movements of the pelvic limb of the horse and
1423   the role of the muscles in the walk and the trot. *Anat Embryol (Berl)* 152:261-272.
1424   Westerman M, Kear BP, Aplin K, Meredith RW, Emerling C, and Springer MS. 2012.
1425   Phylogenetic relationships of living and recently extinct bandicoots based on nuclear and
1426   mitochondrial DNA sequences. *Mol Phylogenet Evol* 62:97-108.
1427   Wible JR, Rougier GW, and Novacek MJ. 2005. Anatomical evidence for superordinal/ordinal
1428   eutherian taxa in the Cretaceous. *The Rise of Placental Mammals*. Baltimore: Johns
1429   Hopkins University Press, 15-36.
1430   Wible JR, Rougier GW, Novacek MJ, and Asher RJ. 2007. Cretaceous eutherians and Laurasian
1431   origin for placental mammals near the K/T boundary. *Nature* 447:1003-1006.

1432   Wilson DE, and Reeder DM. 2005. Mammal Species of the World. 3rd ed. Baltimore: Johns
1433   Hopkins University Press.
1434   Wilson GP, Evans AR, Corfe IJ, Smits PD, Fortelius M, and Jernvall J. 2012. Adaptive radiation
1435   of multituberculate mammals before the extinction of dinosaurs. *Nature* 483:457-460.
1436   Wren TA, Beaupre GS, and Carter DR. 2000. Mechanobiology of tendon adaptation to
1437   compressive loading through fibrocartilaginous metaplasia. *J Rehabil Res Dev* 37:135-
1438   143.
1439   Yuan CX, Ji Q, Meng QJ, Tabrum AR, and Luo ZX. 2013. Earliest evolution of multituberculate
1440   mammals revealed by a new Jurassic fossil. *Science* 341:779-783.
1441   Zack SP, Penkrot TA, Krause DW, and Maas MC. 2005. A new apheliscine "condylarth"
1442   mammal from the late Paleocene of Montana and Alberta and the phylogeny of
1443   "hyopsodontids". *Acta Palaeontologica Polonica* 50:809-830.
1444   Zalmout IS. 2008. Late Eocene sea cows (Mammalia, Sirenia) from Wadi al Hitan in the Fayum
1445   Basin, Egypt. University of Michigan.
1446   Zheng X, Bi S, Wang X, and Meng J. 2013. A new arboreal haramiyid shows the diversity of
1447   crown mammals in the Jurassic period. *Nature* 500:199-202.
1448   Zhou CF, Wu S, Martin T, and Luo ZX. 2013. A Jurassic mammaliaform and the earliest
1449   mammalian evolutionary adaptations. *Nature* 500:163-167.
1450

1451   FIGURES

1452

1453   Figure 1. Generalized knee showing sesamoid bones found in various mammals, although

1454   possibly no species includes all of these (patella, lunula, cyamella, fabella and parafibula). Also

1455   shown are relevant muscles, ligaments and other anatomical elements that lie close to the

1456   sesamoids of the knee joint. The knee is in medial view and the medial collateral ligament has

1457   been removed.

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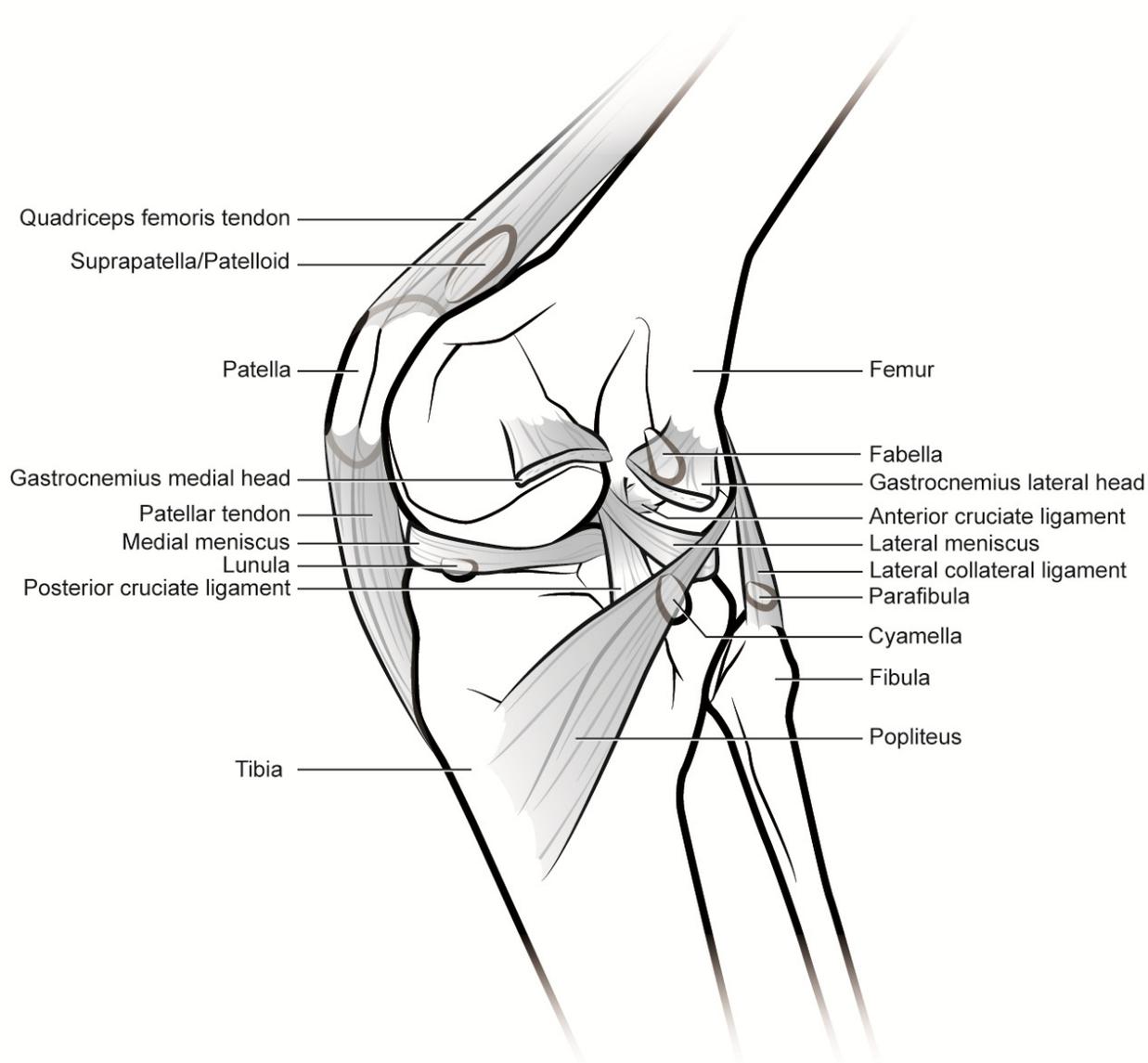
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1460   Figure 2. Generalized tetrapod with anatomical/developmental axes defined for the hindlimb:

1461   cranial/caudal (towards the head/tail respectively), proximal/distal (toward/further from the trunk

1462   respectively), dorsal/ventral (towards the back/belly respectively).

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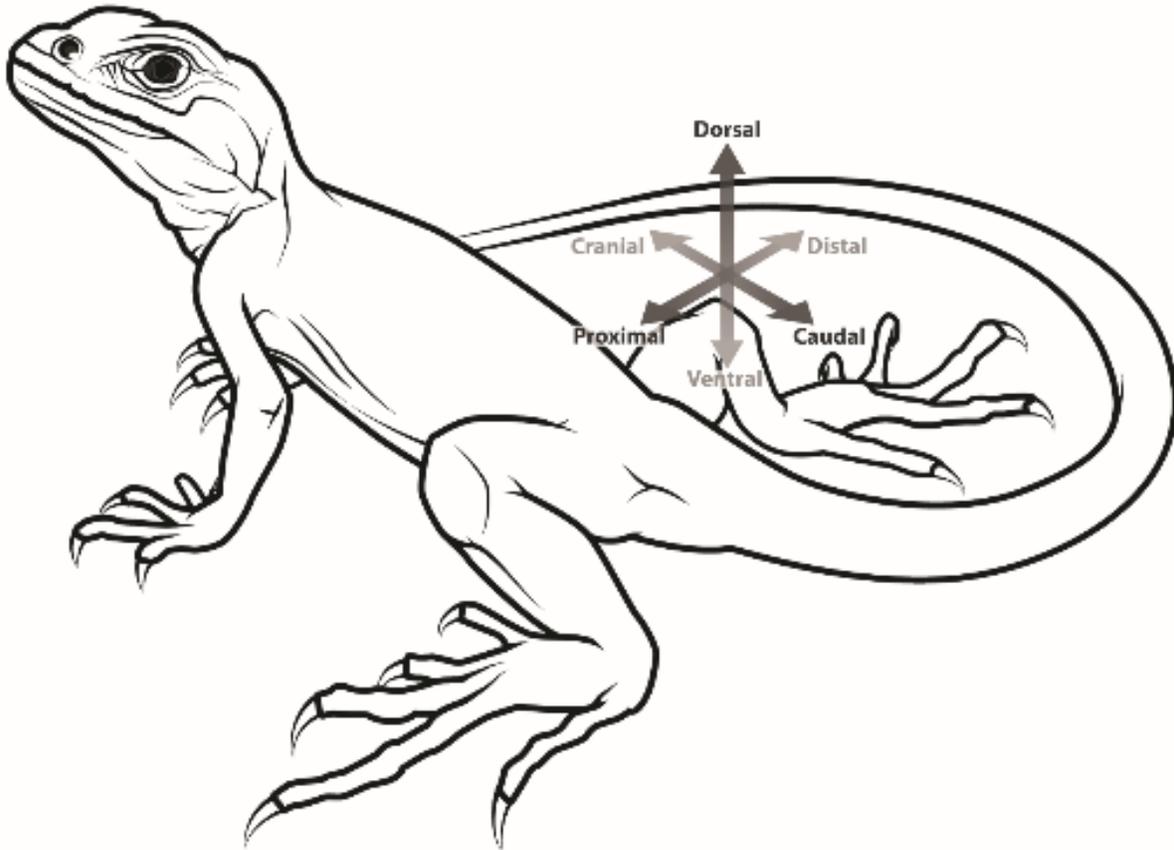
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1465   Figure 3. Reconstruction of ancestral patellar states in Tetrapoda, showing the major extant

1466   clades. Reconstruction was performed using Mesquite's parsimony algorithm and unordered

1467   character states, where 0 (black) = absent patella, 1 (yellow) = soft tissue patella/patelloid, and 2

1468   (blue) = ossified patella; see Methods for further details. The distribution of the ossified patella

1469   among extant clades has been interpreted as three occasions of independent evolution (in Aves,

1470   Squamata, and Mammalia) (Dye, 1987, Haines, 1940), a conclusion strongly reinforced by

1471   specific fossil evidence (absence or equivocality of a patella in all outgroups). Reconstruction

1472   within Mammalia is explored in more depth in Figures 5-7. MYA= millions of years from

1473   present.

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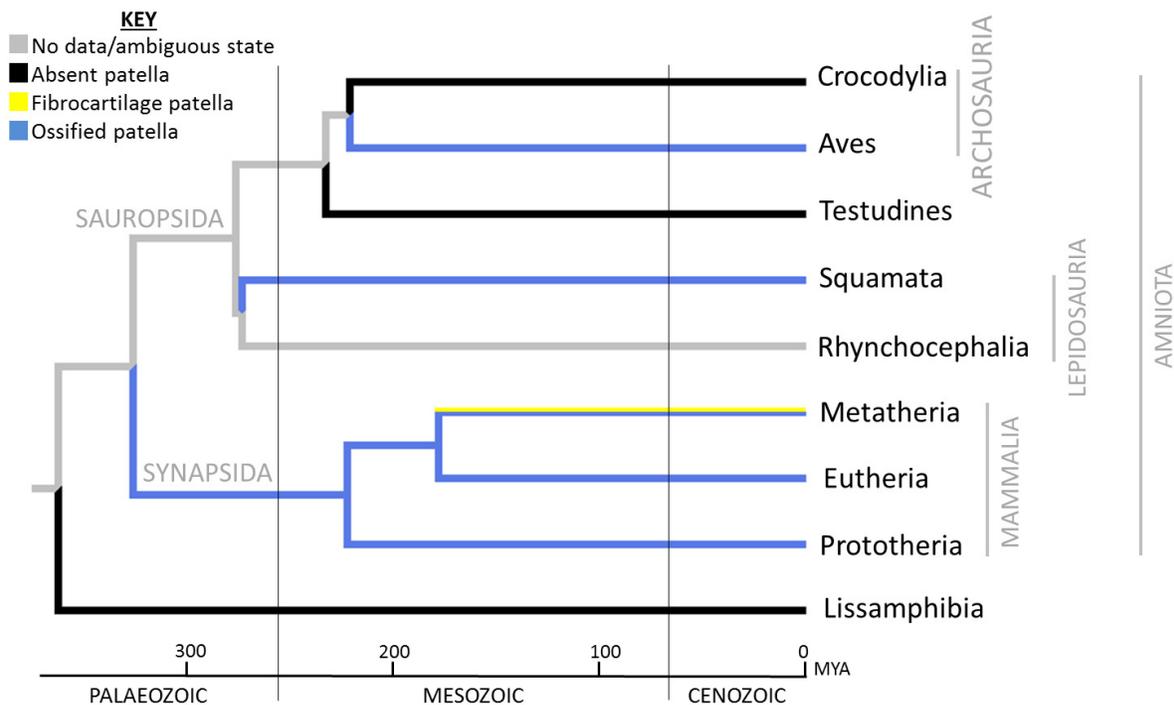
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1476   Figure 4. Examples of tetrapods with or without patellae. A, B. *Ornithorhynchus anatinus*

1477   (Monotremata: duck-billed platypus, Redpath Museum specimen 2458). C, D. *Tachyglossus*

1478   *aculeatus* (Monotremata: echidna, Redpath Museum specimen 2463). E, F. *Didelphis virginiana*

1479   (Metatheria: North American opossum, Redpath Museum specimen 5019). G, H. *Procavia*

1480   *capensis* (Eutheria: Afrotheria: Cape hyrax, Uncatalogued Horniman Museum specimen,

1481   London, UK). I, knee of patient with Meier-Gorlin Syndrome (Guernsey et al. 2010). For more

1482   images of mammalian patellae (or lack thereof in some marsupials), see Figures S1-S3.

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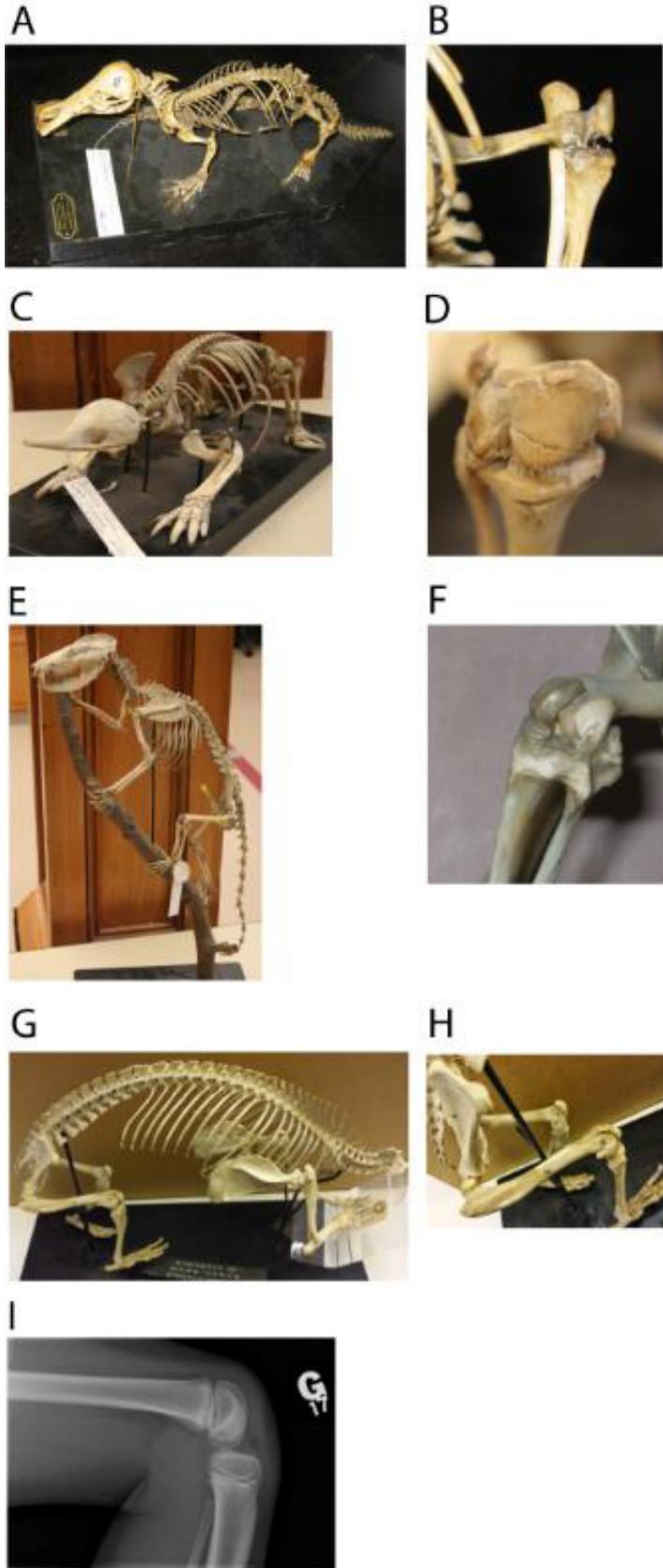
1484

1485   Figure 5. Reconstruction of ancestral patellar state in Mesozoic mammals, using Mesquite's

1486   parsimony algorithm and unordered character states, where 0 (black) = absent patella, 1 (yellow)

1487   = soft tissue (i.e. fibrocartilaginous in adults) patella/patelloid, and 2 (blue) = ossified patella.

1488   Uncertain patellar state is indicated by grey branches and question mark (?) following taxon

1489   name, and key fossils with hindlimb material are denoted by †. This reconstruction suggests that

1490   a bony patellar sesamoid has evolved at least five times within Mammaliaformes. Reconstruction

1491   using ordered parsimony and maximum likelihood methods similarly resulted in five instances of

1492   ossified patellar evolution. An alternative topology with †*Eomaia* placed on the therian stem

1493   (after O'Leary et al., 2013), shown in Figure S4, similarly found 4-6 instances of bony patella

1494   evolution. Evolution within Metatheria is explored in more detail in Figure 6, and within

1495   Eutheria in Figure 7. MYA= millions of years from present.

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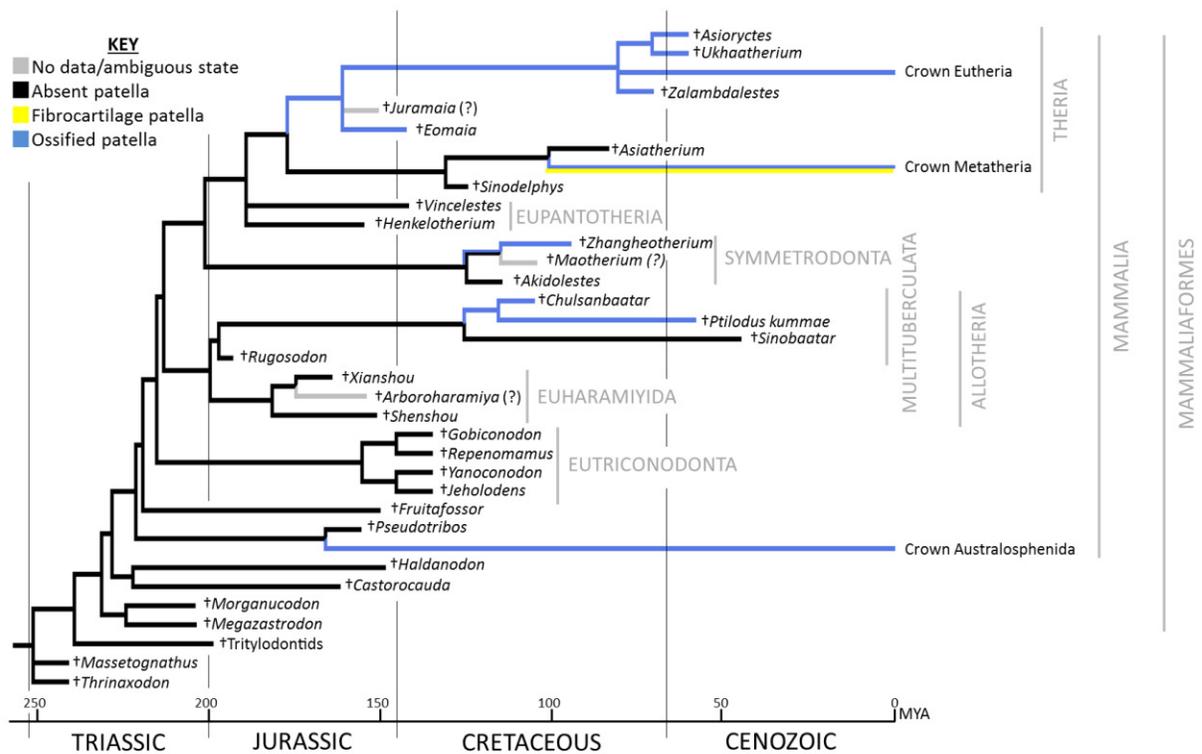
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1498   Figure 6. Reconstruction of ancestral patellar state in Metatheria, using Mesquite's parsimony

1499   algorithm and unordered character states, where 0 (black) = absent patella, 1 (yellow) = soft

1500   tissue (i.e. fibrocartilaginous in adults) patella/patelloid, and 2 (blue) = ossified patella. Uncertain

1501   patellar state is indicated by grey branches and question mark (?) following taxon name, and key

1502   fossils with hindlimb material are denoted by †. The reconstruction suggests that the ossified

1503   patella evolved between 1-5 times in Metatheria, with loss and reversion (to a fibrocartilaginous

1504   patella/patelloid and back) or as independent instances. States 0 (no patella) and 1 (fibrocartilage

1505   patella in adults) are equally parsimonious at the base of the tree. Ordered parsimony

1506   reconstruction yields similar results but state 1 is most parsimonious ancestrally. Maximum

1507   Likelihood analysis results in five independent instances of patellar evolution (in Borhyaenoidea,

1508   Caenolestidae, Notoryctidae, Thylacomyidae + Peramelidae, and Tarsipedidae), with an

1509   ancestral state of either 0 or 1 depending on the states assigned to the earliest fossils such as

1510   *Sinodelphys*. An alternative topology with Microbiotheriidae nested slightly further within

1511   Marsupialia (after May-Collado et al., 2015), shown in Figure S5, similarly shows between 1-5

1512   instances of bony patella evolution but with more internodes of ambiguous character state (i.e.

1513   equivocal between states 1 and 2). MYA= millions of years from present.

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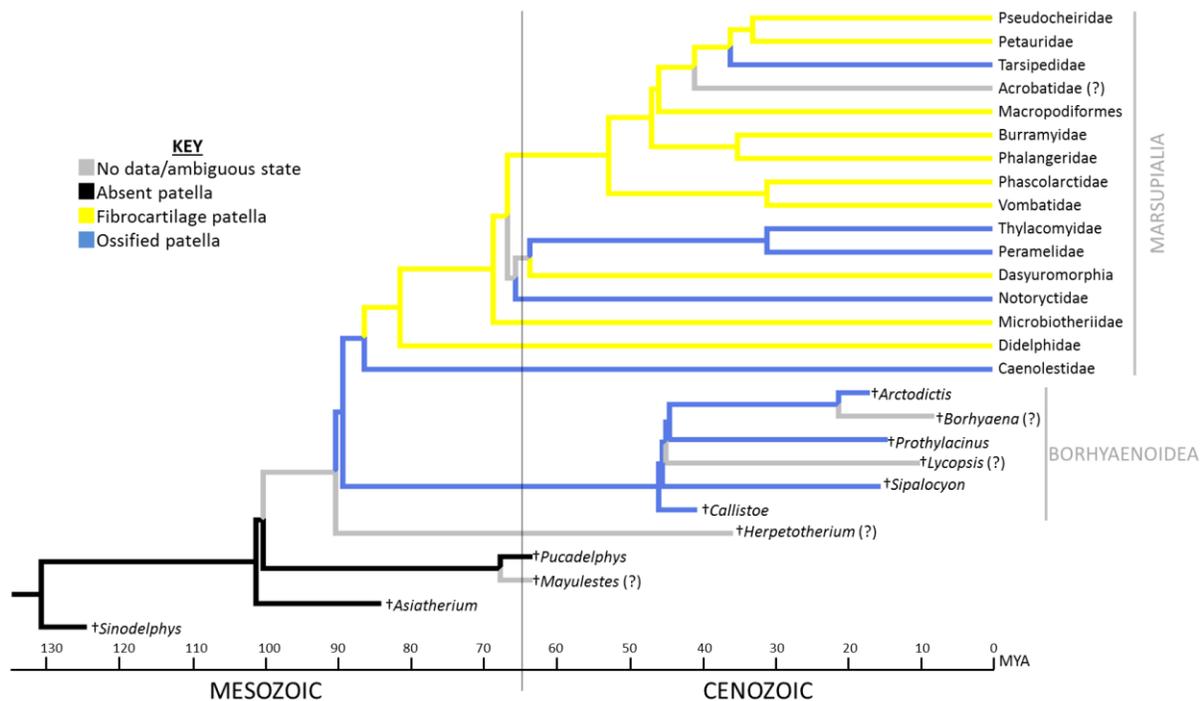
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1517   Figure 7. Reconstruction of ancestral patellar state in Eutheria, using Mesquite's parsimony

1518   algorithm and unordered character states, where 0 (black) = absent patella, 1 (yellow) = soft

1519   tissue (i.e. fibrocartilaginous in adults) patella/patelloid (state not present in Eutheria other than

1520   some bats; see main text), and 2 (blue) = ossified patella. Uncertain patellar state is indicated by

1521   grey branches and question mark (?) following taxon name, and key fossils with hindlimb

1522   material are denoted by †. Our reconstruction suggests that the ossified patella evolved only once

1523   within Eutheria and (as far as is currently known) has only been lost by the bat genus *Pteropus*

1524   (not counting groups which have lost hindlimbs; e.g. *Trichechus manatus*/crown Sirenia,

1525   *Tursiops truncates*/crown Cetacea). Taxa within Euarchontoglires (e.g. rats, mice, guinea pigs,

1526   rabbits, most primates), some Carnivora, and possibly some Chiroptera have been found to

1527   possess a suprapatellar structure similar to the patelloid, shown by vertical black bars at the

1528   appropriate branches. MYA= millions of years from present, Pε = Paleocene, Eo = Eocene, OG

1529   = Oligocene, MI = Miocene (most recent Cenozoic epochs not labelled).

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1531