

Evolution of pinniped UCP1 is not linked to aquatic life but to neonatal thermogenesis and body size

Michael J. Gaudry^a , Thomas Jacob Fyda^a, and Martin Jastroch^{a,1}

Yuan et al. (1) sequenced the genomes of 17 marine mammals, providing an excellent basis to further elucidate mammalian aquatic evolution. Surprisingly, in their examination of the previously published Antarctic fur seal (*Arctocephalus gazella*) genome (2), Yuan et al. report the pseudogenization of uncoupling protein 1 (*UCP1*), the key driver of brown adipose tissue (BAT)-mediated nonshivering thermogenesis (NST) (3), concluding that this underscores the strategic importance of prioritizing insulation rather than heat production in aquatic marine mammals. Notably, the Antarctic fur seal is the most polar pinniped species examined in the dataset and, hence, most expected

to rely on *UCP1*-mediated NST during cold exposure, all other factors set aside (allometry, insulation, etc.). Therefore, we aimed to verify this *UCP1* pseudogenization by comprehensively examining the raw Sequence Read Archive (SRA) data of the Antarctic fur seal.

We contest that, while the assembled Antarctic fur seal genome does display seeming mutations in *UCP1* exons 1 and 6 (Accession: UIRR01000066.1), these are not supported by SRA data. We retrieved 170 sequence reads from the SRA database (Accession: SRX1338453–SRX1338509) spanning these sites of contention, all of which reveal that the

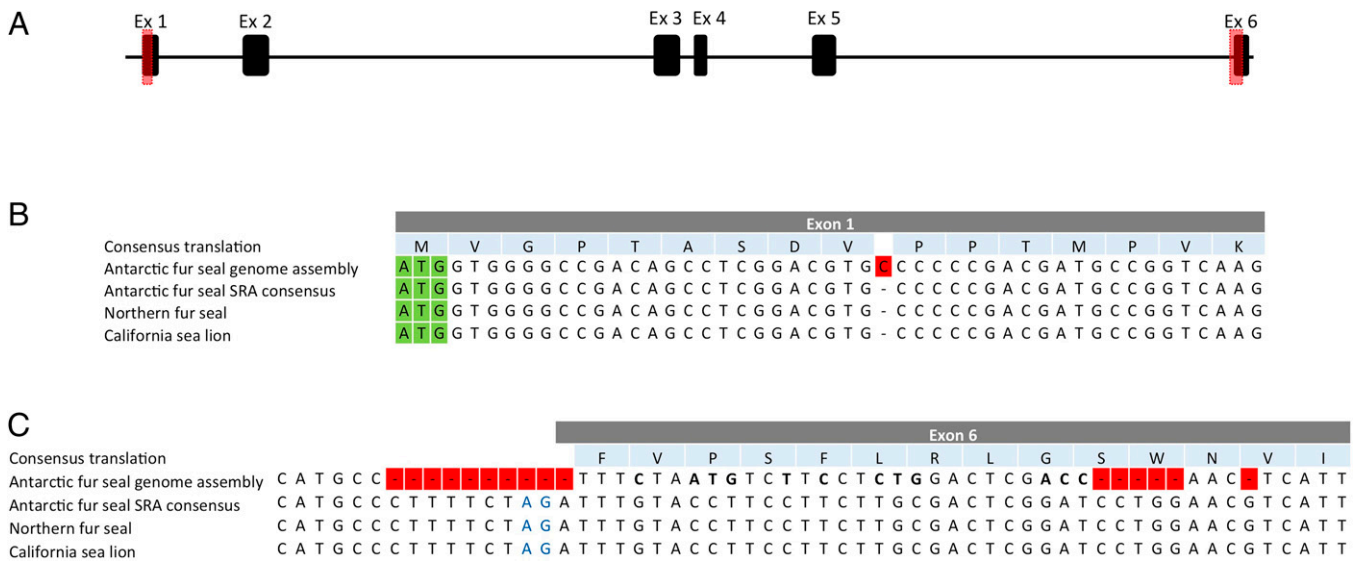


Fig. 1. Schematic of the *UCP1* gene (A) with red regions highlighting the locations of exon 1 (B) and exon 6 (C) alignments of the Antarctic fur seal (*A. gazella*) genome (Accession: UIRR01000066.1), SRA consensus sequence (Accession: SRX1338453–SRX1338509), northern fur seal (*Callorhinus ursinus*; Accession: QLOG01010939.1), and California sea lion (*Zalophus californianus*; Accession: PISZ01002091.1). The ATG start site of exon 1 and nucleotides comprising the AG splice site of intron 5 are highlighted in green and blue, respectively. The apparent frame-shift mutations of the misassembled Antarctic fur seal genome are highlighted in red, while the SRA consensus reveals the highly conserved true identities of these sites. The consensus amino acid virtual translation is shown above the nucleotide alignment.

^aDepartment of Molecular Biosciences, The Wenner-Gren Institute, Stockholm University, Stockholm SE-106 91, Sweden

Author contributions: M.J.G. designed research; M.J.G. performed research; M.J.G. and T.J.F. analyzed data; and M.J.G. and M.J. wrote the paper.

The authors declare no competing interest.

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¹To whom correspondence may be addressed. Email: martin.jastroch@su.se.

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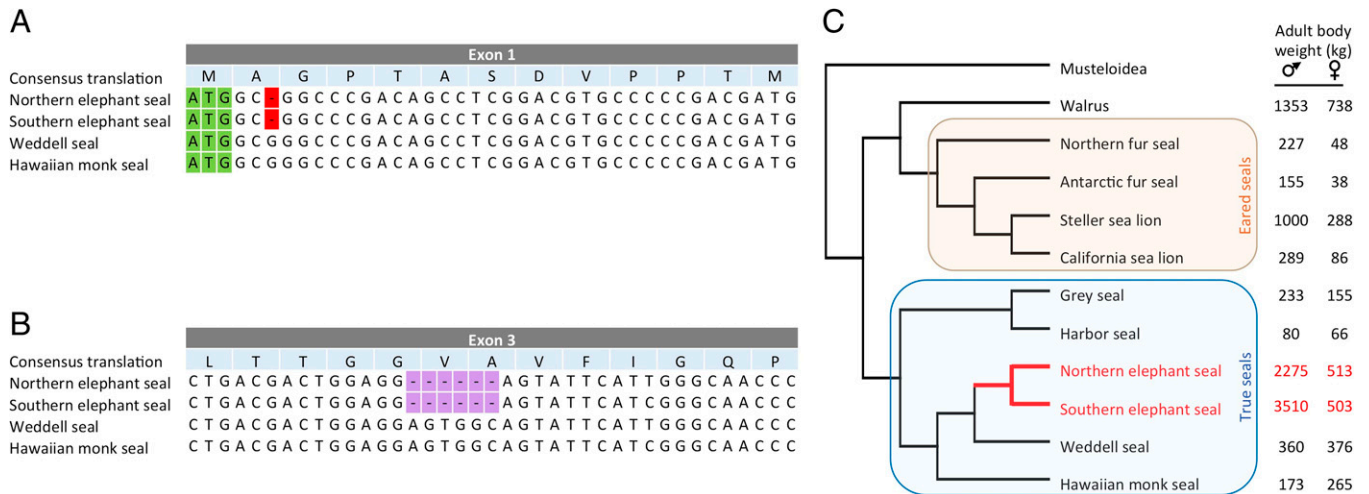


Fig. 2. Alignment of the northern elephant seal (*M. angustirostris*; Accession: PITE01002540.1) and southern elephant seal (*M. leonina*; Accession: JAAMPH010000052.1) potential *UCP1* pseudogenes displaying an early frameshift mutation (red) in exon 1 following the ATG start site (green) (A) and a 6-bp in-frame deletion in exon 3 (purple) (B) in comparison to the intact loci of the Hawaiian monk seal (*Neomonachus schauinslandii*; Accession: NINY01007775.1) and Weddell seal (*Leptonychotes weddellii*; Accession: APMU01141180.1 and APMU01115166.1). The consensus amino acid virtual translation is shown above the nucleotide alignment. (C) Phylogeny of pinnipeds (based on refs. 1 and 9), with adult male and female body weights (4). Lineages with black branches indicate intact *UCP1*, while red branches of the elephant seals denote apparent *UCP1* pseudogenes.

Antarctic fur seal retains an intact highly conserved *UCP1* locus (Fig. 1). The raw data strongly suggest genome misassemblies rather than authentic sites of inactivation. Thus, the intact Antarctic fur seal *UCP1* remains under strong selective pressures likely due to the cold ecological niche exploited by the species.

Instead, we highlight that, if at all, the only pinnipeds exhibiting potential *UCP1* pseudogenes are the northern and southern elephant seals (*Mirounga angustirostris* and *Mirounga leonina*, respectively), which have, unfortunately, not been examined by Yuan et al. (1). Both species share a frameshift deletion in exon 1 that may produce a nonsensical messenger RNA or at least a truncated open reading frame, and a unique 6-bp in-frame deletion in exon 3 (Fig. 2). Interestingly, elephant seals are the largest extant pinnipeds and carnivores, with males reaching up to ~3,500 kg (despite massive body size sexual dimorphism) (4). Southern elephant seal pups are ~38 kg at birth and, remarkably, gain over 3 kg/d before weaning at ~22 d and ~120 kg (5). Thus, we posit that *UCP1* pseudogenization in pinnipeds is not linked to aquatic life but to the evolution of large body size.

While we generally agree with the conclusion that insulation rather than *UCP1*-mediated NST is prioritized in aquatic marine mammals given the high thermal conductivity of water (~24.1 times higher than air) (6), we assert that only fully aquatic mammals (cetaceans and sirenians) support this conclusion. Indeed, several pinnipeds are known to display both BAT and *UCP1* as neonates (7), presumably the most critical life stage for supplemental heat production. The overwhelming retention and conservation of *UCP1* in this lineage of semiaquatic mammals, including the Antarctic fur seal, is instead an indicator of the importance of NST when birthing and rearing young on land, while *UCP1* inactivation in elephant seals is linked to body size, as suggested previously for other terrestrial mammals (6, 8).

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