In the Siberian cat breed, two variants were identified in the \textit{CORIN} (Corin, serine peptidase) gene, a suppressor of the \textit{ASIP} (agouti signaling protein) pathway (Enshell-Seijffers et al., 2008) that causes golden coat modifications characterized by enlarged subapical phaeomelanin bands in hairs and reduced dark tips (Abitbol et al., 2022; Beauvois et al., 2021). These modifications, called sunshine and extreme-sunshine, are similar to the golden modification of tigers (Xu et al., 2017). In British cats, breeders from Germany and Russia have reported since the 2010s a coat modification that is distinct from the known golden shaded (Vella et al., 1999) and golden ticked phenotypes (Lyons et al., 2021). This modification was supposed to be polygenic as several phenotypes differing in their warm tone and countershading were observed, ranging from a classical golden ticked phenotype to a ‘copper’ phenotype characterized by a red mantle with marked ivory belly and ivory spots on the upper sides of the paws (Figure 1a–d). However, careful examination of pedigree data indicated a probable autosomal...
recessive inheritance pattern. DNA and phenotypic data from these copper British cats and from control cats were collected. Twenty-five British cats (including 10 copper cats) were genotyped using the Illumina Feline 63k SNP array, among which 60,599 SNPs yielded usable results (minor allele frequency >5%, genotyping
FIGURE 1 The copper phenotype in British cats is governed by a CORIN nonsense allele. (a) Golden ticked phenotype in a black tabby British cat. Note the blonde tone and the agouti phenotype owing to agouti banded hairs. (b–d) Copper phenotype variations in black tabby British cats. (b) Note the red tone with a discrete lightening of the belly, ivory marks on the uppersides of the paws and the black tail tip. (c) Note the blonde to apricot tone with marked ivory belly and ivory marks on the uppersides of the paws. (d) Note the red mantle with marked light ivory to white belly and large ivory marks on the uppersides of the paws. The three copper cats (b–d) were $T/T$ homozygous for the CORIN:c.2425C>T variant and showed tipped hairs. The golden ticked cat (a) showed agouti ticked hairs and was heterozygous for the CORIN:c.2425C>T variant (Table S3, Figure S2). (e) Manhattan plot of the genome-wide association study. The plots represent the $P_{raw}$ and $P_{Bonferroni}$ values of each SNP included in the case–control association study. The association study compared the 10 copper British cats with 15 control British cats. A suggestive association with chromosome B1 was detected. The three SNPs with the highest association were chrB1.188265817, chrB1.188367525 and chrB1.188505613, with a $P_{raw}$ value of $2.21 \times 10^{-7}$ and a $P_{Bonferroni}$ value of 0.11 (Table S1). UN, Unknown. (f) Schematic of the 13 domains of CORIN (Appendix S1). The CORIN:c.839G>A missense variant of extreme-sunshine Siberian cats, the CORIN:c.1759C>T missense variant of golden tigers and the CORIN:c.2383C>T missense variant of sunshine Siberian cats are depicted in black. The CORIN:c.2425C>T nonsense variant of copper British cats is depicted in red. 

rate >95%). All 25 cats had genotyping rates >95% and all were conserved for the analysis. Following basic case–control analysis, the genomic inflation factor was 1.59 and the 25 highest significant associations were identified for 25 SNPs, among which 18 markers were located on chromosome B1 (Appendix S1, Figure 1e, Table S1). After Bonferroni correction of the $P_{raw}$ values for multiple tests, no SNP had a significant $P_{Bonferroni}$ value (Figure 1e, Table S1). Seventeen of the 18 SNPs from chromosome B1 were located between position 164738782 bp and position 175627824 bp (Table S1) according to Felis_catus 9.0 reference genome and defined the genome-wide association study candidate region. This region contains a strong candidate gene, CORIN (chromosome B1: 167 578 182 bp to 167835768 bp, Felis_catus 9.0). Exons and exon–intron boundaries from CORIN were sequenced in two copper cats and compared with the reference feline sequence (Appendix S1, Table S2). Three variants were identified. We found the previously described CORIN:c.1449C>G SNP (rs43981625, ensembl.org; Beauvois et al., 2021) predicted to be a neutral variant (Appendix S1) and a synonymous CORIN:c.2684C>T variant. In exon 19, we found that the two copper cats were $T/T$ homozygous for a CORIN:c.2425C>T nonsense variant predicted to change an arginine at position 809 in the protein into a stop codon: CORIN:p.(Arg809Ter).

We genotyped a total of 84 British cats for the CORIN:c.2425C>T variant. All 30 copper cats were $T/T$ homozygous. The copper cat group included cats with or without a marked ivory belly but showing a gold to red tone and ivory marks on the uppersides of the paws (Figure 1b–d). Among 54 British control cats, 20 were $C/T$ heterozygous for the CORIN:c.2425C>T variant and included five copper obligate carriers. Additionally, in the group of 17 golden ticked and golden shaded British control cats, 13 individuals were $C/T$ heterozygous and four cats were wild-type homozygous (Table S3).

We searched for the CORIN:c.2425C>T variant in the 340 cats of the 99 Lives Cat Genome Consortium for sharing feline genome sequence information and Caroline Dufaure de Citres (Antagene) for technical assistance. The authors thank the owners, breeders and feline judges for providing samples, hairs and pictures, especially Elizaveta Lipovenko, Linda Persson-Wahlqvist and Eleonora Ruggiero for their great help. Feline DNA samples are part of the Feli-DNA biobank, which is part of the CRB-Anim infrastructure (ANR-11-INBS-0003, in the framework of the ‘Investing for the Future’ program, PLAl).

ACKNOWLEDGEMENTS
The authors wish to thank the 99 Lives Cat Genome Consortium for sharing feline genome sequence information and Caroline Dufaure de Citres (Antagene) for technical assistance. The authors thank the owners, breeders and feline judges for providing samples, hairs and pictures, especially Elizaveta Lipovenko, Linda Persson-Wahlqvist and Eleonora Ruggiero for their great help. Feline DNA samples are part of the Feli-DNA biobank, which is part of the CRB-Anim infrastructure (ANR-11-INBS-0003, in the framework of the ‘Investing for the Future’ program, PLAl).

CONFLICT OF INTEREST
The authors declare that they have no competing interests.
DATA AVAILABILITY STATEMENT
SNP genotyping data were deposited at OSF (https://osf.io/xe9rn/?view_only=3c8858b9ff1c4a0c86e2e6681bcaa2ad).

Genomic sequences of CORIN exon 19 from wild-type and copper cats (Felis catus) were submitted to GenBank. Accession numbers are GenBank ID: MW288825 for the wild-type allele and GenBank ID: ON640807 for the CORIN:c.[2425C>T] variant allele. Sequences for the cat analysis of the 99 Lives project (Buckley et al., 2020) are available under BioProject accession IDs PRJNA308208 and PRJNA288177 at the sequence read archive (https://www.ncbi.nlm.nih.gov/sra).

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SUPPORTING INFORMATION
Additional supporting information may be found in the online version of the article at the publisher’s website.

How to cite this article: Abitbol, M., Dargar, T. & Gache, V. (2022) Golden cats: A never-ending story!. Animal Genetics, 53, 715–718. Available from: https://doi.org/10.1111/age.13228