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Georgian white coat color of red fox (*Vulpes vulpes*) maps to fox chromosome 2 in the region containing *KIT* gene

A.V. Kukekova^{1,§}, J.L. Johnson¹, A.V. Kharlamova², A.V. Vladimirova², D.V. Shepeleva², R.G. Gulevich², and L.N. Trut²

¹Animal Sciences Department, College of ACES, University of Illinois at Urbana-Champaign, IL 61801, USA

²Institute of Cytology and Genetics of the Russian Academy of Sciences, Novosibirsk, 630090, Russia

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The farm breeding of red foxes began in Eastern Canada in the late 19th century.¹ Through fox farm breeding, several new coat color variants have been identified, with the Georgian white (GW) morph first being described at Bakurian farm in Georgia in 1943.^{2,3} GW foxes are produced by breeding GW and standard silver foxes and are heterozygous for the *GW* allele. They are characterized by white coat color, brown eyes, a black nose and black spots on the head, along the spine and on some other parts of the body (Fig. 1). In a breeding between two GW foxes, offspring homozygous for the *GW* allele are underrepresented, which was attributed to the death of some homozygous embryos before implantation.³ The offspring homozygous for the *GW* allele that are born alive are almost completely white and die at 1–2 months of age.³ Interestingly, the shortage of *GW* homozygous offspring in breedings between GW foxes can be reduced by additional illumination of the dam during pregnancy.³

Blood samples were collected from 13 three-generation pedigrees produced by breeding GW and standard silver foxes (88 individuals, including 55 foxes in the third generation) at the Institute of Cytology and Genetics of the Russian Academy of Sciences in Novosibirsk, Russia. DNA was extracted using DNA Maxi Blood Kit (Qiagen). The pedigrees were genotyped with 224 dog microsatellites (Table S1) as described.^{4–6} All genotypes were checked for Mendelian segregation and manually corrected for errors. Linkage mapping using the Twopoint function of CRI-MAP version 2.503^{7,8} identified the most significant linkage between GW and markers on fox chromosome 2 (VVU2): *FH2890* ($\theta = 0.0$; LOD = 16.26), *FH3006* ($\theta = 0.0$; LOD = 13.85) and *AHT121* ($\theta = 0.0$; LOD = 11.44) (Table S2). Multipoint linkage mapping and haplotype analysis placed the *GW* locus in the interval

[§]Corresponding author: Anna V. Kukekova, Department of Animal Sciences, The University of Illinois at Urbana-Champaign, 206 Edward R. Madigan Laboratory, 1201 West Gregory Drive, Urbana, IL 61801, Phone: 217-300-2425, Fax: 217-244-5617, avk@illinois.edu.

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defined by markers *REN278L10* and *REN150M24* (Fig. 2; Fig. S1). This is a region with a suppressed recombination rate, and the marker *REN150M24* could not be assigned a unique location. On the fox map constructed with a larger number of pedigrees,⁶ the interval between markers *REN278L10* and *REN150M24* spans 16.1 cM.^{4,6} This interval is syntenic to three dog chromosomes: CFA2, 9, and 13 (Table S3).⁶

The part of CFA13 that is syntenic to the *GW* interval on VVU2 includes the *KIT* gene (Fig. 2), mutations in which are responsible for white spotting in multiple mammalian species.⁹ Recently, we have shown that a mutation in the *KIT* gene causes platinum coat color in foxes.¹⁰ Allelic interaction among the *GW* and platinum coat colors has previously been established through cross-breeding of *GW* and platinum foxes.³ The mapping of the *GW* allele to this interval on VVU2 is thus consistent with the results of the experimental breedings³ and suggests that *GW* is also caused by a mutation in the *KIT* gene. Little is known about the role of light in regulating gene expression in mammals, and further analysis of the *GW* phenotype could contribute to our understanding of these mechanisms.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.
Fox heterozygous for the Georgian white allele.

Figure 2.

Meiotic linkage map fox chromosome 2 (VVU2) constructed with pedigrees informative for the Georgian white phenotype. The most likely location of the *GW* locus on VVU2 with LOD support 2.0 is indicated on the left. The map is aligned against the dog genome; positions of markers and the *KIT* gene (chr13: 47,108,519-47,190,020 bp) in CamFam3.1 are shown on the right.