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Anorexia nervosa (AN) is a chronic psychiatric disease characterized by a refusal to maintain body weight at or above 85% of that which is normal for height, body dysmorphia, and fear of gaining weight. Genetic studies have had limited success identifying risk loci and a recent genome-wide association study of 1033 AN cases and 3733 controls found no significantly associated loci; however, it identified several genes with single nucleotide polymorphisms (SNPs) of nominal significance: AKAP6, FAM155A, LRP2, NTNG1, VGLL4, and ZNF804B (Wang et al., 2011). We attempted to replicate these associations in an independent cohort of 396 female AN cases of European descent (mean age = 32.4 ± 14.25) obtained from the NIMH Center for Collaborative Studies on Mental Disorders (Kaye et al., 2008) and 690 age-matched and education-matched European controls (mean age = 26.34 ± 8.33). Controls were collected as part of the AN trios study, and never met the criteria for an eating disorder (Reba et al., 2005) (more detailed methodology provided in online supplement, Supplemental digital content 1, http://links.lww.com/PG/A106). Overall, 12 SNPs were selected for genotyping, rs2383378 and rs12894779 in AKAP6, rs11842161 and rs4511387 in FAM155A, rs830998, rs830997, rs2075252, and rs4667591 in LRP2, rs10494067 in NTNG1, rs6782029 and rs2616551 in VGLL4, and rs6959888 in ZNF804A. Genotyping was performed using TaqMan genotyping assays (Applied Biosystems Inc., Foster City, California, USA) as per manufacturer protocol. χ²-Tests of allelic association were performed using PLINK v1.04 (Purcell et al., 2007) to test for allelic association with AN. rs2616551 in VGLL4 was found to be nominally associated with AN [Minor allele frequency (MAF) in cases = 17%, controls = 21%, χ² = 4.3, P = 0.04, odds ratio = 0.79]. These analyses did not correct for population stratification, however, rs2616551 was associated with AN in the genome-wide association study performed by Wang et al. (2011) (P = 0.0005, odds ratio = 0.78). Recent studies of complex genetic traits have found both common and rare genetic variation to influence liability to disease. Therefore, we performed next generation sequencing (NGS) of a 9.4 kb amplicon of VGLL4 capturing 80% of the coding region of VGLL4 with the aim of finding rare coding variation in VGLL4 increasing risk for AN. An additional 554 AN samples (mean age = 26.2 ± 8.14) collected as part of the Price Foundation Anorexia Nervosa Affected Relative Pair dataset (Kaye et al., 2000) and the AN Trios study (Reba et al., 2005) were used, to provide 950 AN individuals in total for NGS. NGS was performed using SOLiD
sequencing (Life Technologies, Grand Island, New York, USA) at the Penn Genome Frontiers Institute. Sequence reads were aligned to the reference sequence for VGLL4 (build hg19) using Bowtie (version 0.12.7) (Langmead et al., 2009), SAMtools (version 0.1.18), and VarScan (version 2.2.7). A total of 59 variants were identified and 40 of these were novel. Only one SNP was coding (synonymous), and therefore none of the 59 variants were genotyped in additional AN populations. This should be considered a limitation of this study as noncoding variation is known to influence disease risk. However, because of the nominal association of VGLL4 in two independent AN cohorts, this remains a candidate gene worthy of future study in AN populations.

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Conflicts of interest
There are no conflicts of interest.

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