

Are you aware of the frequency of obesity-associated gene variants?

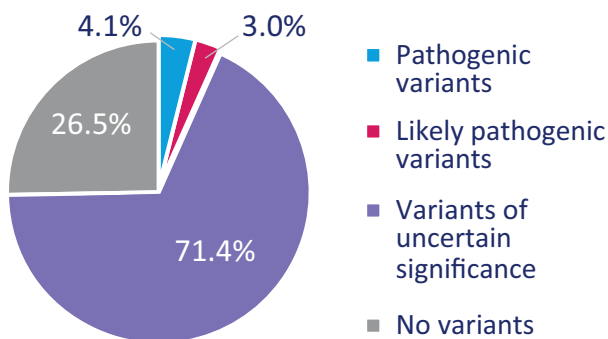
It is likely that the true prevalence of rare genetic diseases of obesity has previously been underestimated because genetic testing is often not done in individuals with obesity

Uncovering Rare Obesity® is a no-charge, comprehensive genetic testing program for rare genetic diseases of obesity sponsored by Rhythm Pharmaceuticals, Inc.

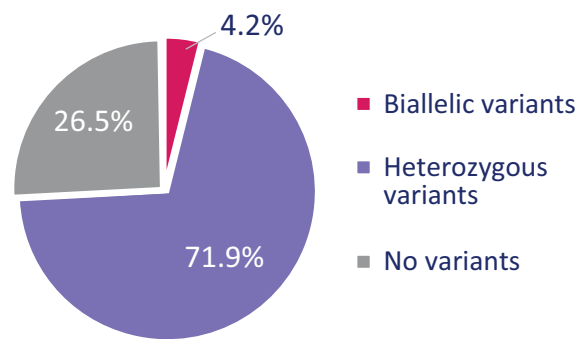
To be eligible for testing through the Uncovering Rare Obesity® program, patients must be located in the United States or its territories, and:

- ≤18 years of age with body mass index (BMI) ≥97th percentile, OR
- ≥19 years of age with BMI ≥40 kg/m² and a history of childhood obesity, OR
- an immediate family member of select, previously tested patients, OR
- showing clinical symptoms of Bardet-Biedl syndrome (BBS)

Sequences from 11,671 individuals were analyzed using the expanded 79-gene and 1-chromosomal region panel^a



73.5% of individuals had at least 1 pathogenic variant, likely pathogenic variant, or variant of uncertain significance in one of the 79 genes.



73.5% of individuals had biallelic or heterozygous variants. Includes homozygous and presumed compound heterozygous variants.

Of the total population, 2.9% of individuals carried pathogenic or likely pathogenic variants that also met the mode of inheritance^b

^aPatients may have >1 variant and therefore may be represented in >1 section of the pie charts. ^bMode of inheritance criteria were defined as ≥2 alleles in autosomal recessive conditions or ≥1 allele in autosomal dominant conditions.

Most frequent variants:

ALMS1 - 9.22% (n=1076)	IFT172 (BBS20) - 3.41% (n=398)	LEPR - 2.51% (n=293)	POMC - 2.13% (n=249)
CEP290 (BBS14) - 4.87% (n=568)	RPGRIP1L - 3.34% (n=390)	MAGEL2 - 2.49% (n=291)	BBS9 - 2.02% (n=236)
PLXNA4 - 3.50% (n=408)	PLXNA3 - 3.18% (n=371)	MKS1 (BBS13) - 2.41% (n=281)	NCOA1 - 2.02% (n=236)
MC4R - 3.49% (n=407)	PLXNA2 - 3.10% (n=362)	CREBBP - 2.26% (n=264)	BBS1 - 1.98% (n=231)
PLXNA1 - 3.44% (n=401)	SH2B1 - 2.58% (n=301)	SEMA3G - 2.23% (n=260)	PCSK1 - 1.92% (n=224)

Uncovering Rare Obesity® panel

ADCY3	BBS2	CPE	IFT172 (BBS20)	LEPR	MRAP2	PHF6	PROK2	SEMA3C	TRIM32 (BBS11)
AFF4	BBS4	CREBBP	IFT27 (BBS19)	LZTFL1 (BBS17)	NCOA1 (SRC1)	PHIP	RAB23	SEMA3D	TRPC5
ALMS1	BBS5	CUL4B	IFT74 (BBS22)	MAGEL2	NR0B2	PLXNA1	RAI1	SEMA3E	TTC8 (BBS8)
ARL6 (BBS3)	BBS7	DNMT3A	INPP5E	MC3R	NRP1	PLXNA2	RPGRIP1L	SEMA3F	TUB
BBIP1 (BBS18)	BBS9 (PTHB1)	DYRK1B	ISL1	MC4R	NRP2	PLXNA3	RPS6KA3	SEMA3G	UCP3
BBS10	BDNF	EP300	KIDINS220	MECP2	NTRK2	PLXNA4	SDCCAG8 (BBS16)	SH2B1	VPS13B
BBS12	CFAP418 (BBS21)	GNAS	KSR2	MKKS (BBS6)	PCNT	POMC	SEMA3A	SIM1	WDPCP (BBS15)
BBS1	CEP290 (BBS14)	HTR2C	LEP	MKS1 (BBS13)	PCSK1	PPARG	SEMA3B	TBX3	16p11.2 chromosomal region