Title: Bardet-Biedl Syndrome *GeneReview* Table 8

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Note: The following information is provided by the authors listed above and has not been reviewed by *GeneReviews* staff.

Table 8. *MKKS/BBS6* Pathogenic Allelic Variants

Gene	Mutation	Exon	Reference
BBS6	p.A242S heterozygote	3	Katsanis et al 2001
BBS6	p.Q147X heterozygote	3	Katsanis et al 2001
BBS6	p.Q147X heterozygote	3	Katsanis et al 2001
BBS6	p.Y37C homozygous	3	Katsanis et al 2001
BBS6	p.C499S heterozygote	6	Katsanis et al 2001
MKKS	p.H84Y homozygote	3	Stone et al 2000
MKKS	p.A242S homozygote	3	Stone et al 2000
MKKS	p.Y37C heterozygote	3	Stone et al 2000
MKKS	p.W405fsX413 heterozygote	5	Stone et al 2000
BBS6	p.Y37C homozygote	3	Katsanis et al 2000, Katsanis et al 2001
BBS6	p.D143fsX157 heterozygote	3	Katsanis et al 2000
BBS6	p.L227P heterozygote	3	Katsanis et al 2000
BBS6	p.F94fsX103 homozygote	3	Katsanis et al 2000, Slavotinek et al 2000
BBS6	p.D143fsX157 homozygote	3	Katsanis et al 2000, Slavotinek et al 2000
BBS6	p.F94fsX103 heterozygote	3	Katsanis et al 2000
BBS6	p.D143fsX157 heterozygote	3	Katsanis et al 2000
BBS6	p.T57A heterozygote	3	Katsanis et al 2000
BBS6	p.G52D heterozygote	3	Slavotinek et al 2000
BBS6	p.Y264X heterozygote	3	Slavotinek et al 2000
BBS6	p.A242S heterozygote	3	Beales et al 2001
BBS6	p.A242S heterozygote	3	Slavotinek et al 2000
BBS6	p.Q147X homozygote	3	Beales et al 2001

Gene	Mutation	Exon	Reference
BBS6	p.D285A homozygote	3	Beales et al 2001
BBS6	p.R518H homozygote	6	Beales et al 2001
BBS6	p.I32M homozygote	3	Beales et al 2001
BBS6	p.S235P homozygote	3	Beales et al 2001
BBS6	p.C499S homozygote	6	Beales et al 2001
BBS6	p.S511A homozygote	6	Beales et al 2001
BBS6	c.431-441del homozygote	3	Slavotinek et al 2002
BBS6	c.876-877 insCCTG heterozygote	3	Slavotinek et al 2002
BBS6	p.G345E homozygote	4	Slavotinek et al 2002
BBS6	p.R155L	3	Slavotinek et al 2002
BBS6	p.I339V	4	Slavotinek et al 2002

.0001 BBS6, H84Y. A homozygous histidine to tyrosine missense mutation was found together with A242S in all affected Amish individuals with McKusick-Kaufman syndrome [Stone et al 2000]. It has been predicted that this substitution may disrupt protein function by interfering with ATP hydrolysis in the equatorial domain of the protein.

.0002 BBS6, A242S. A homozygous alanine to serine missense mutation was found together with H84Y in all affected Amish individuals with Mckusick-Kaufman syndrome [Stone et al 2000]. However, unlike H84Y, this mutation has not been predicted to disrupt protein function. It has also been found in one unaffected control from Newfoundland [Beales et al 2001], in heterozygous form in an individual with BBS who had hypothyroidism [Slavotinek et al 2002], and in affected and unaffected siblings in a Newfoundland family [Katsanis et al 2001]. It has been proposed that either this allele is actually a rare polymorphism, or else that BBS arises through multiallelic inheritance [Katsanis et al 2001].

.0003 BBS6, Y37C. A tyrosine to cysteine missense mutation was found in an infant with MKKS in compound heterozygous form along with a two base pair deletion in exon 5 (W405fsX413) [Stone et al 2000]. Y37C was also identified in homozygous form in an individual with BBS who carried an additional mutation in *BBS2* (N70S) [Katsanis et al 2001].

.0004 BBS6, W405fsX413. This two base pair deletion in exon 5 of *BBS6* was found in compound heterozygous form with Y37C in an infant with MKKS [Stone et al 2000].

.0005 BBS6, D143fsX157. This mutation is a complex deletion that predicts the introduction of a premature termination codon at residue 157 of *BBS6* and was identified in homozygous form in all affected individuals from two Newfoundland BBS families [Katsanis et al 2000]. In addition, it was also found in compound

heterozygous form in an affected individual together with D143fsX157, and with L227P in an affected individual from Newfoundland [Katsanis et al 2000].

.0006 BBS6, L227P. This missense mutation was found in compound heterozygous form in an affected individual from Newfoundland together with D143fsX157 [Katsanis et al 2000].

.0007 BBS6, F94fsX103. This mutation has been identified in the homozygous form in all affected individuals from three BBS families from Newfoundland [Katsanis et al 2000, Slavotinek et al 2000]. In addition, it was also found in compound heterozygous form in an affected individual together with D143fsX157 [Katsanis et al 2000].

.0008 BBS6, T57A. This missense mutation was identified in heterozygous form in an individual with BBS and was not found in 192 control chromosomes [Katsanis et al 2000].

.0009 BBS6, G52D. A Hispanic BBS proband was found to be a compound heterozygote for a glycine to aspartic acid missense mutation (G52D), and a nonsense mutation (Y264X) in BBS6 [Slavotinek et al 2000].

.0010 BBS6, Y264X. A Hispanic BBS proband was found to be a compound heterozygote for a nonsense mutation (Y264X), and a missense mutation (G52D) in BBS6 [Slavotinek et al 2000].

.0011 BBS6, Q147X. This nonsense mutation was identified in heterozygous form in an individual with BBS who also carried two nonsense mutations in *BBS2* (Y24X & Q59X) [Beales et al 2001, Katsanis et al 2001].

.0012 BBS6, D285A. This missense mutation was identified in homozygous form in affected individuals from a BBS pedigree [Beales et al 2001].

.0013 BBS6, R518H. This missense mutation was identified in homozygous form in affected individuals from a BBS pedigree [Beales et al 2001].

.0014 BBS6, I32M. This missense mutation was identified in homozygous form in affected individuals from a BBS pedigree [Beales et al 2001]. It was suggested that this would result in the introduction of an alternative methionine start codon.

.0015 BBS6, S235P. This missense mutation was identified in homozygous form in affected individuals from a BBS pedigree [Beales et al 2001]. It was suggested that this change would result in a structural change to the BBS6 protein.

.0016 BBS6, C499S. This missense mutation was identified in homozygous form in an individual with BBS along with two other nonsense mutations in *BBS6* (L168fsX170 and R216X) [Katsanis et al 2001].

.0017 BBS6, S511A. This missense mutation was identified in homozygous form in affected individuals from a BBS pedigree [Beales et al 2001].

.0018 BBS6, c.431-441del. A homozygous deletion of 10 base pairs in exon 3 of *BBS6* that predicts a frameshift resulting in a premature stop codon at residue 152 was identified in an individual with BBS [Slavotinek et al 2002].

.0019 BBS6, c.876-877insCCTG. A heterozygous insertion of 4 base pairs in exon 3 of BBS6 was identified that predicts a frameshift resulting in a premature

stop codon at residue 327 in an individual with atypical BBS [Slavotinek et al 2002].

.0020 BBS6, p.G345E. This homozygous missense mutation was identified in an individual with BBS [Slavotinek et al 2002].

.0021 BBS6, p.R155L. This missense mutation was identified in heterozygous form in an individual with BBS [Slavotinek et al 2002].

.0022 BBS6, p.I339V. This missense mutation was identified in heterozygous form in an individual with BBS [Slavotinek et al 2002].

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