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HUMAN GENE MUTATIONS

Paul D. Lewis

Novel human pathological mutations

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Gene Symbol: CRB1

Disease: Leber congenital amaurosis

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Small Deletions (< 21 bp)

Accession Number	Codon Number/location	Deletion
Hd0510	166	GATGGaattgatggTTACT

Comments:

Gene Symbol: BMPR1A

Disease: Hereditary mixed polyposis syndrome

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Small Deletions (< 21 bp)

Accession Number	Codon Number/location	Deletion
Hd0511	42	GACCAG^AAAaagtcagaaaaTGGAGTA

Comments: Cause frame-shift and stop at codon 69 (TGA)

Gene Symbol: VHL

Disease: von Hippel–Lindau syndrome

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Small Deletions (< 21 bp)

Accession Number	Codon Number/location	Deletion
Hd0512	57	GCC^GGgCGGCCG

Comments: Apparently isolated case with multiple cerebellar haemangioblastomas. Ref. Seq.: L15409. Formal notation: c.171delG

Gene Symbol: CYP1B1

Disease: Glaucoma, Primary congenital

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Small Deletions (< 21 bp)

Accession Number	Codon Number/location	Deletion
Hd0513	152	AGCATG^atGCGCAAC

Comments: Mutation: c.454–455delAT, GenBank accession U56438

Gene Symbol: SERPINC1

Disease: Antithrombin deficiency

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Small Deletions (< 21 bp)

Accession Number	Codon Number/location	Deletion
Hd0514	417	AAGTT^CCTCTgAACACTATT

Gene Symbol: CYP1B1

Disease: Primary congenital glaucoma

J. Nirmaladevi, T. Karthiyayini, G. Kumaramanickavel

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Small Deletions (< 21 bp)

Accession Number	Codon Number/location	Deletion
Hd0515	132/E2	CGGCCGC^AGCAtGGCT

Comments: Truncated dioxin-inducible cytochrome p450 protein

Gene Symbol: APC

Disease: Familial adenomatous polyposis coli

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Small Deletions (< 21 bp)

Accession Number	Codon Number/location	Deletion
Hd0518	1060	ATGAA^ATaaaacAAAGTGAGCAAAG

Comments: Patient with classical familial adenomatous polyposis coli

Gene Symbol: SPAST

Disease: Spastic paraparesis

C. Depienne, C. Tallaksen, J.Y. Lephay, B. Bricka, S. Poea-Guyon, B. Fontaine, P. Labauge, A. Brice, A. Durr

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Small Deletions (< 21 bp)

Accession Number	Codon Number/location	Deletion
Hd0519	Glu452GlyfsX456	A^GAAG

Gene Symbol: SCN8A

Disease: Ataxia

M.H. Meisler, M.M. Trudeau, J.C. Dalton, J.W. Day, L.P.W. Ranum

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Small Deletions (< 21 bp)

Accession Number	Codon Number/location	Deletion
Hd0520	1719	CGCCCC^CctGAC

Comments: P1719FSX1724

Gene Symbol: FECH

Disease: Porphyria, erythropoietic

E. Di Pierro, V. Brancaleoni, V. Moriondo, V. Besana, M.D. Cappellini

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Gross Deletions

Accession Number	Description
Hg0501	Sequence analysis on the RNA showed loss of exons 3 and 4. DNA analysis revealed the presence of a 5,576 bp deletion defined by two short direct repeats of about 40 bp and two Alu sequences. The first breakpoint was located in intron 2 at nucleotide 12490, the second was located in intron 4 at nucleotide 18067.

Comments: Genebank accession number of FECH sequence is AJ250235

Gene Symbol: CRB1

Disease: Leber congenital amaurosis

E. Vallespin, D. Cantalapiedra, M. Garcia-Hoyos, R. Riveiro, C. Villaverde, M.J. Trujillo-Tiebas, C. Ayuso

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Missense/Nonsense Mutations (single base-pair substitutions)

Accession Number	Codon Number/location	Nucleotide substitution	Amino acid substitution
Hm0534	1330	GAG-TAG	Glu-Ter

Gene Symbol: FOXE1

Disease: Nonsyndromic cleft palate

D. Teti, Mario Venza, Maria Visalli, Emanuele Bellacchio, Claudia Torino, Teresa Arrigo, Bruno Dallapiccola

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Missense/Nonsense Mutations (single base-pair substitutions)

Accession Number	Codon Number/location	Nucleotide substitution	Amino acid substitution
Hm0535	49	CTG-CCG	Leu-Pro

Comments: Protein modeling suggested that the mutation L49P causes the distortion of the terziary structure of FOXE1 protein, which could impair the binding for the consensus sequences and influence the molecular recognition of nucleic acids by the transcription factor.

Gene Symbol: ABCA4

Disease: Stargardt disease 1

R.Riveiro-Alvarez, M.J. Trujillo, D. Cantalapiedra, E. Vallespin, C. Villaverde, D. Valverde, C. Ayuso

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Missense/Nonsense Mutations (single base-pair substitutions)

Accession Number	Codon Number/location	Nucleotide substitution	Amino acid substitution
Hm0536	1315	cCAG-TAG	Gln-Ter

Comments: Mutations in the ABCA4 gene have been associated with autosomal recessive Stargardt disease (STGD1), cone-rod dystrophy (CRD), and retinitis pigmentosa (RP). We employed a recently developed genotyping microarray, the ABCR400-chip, to search for known ABCA4 mutations. In those patients with STGD1 on whom we identified at least one ABCA4 mutation, we performed direct sequencing. This molecular analysis revealed us novel missense, nonsense and splicing mutations. In conclusion, we have shown that the ABCA4 mutation chip is an efficient first screening tool for arSTGD.

Gene Symbol: ABCA4

Disease: Stargardt disease 1

R.Riveiro-Alvarez, M.J. Trujillo, D. Cantalapiedra, E. Vallespin, C. Villaverde, D. Valverde, C. Ayuso

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Missense/Nonsense Mutations (single base-pair substitutions)

Accession Number	Codon Number/location	Nucleotide substitution	Amino acid substitution
Hm0537	1961	cGGA-AGA	Gly-Arg

Comments: Mutations in the ABCA4 gene have been associated with autosomal recessive Stargardt disease (STGD1), cone-rod dystrophy (CRD), and retinitis pigmentosa (RP). We employed a recently developed genotyping microarray, the ABCR400-chip, to search for known ABCA4 mutations. In those patients with STGD1 on whom we identified at least one ABCA4 mutation, we performed direct sequencing. This molecular analysis revealed us novel missense, nonsense and splicing mutations. In conclusion, we have shown that the ABCA4 mutation chip is an efficient first screening tool for arSTGD.

Gene Symbol: ABCA4

Disease: Stargardt disease 1

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Missense/Nonsense Mutations (single base-pair substitutions)

Accession Number	Codon Number/location	Nucleotide substitution	Amino acid substitution
Hm0538	2187	gCAG-TAG	Gln-Ter

Comments: Mutations in the ABCA4 gene have been associated with autosomal recessive Stargardt disease (STGD1), cone-rod dystrophy (CRD), and retinitis pigmentosa (RP). We employed a recently developed genotyping microarray, the ABCR400-chip, to search for known ABCA4 mutations. In those patients with STGD1 on whom we identified at least one ABCA4 mutation, we performed direct sequencing. This molecular analysis revealed us novel missense, nonsense and splicing mutations. In conclusion, we have shown that the ABCA4 mutation chip is an efficient first screening tool for arSTGD.

Gene Symbol: TNFSF5

Disease: Hyper-IgM syndrome

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Missense/Nonsense Mutations (single base-pair substitutions)

Accession Number	Codon Number/location	Nucleotide substitution	Amino acid substitution
Hm0539	167	GGA-GTA	Gly-Val

Gene Symbol: CRB1

Disease: Leber congenital amaurosis

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Missense/Nonsense Mutations (single base-pair substitutions)

Accession Number	Codon Number/location	Nucleotide substitution	Amino acid substitution
Hm0540	1001	ATT-AAT	Ile-Asn

Gene Symbol: CYP1B1

Disease: glaucoma, primary congenital

J.F.F. Brinkmann, C.P.E. Ottenheim, R.H.C. Zegers, P.T.V.M. de Jong, A.A.B. Bergen

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Missense/Nonsense Mutations (single base-pair substitutions)

Accession Number	Codon Number/location	Nucleotide substitution	Amino acid substitution
Hm0541	159	cCAG-cTAG	Gln-Stop

Comments: Mutation: c.475C > T, p.Q159X (stop codon), GenBank accession U56438

Gene Symbol: PRSS1

Disease: Pancreatitis, hereditary

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Missense/Nonsense Mutations (single base-pair substitutions)

Accession Number	Codon Number/location	Nucleotide substitution	Amino acid substitution
Hm0542	98	cCAA-AAA	Gln-Lys

Gene Symbol: SLC3A1

Disease: Cystinuria

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Missense/Nonsense Mutations (single base-pair substitutions)

Accession Number	Codon Number/location	Nucleotide substitution	Amino acid substitution
Hm0543	179	GAT-TAT	Asp-Tyr

Gene Symbol: CYP1B1

Disease: Primary congenital glaucoma

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Missense/Nonsense Mutations (single base-pair substitutions)

Accession Number	Codon Number/location	Nucleotide substitution	Amino acid substitution
Hm0544	292	ATG-AAA	Met-Lys

Comments: Mutated dioxin-inducible cytochrome p450 protein

Gene Symbol: SLC7A9

Disease: Cystinuria

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Missense/Nonsense Mutations (single base-pair substitutions)

Accession Number	Codon Number/location	Nucleotide substitution	Amino acid substitution
Hm0545	73	GGG-AGG	Gly-Arg

Gene Symbol: SLC3A1

Disease: Cystinuria

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Missense/Nonsense Mutations (single base-pair substitutions)

Accession Number	Codon Number/location	Nucleotide substitution	Amino acid substitution
Hm0546	562	GAG-CAG	Glu-Gln

Comments:

Gene Symbol: SLC3A1

Disease: Cystinuria

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Missense/Nonsense Mutations (single base-pair substitutions)

Accession Number	Codon Number/location	Nucleotide substitution	Amino acid substitution
Hm0547	567	AGG-AGC	Arg-Ser

Gene Symbol: RPE65

Disease: Leber's congenital amaurosis

Mamatha Gandra, Srilekha Sundaramurthy, Govindasamy Kumaramanickavel

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Missense/Nonsense Mutations (single base-pair substitutions)

Accession Number	Codon Number/location	Nucleotide substitution	Amino acid substitution
Hm0548	471	CCC-CTC	PRO-LEU

Comments: Pro471Leu mutation has been detected in an Indian LCA patient.

Gene Symbol: MPZ

Disease: Charcot-Marie-Tooth disease

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Missense/Nonsense Mutations (single base-pair substitutions)

Accession Number	Codon Number/location	Nucleotide substitution	Amino acid substitution
Hm0549	101	TGG-TAG	Trp-Term

Gene Symbol: GJB1

Disease: Charcot-Marie-Tooth disease

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Missense/Nonsense Mutations (single base-pair substitutions)

Accession Number	Codon Number/location	Nucleotide substitution	Amino acid substitution
Hm0550	170	GTC-GAC	Val-Asp

Comments: c.509T > A

Gene Symbol: MPZ

Disease: Charcot-Marie-Tooth disease

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Missense/Nonsense Mutations (single base-pair substitutions)

Accession Number	Codon Number/location	Nucleotide substitution	Amino acid substitution
Hm0551	144	CTG-CCG	Leu-Pro

Comments: c.434T > C

Gene Symbol: SPAST (SPG4)

Disease: Spastic paraparesis

C. Depienne, C. Tallaksen, J.Y. Lephay, B. Bricka, S. Poea-Guyon, B. Fontaine, P. Labauge, A. Brice, A. Durr

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Missense/Nonsense Mutations (single base-pair substitutions)

Accession Number	Codon Number/location	Nucleotide substitution	Amino acid substitution
Hm0552	385	GGG-TGG	Gly-Trp

Comments: Sporadic spastic paraplegia

Gene Symbol: SPAST

Disease: Spastic paraparesis

C. Depienne, C. Tallaksen, J.Y. Lephay, B. Bricka, S. Poea-Guyon, B. Fontaine, P. Labauge, A. Brice, A. Durr

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Missense/Nonsense Mutations (single base-pair substitutions)

Accession Number	Codon Number/location	Nucleotide substitution	Amino acid substitution
Hm0553	444	GAT-GAG	Asp-Glu

Comments: Sporadic spastic paraplegia

Gene Symbol: SPAST

Disease: Spastic paraparesis

C. Depienne, C. Tallaksen, J.Y. Lephay, B. Bricka, S. Poea-Guyon, B. Fontaine, P. Labauge, A. Brice, A. Durr

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Missense/Nonsense Mutations (single base-pair substitutions)

Accession Number	Codon Number/location	Nucleotide substitution	Amino acid substitution
Hm0554	581	CGA-TGA	Arg-Stop

Comments: Sporadic spastic paraplegia

Gene Symbol: SPAST

Disease: Spastic paraparesis

C. Depienne, C. Tallaksen, J.Y. Lephay, B. Bricka, S. Poea-Guyon, B. Fontaine, P. Labauge, A. Brice, A. Durr

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Missense/Nonsense Mutations (single base-pair substitutions)

Accession Number	Codon Number/location	Nucleotide substitution	Amino acid substitution
Hm0555	461	CTA-CCA	Leu-Pro

Comments: Sporadic spastic paraplegia

Gene Symbol: SPAST

Disease: Spastic paraparesis

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Missense/Nonsense Mutations (single base-pair substitutions)

Accession Number	Codon Number/location	Nucleotide substitution	Amino acid substitution
Hm0556	503	CGG-TGG	Arg-Trp

Comments: Sporadic spastic paraplegia

Gene Symbol: SPAST

Disease: Spastic paraparesis

C. Depienne, C. Tallaksen, J.Y. Lephay, B. Bricka, S. Poea-Guyon, B. Fontaine, P. Labauge, A. Brice, A. Durr

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Missense/Nonsense Mutations (single base-pair substitutions)

Accession Number	Codon Number/location	Nucleotide substitution	Amino acid substitution
Hm0557	238	CCC-ACC	Pro-Thr

Comments: Sporadic spastic paraplegia

Gene Symbol: AVP

Disease: Diabetes insipidus, neurohypophyseal

A.P. Abbes, H. Engel, E.J.M. Bruggeman, A.A.M. Franken

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Missense/Nonsense Mutations (single base-pair substitutions)

Accession Number	Codon Number/location	Nucleotide substitution	Amino acid substitution
Hm0558	65	cTGC-TTC	Cys-Phe

Comments: Dutch kindred

Gene Symbol: AVP

Disease: Diabetes insipidus, neurohypophyseal

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Missense/Nonsense Mutations (single base-pair substitutions)

Accession Number	Codon Number/location	Nucleotide substitution	Amino acid substitution
Hm0559	87	gTCC-gTAC	Ser-Tyr

Comments: Dutch kindred

Gene Symbol: AVP

Disease: Diabetes insipidus, neurohypophyseal

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Missense/Nonsense Mutations (single base-pair substitutions)

Accession Number	Codon Number/location	Nucleotide substitution	Amino acid substitution
Hm0560	98	cTGC-cTCT	Cys-Ser

Comments: Welsh kindred

Gene Symbol: AVP

Disease: Diabetes insipidus, neurohypophyseal

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Missense/Nonsense Mutations (single base-pair substitutions)

Accession Number	Codon Number/location	Nucleotide substitution	Amino acid substitution
Hm0561	92	gTGC-AGC	Cys-Ser

Comments: French kindred

Gene Symbol: ABCA4

Disease: Stargardt disease 1

R. Riveiro-Alvarez, M.J. Trujillo, D. Cantalapiedra, E. Vallespin, C. Villaverde, D. Valverde, C. Ayuso

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Splicing Mutations (single base-pair substitutions)

Accession Number	Intron designation	Donor/acceptor	Relative location	Nucleotide substitution
Hs0512	22	Donor	-2	A-T

Comments: Mutations in the ABCA4 gene have been associated with autosomal recessive Stargardt disease (STGD1), cone-rod dystrophy (CRD), and retinitis pigmentosa (RP). We employed a recently developed genotyping microarray, the ABCR400-chip, to search for known ABCA4 mutations. In those patients with STGD1 on whom we identified at least one ABCA4 mutation, we performed direct sequencing. This molecular analysis revealed us novel missense, nonsense and splicing mutations. In conclusion, we have shown that the ABCA4 mutation chip is an efficient first screening tool for arSTGD.

Gene Symbol: PRPF31

Disease: Retinitis pigmentosa

Mamatha Gandra, Sreelekha Sundaramurthy, Govindasamy Kumaramanickavel

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Splicing Mutations (single base-pair substitutions)

Accession Number	Intron designation	Donor/acceptor	Relative location	Nucleotide substitution
Hs0513	6	Donor		G-A

Comments: G/A substitution at +1 of Intron6

Gene Symbol: PRPF31

Disease: Retinitis pigmentosa

Mamatha Gandra, Sreelekha Sundaramurthy, Govindasamy Kumaramanickavel

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Splicing Mutations (single base-pair substitutions)

Accession Number	Intron designation	Donor/acceptor	Relative location	Nucleotide substitution
Hs0514	6	Donor		G-A

Comments: G/A +1Intron6, A splicing mutation found in an Indian autosomal dominant retinitis pigmentosa family

Gene Symbol: SPAST

Disease: spastic paraparesis

C. Depienne, C. Tallaksen, J.Y. Lephay, B. Bricka, S. Poea-Guyon, B. Fontaine, P. Labauge, A. Brice, A. Durr

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Splicing Mutations (single base-pair substitutions)

Accession Number	Intron designation	Donor/acceptor	Relative location	Nucleotide substitution
Hs0515	Intron 1	Donor	+1	G-A

Comments: Sporadic spastic paraplegia

Gene Symbol: SPAST

Disease: Spastic paraparesis

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Splicing Mutations (single base-pair substitutions)

Accession Number	Intron designation	Donor/acceptor	Relative location	Nucleotide substitution
Hs0516	Intron 1	Donor	+1	G-T

Comments: Sporadic spastic paraplegia