GLYOXYLATE REDUCTASE/HYDROXYPYRUVATE REDUCTASE (*GRHPR*) GENE (PRIMARY HYPEROXALURIA TYPE 2)

MUTATION DATA BASE

REFERENCE SEQUENCES:
c.DNA: NM_012203
g.DNA: NG_008135.1

Nomenclature: HGVS guidelines (http://www.hgvs.org/rec.html)

Table 1: Polymorphic variants and those of unknown significance
Table 2: Missense and nonsense mutations
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Date: 23 August 2017 (future updates will not be made)
Curator: Dr Gill Rumsby

Table 1: Polymorphisms and variants of unknown significance

Location	Sequence variant	Codon/Effect	Frequency in controls	% activity	Reference
intron 1	c.[83+51delG]	n/a			Rumsby and Williams unpublished
Intron 2	c.[215-11C>T]	n/a			Rumsby and Williams unpublished
Intron 3	c.[288-11C>T]	n/a			Rumsby and Williams unpublished
Intron 4	c.[493+27C>T]	n/a			Rumsby and Williams unpublished
Intron 5	c.[494-68A>G]	n/a			Rumsby and Williams unpublished
Exon 6	c.[509G>A]	p.Arg170Gln rs12002324	0.0104 (A)		Rumsby and Williams unpublished
Exon 6	c.[579A>G]	p.Ala193Ala	0.14 (A) 0.86 (G)	100%	Cregeen et al., 2003
Intron 6	c.[598+145G>T]	n/a			Rumsby and Williams unpublished
Intron 7	c.[734+9G>A]	n/a			Rumsby and Williams unpublished
Exon 8	c.[740A>G]	p.[Asp247Gly]		Predicted benign (Sift/Polyphen)	Rumsby and Williams unpublished
Intron 8	c.[866-25_866-24[(8_9)]	CT repeat			Cregeen et al., 2003
Exon 9	c.[871C>T]	p.Leu291Leu			Rumsby and Williams unpublished

Exon 9	c.[963G>A]	p.Pro321Pro			Rumsby and Williams unpublished

Table 2: Missense and Nonsense mutations

Location	Sequence variant	Codon/Effect	Frequency in PH2 patients	In vitro activity/how proven	References
Exon 2	c.[102G>A]	p.Trp34X			Rumsby unpublished
Exon 2	c.[203T>C]	p.Leu68Pro		modelling	Rumsby unpublished
Exon 3	c.[287G>T]	p.Arg96Leu		SIFT, Polyphen 2 prediction	Rumsby, unpublished
Exon 4	c.[295C>T]	p.Arg99X	6%	n/a	Webster et al, 2000
Exon 4	c.[337G>A]	p.Glu113Lys		0%	Takayama et al., 2007
Exon 5	c.[478G>A]	p.Gly160Arg		modelling (coenzyme binding)	Rumsby and Williams unpublished
Exon 6	c.[494G>A]	p.Gly165Asp	13%	GR activity 1.5% of control	Webster et al., 2000
Exon 7	c.626C>T	p.Ser209Phe		Prediction	Hopp et al.,2015
Exon 7	c.[743T>A]	p.Val248Asp		SIFT, polyphen2	Rumsby and Williams unpublished
Exon 9	c.889G>A	p.Ala297Thr		Prediction	Hopp et al., 2015
Exon 9	c.[904C>T]	p.Arg302Cys	3%	GR activity 5.6% of control	Cregeen et al., 2003
Exon 9	c.[905G>A]	p.Arg302His		Not tested, affects same amino acid as 904C>T	Rumsby unpublished
Exon 9	c.905G>C	p.Arg302Pro		Prediction	Hopp et al.,2015
Exon 9	c.[934A>G] (*sic*. C.975A>G)	p.Asn312Asp		0%	Levin-Iaina et al. 2009

Exon 9	c.[965T>G]	p.Met322Arg	11%	0%	Webster et al., 2000
Exon 9	c.[965T>C]	p.Met322Thr		Not tested, affects same amino acid as 965T>G	Rumsby unpublished

Table 3: Splice site mutations

Location	Sequence variant	Codon/Effect	Frequency in PH2 patients	In vitro activity/how proven	References
intron 1	c.[84-2A>G]	missplicing	8%	liver mRNA shows exon skipping	Cregeen et al., 2003
Exon 3-intron 3	c.287_287+4delGGTTAAinsCCC	Donor splice site eliminated		Prediction	Hopp et al., 2015
Exon 4-intron 4	c.[403_404+2delAAGT]*	missplicing	18%	Liver mRNA shows incorporation of part of intron 4 (Cregeen et al., 2003)	Webster et al., 2000 Cregeen et al., 2003
Intron 4	c.[404+1_4del]	missplicing		May be same as c.[403_404+2delAAGT]	Williams and Rumsby, unpublished
Intron 4	c.404+5G>A	missplicing		Prediction (WT 0.99, Mut 0.34)	Hopp et al.,2015
Intron 5	c.[493+2T>A]	missplicing			Rumsby unpublished
Intron 7	c.734+1G>A	Donor splice site eliminated		prediction	Hopp et al., 2015
Intron 7	c.[735-1G>A]	missplicing			Webster et al., 2000

*Previously reported as c.403_405+2delAAGT

Table 4: Deletions and insertions

Location	Sequence variant	Codon/Effect	Frequency in PH2 patients	How proven	References
5'UTR	c.-4_-3delinsAT	Introduction of new start site plus fs		In vitro loss of transcription	Fu et al., 2014
Exon 1	c.[45delA]	frame shift			Rumsby and Williams unpublished
intron 1	c.[84-8_84-5delCCCC;84-13_84-12delCC]	?missplicing	3%		Cregeen et al. 2003
Exon 2	c.[103delG]	p.Asp35Thrfs*11	37%		Webster et al., 2000
					Cregeen et al., 2003
Exon 2	c.248_249delTG	Frameshift			Takayama et al., 2013
Exon 2	c.271delG	p.Asp91fs			
Exon 4	c.288-2_288delAGT	Missplicing?			Rumsby et al unpublished
Exon 4	c.346_347ins (size of insertion unknown) NG_008135.1:g.[8888_8892delins7465_7744;8897_8910dup]	p.116fs			Rumsby et al unpublished
Exon 4	c.[375delG]	Frameshift,termination at codon 133	3%		Cregeen et al., 2003
Exon 4/intron 4 boundary	c.[403_404+2delAAGT]*	Missplicing (see table 3)	18%		Webster et al., 2000
					Cregeen et al., 2003
Intron 4	c.[404+1_404+4delGTAA]	missplicing			Williams and Rumsby, unpublished

Exon 5	c.454dupA	p.Thr152fs			Hopp et al.,2015
Exon 6	c.[540delT]	Frameshift, termination at codon 181	3%		Cregeen et al., 2003
Exon 7	c.[608_609delCT]	Frameshift, termination at codon 210	9%		Cregeen et al., 2003
Exon 7	c.694delC	p.Gln232Argfs*3		Expression studies	Fu et al.,2014
Exon 8	c.769dupG	p.Gln256fs			Hopp et al.,2015
Exon 8	c.783delT	p.Lys262Argfs*9			Rumsby, unpublished
Exon 8	c.[864_865delTG]	frameshift, termination at codon 310			Lam et al., 2001
Exon 9	c.890_891dupCC	p.Thr298fs			Hopp et al.,2015

*Previously reported as c.403_405+2delAAGT