Supplemental_Table_S4. Correlation between splice site variants and clinical features in STGD1 patients.
All variants were previously found in a compound heterozygous manner (Cornelis et al. 2017 and references therein), except for eight variants, i.e. c.160+5G>C, c.302+4A>C, c.768G>T, c.4253+4C>T, c.4667G>C, c.5461-10T>C, c.5461-8T>G and c.6729+5_6729+19del. When clinical information was available for the homozygous cases, this was used to assess the severity of the corresponding variant. If more than one patient carried a variant, we assessed the clinical phenotype of the case(s) for which the second variant was known, and if this variant could be classified either as severe variant (stop mutation, frameshift mutation, canonical splice site mutation) or as mild variant based on statistics (p.[Gly863Ala, Gly863del], p.(Ala1038Val), p.(Gly1961Glu), c.5714+5G>A, and p.(Arg2030Gln)(Cornelis et al. 2017). A non-canonical splice variant was deemed mild if the second allele was severe and the patient showed an intermediate STGD1 phenotype. It was considered severe if the second allele was severe and the patient showed early-onset STGD1 (onset ≤ 10 yrs). The variant was also considered severe if the second allele was mild and the patient showed an intermediate STGD1 phenotype. For 25/47 variants, we observed concordance between the *in vitro* splice assay result and the clinical assessment in one or more patients; for 22/47 variants a conclusion was not possible.

DNA variant	% correctly spliced mRNA	Classification variant based on RNA splice study	Number of alleles in *ABCA4* LOVD	Classification NCSS variant based on clinical data	Concor-dance variant classifi-cation	Reference (PMID)
c.160+5G>C	34,3	Moderate	3	Moderate	Yes	Sciezynska et al. 2015 (26593885)
c.161G>T	0	Severe	1	n.a.	n.a.	Oishi et al. 2014 (25324289)
c.302+4A>C	0	Severe	4	Severe	Yes	Siemiatkowska et al. 2011 (22128245)
c.303-3C>G	0	Severe	0[1]	Severe	Yes	This study
c.768G>T	0	Severe	140	Severe	Yes	Maugeri et al. 1999 (10090887)
c.859-9T>C	75,7	Mild	6	Mild	Yes	Duncker et al. 2015 (26551331); Alapati et al. 2014 (25082885); this study
c.1100-6T>A	0	Severe	1	n.a.	n.a.	Zernant et al. 2011 (21911583)
c.1937+13T>G	14#	Severe	0[1]	n.a.	n.a.	This study
c.2382+5G>C*	47,9#	Moderate	1	n.a.	n.a.	Riveiro-Alvarez et al. 2013 (23755871)
c.2588G>C*	60#	Mild[2]	291	Mild	Yes	Maugeri et al. 1999 (10090887); Zernant et al. 2017 (28446513)
c.2919-10T>C	61,1	Moderate	0[3]	n.a.	n.a.	Schulz et al. 2017 (28118664)
c.2919-6C>A	79,6	Mild	1	n.a.	n.a.	Ozgul et al. 2004 (15108289)
c.3050+5G>A	0	Severe	13	Severe	Yes	Rivera et al. 2000 (10958763)
c.3522+5del	53,0	Moderate	2	Moderate	Yes	Zernant et al. 2011 (21911583)
c.3607G>A	10,9	Severe	1	n.a.	n.a.	Stennirri et al. 2004 (15192030)
c.3607+3A>T	0	Severe	1	Severe	Yes	Boulanger-Scemama et al. 2015 (26103963)
c.3812A>G	0	Severe	1	n.a.	n.a.	Zernant et al. 2011 (21911583)
c.3813G>C	0	severe	1	n.a.	n.a.	Lambertus et al. 2015 (25444351)
c.3862+3A>G	53,4	Moderate	1	n.a.	n.a.	Alapati et al. 2014 (25082885)
c.4128G>A	0	Severe	1	n.a.	n.a.	Passerini et al. 2010 (19265867)
c.4253+4C>T	7,8	Severe	13	Severe	Yes	Sanchez et al. 2014 (25342620)
c.4253+5G>A	0	Severe	11	Severe	Yes	Paloma et al. 2001 (11385708)
c.4253+5G>T	5,4	Severe	4	Severe	Yes	Lewis et al. 1999 (9973280)
c.4538A>G	0$	Severe	2	n.a.	n.a.	Fujinami et al. 2013 (23982839)
c.4538A>C	4,3$	Severe	1	Severe	Yes	Fishman et al. 1999 (10206579)
c.4634G>A	100	Benign	1	n.a.	n.a.	Fujinami et al. 2013 (23982839)
c.4667G>C	0	Severe	2	Moder./Severe	Yes	Chacon-Camacho et al. 2013 (23419329)
c.4773G>C	0	Severe	2	n.a.	n.a.	Fujinami et al. 2013 (23982839) Burke et al. 2014 (24677105)
c.4773+3A>G	24,6	Severe	8	Moder./Severe	Yes	Miraldi et al. 2014 (24457364)
c.4773+5G>A	29,1	Severe	1	Severe	Yes	Duno et al. 2012 (22229821)
c.5196+3_5196+6del	0	Severe	1	Severe	Yes	Kitiratschky et al. 2008 (18285826)
c.5196+3_5196+8del	100	Benign	1	n.a.	n.a.	Rozet et al. 1998 (9781034)
c.5312+3A>T	0	Severe	2	Severe	Yes	Xi et al. 2009 (19352439)
c.5313-3C>G	0	Severe	1	Severe	Yes	Downes et al. 2012 (23143460)
c.5460+5G>A	0	Severe	1	n.a.	n.a.	Riveiro-Alvarez et al. 2013 (23755871)
c.5461-10T>C	0	Severe	214	Severe	Yes	Sangermano et al. 2016 (26976702)
c.5461-8T>G	0	Severe	0[1]	Severe	Yes	This study
c.5584G>C	0	Severe	1	n.a.	n.a.	Huang et al. 2015 (25356976)
c.5584+5G>A	0	Severe	6	n.a.	n.a.	Webster et al. 2001 (11328725)
c.5584+6T>C	0	Severe	5	n.a.	n.a.	Rosenberg et al. 2007 (17982420)
c.5585-10T>C	100	Benign	2	n.a.	n.a.	Rosenberg et al. 2007 (17982420)
c.5714+5G>A	39,8	Moderate	116	Moder./Mild[4]	Yes	Cremers et al. 1998 (9466990); Cornelis et al. 2017 (28044389)
c.5836-3C>A	0	Severe	1	Severe	Yes	Sciezynska et al. 2015 (26593885)
c.5898+5del	4,5	Severe	2	Severe	Yes	Sodi et al. 2010 (20128570)
c.6478A>G	55,2	Moderate	2	n.a.	n.a.	Duno et al. 2012 (22229821)
c.6479+4A>G	0	Severe	1	n.a.	n.a.	Huang et al. 2015 (25356976)
c.6729+5_6729+19del	0	Severe	4	Severe	Yes	Littink et al. 2010 (20554613)

In general, we classified variants as severe if the correctly splice RNA is present in <30% of the products, moderately severe if between 30% and 70%, and mild if >70%. [1]These variants were not listed in the *ABCA4* LOVD (http://www.LOVD.nl/ABCA4) but present in STGD1 patients described in this study. [2]The variant c.2588G>C (p.[Gly863Ala, Gly863del] was deemed mild in previous studies (Maugeri et al. 1999) and recently was found to only be penetrant as a mild allele when in *cis* with c.5603A>T (p.(Asn1868Ile))(Zernant et al. 2017). [3]This variant was published after the *ABCA4* LOVD was made. [4]The non-canonical splice site variant c.5714+5G>A based on homozygosity analysis was classified as a mild *ABCA4* variant (Cornelis et al. 2017) but in some reported cases clearly shows a moderately severe character (Cremers et al. 1998). For variants c.2382+5G>C and c.2588G>C, nomenclature does not include the skipping of *ABCA4* exon 15 (*). For variants c.1937+13T>G and c.2382+5G>C, the percentage of correctly spliced mRNA was determined by densitometry (Supplemental Table S12), and for variant c.2588G>C by direct analysis of Sanger sequence traces (#). NCSS, non-canonical splice site; n.a.: not applicable. In the NCSS variant classification it denotes that no conclusion could be drawn as the severity of the second allele was not known or when there were no detailed clinical data available. In the concordance variant classification column it indicates that a correlation analysis was not possible. For variants c.4538A>C and c.4538A>G, the percentage of correctly spliced mRNA was not entirely determined due to likely co-migrating gel fragments of similar size ($).