中国大型队列白化病确诊病例基因谱分析

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#这些作者对这项工作做出了同样的贡献。

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小标题：*中国人口白化病谱系*

至编辑

白化病是一种遗传异质性状，全球患病率为 1:17,000。至少有 22 个基因已被确定为人类白化病的致病基因。这些涉及非综合征性白化病中的 10 个基因和 12 个综合征性白化病基因（Fernandez 等人，2021）。由于疾病基因突变是群体特异性的，因此研究中国人群中疾病基因谱和等位基因分布对于该病早期生活的精确干预非常重要。

2008 年 6 月至 2020 年 12 月，从中国人群中招募了 1,146 例非相关患者，这些患者被皮肤科和眼科专家临床诊断为白化病，包括 858 例未报告病例（**补充表 S1**）和 288 例先前报告的病例（**补充文本**）。所有已知的 22 个白化病基因的突变筛选流程如**图 1** 所示。**补充图 S1** 显示了两个具有代表性的确诊病例（一个 HPS-6（患者#1041）和一个 HPS-1（患者#1052））。方法的详细信息在**补充文本**中进行了描述。

两个反式 P/LP（致病性/可能致病性）等位基因的确认分子诊断率为 93.63%（1,073/1,146）。63 名患者（5.50%）仅携带一个突变等位基因，10 名患者（0.87%）未检测到 P/LP 变体。未检测到的等位基因可能位于所使用的技术遗漏的非编码区域，或者可能来自未知的白化病基因。

在 1073 例确诊病例中，OCA-1 是中国最常见的亚型（62.07%），其次是 OCA-2（17.43%）和 OCA-4（10.90%）（**图 2a，补充表 S2**）。这个频谱与我们之前的试点研究略有不同（OCA-1：70.1%，OCA-4：12.6%，OCA-2：10.2%）（魏等人，2010）。欧洲人群中的前 3 个突变基因是相似的（Lasseaux 等人，2018）（**图 2b，补充表 S2**）。然而，在日本人群中，OCA-4 是最常见的亚型，其次是 OCA-1 和 HPS-1（冈村和铃木，2020 年）（**图 2c，补充表 S2**）。因此，我们进一步证实，白化病基因的突变谱是群体特异性的。

除了一名 OCA-3 患者（患者#908）的皮肤相对较白外，所有其他 OCA-3 患者的皮肤色素沉着均正常。大多数患者（9/10）暴露在阳光下的身体部

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位（如手臂和面部）的皮肤颜色随着年龄的增长而逐渐变黑，这与其他 OCA 类型显着不同。此外，六名患者的发色随着年龄的增长而变暗，虹膜的颜色也变暗（**补充表 S3**）。因此，我们得出结论，与非非洲人群中的其他 OCA 类型相比，OCA-3 的表型是轻微的。

我们的实验室首先报告的 OCA-6（魏等人，2013），占欧洲队列白化病的 3.1%（Lasseaux 等人，2018），但在我们的筛查中仅为 0.47%（5/1,146），表明中国 OCA-6 的患病率较低。迄今为止，全世界已报告了 32 例 OCA-6 患者，其表型各不相同。我们的 5 名中国 OCA-6 患者，包括 2 例新报告的病例（患者#1041 和#1042），表现出相对轻度的白化病。

在白化病患者中必须更加关注综合征型白化病，因为我们在该队列中发现 4.80%（55/1,146）HPS 患者。HPS-1（28/55）是中国人群中 HPS 的主要形式，其次是 HPS-3（9/55）和 HPS6（9/55）。HPS-3、HPS-5 或 HPS-6 患者通常仅表现为眼白化病。由于 HPS 的不同亚型对手术前给予 DDAVP 以防止出血的反应不同（马等人，2016），并且不同的 HPS 亚型可能在结肠炎和肺纤维化方面具有不同的并发症（Fernandez 等人，2021），HPS 亚型的精确基因分型很重要。

该队列总共确定了 486 种不同的等位基因，包括之前报告的 285 个等位基因和本研究中报告的 199 个等位基因。在这 199 个等位基因中，182 个被归类为白化病致病等位基因，17 个是意义不确定的变体（**补充表 S4**）。

除了位点异质性外，每个白化病基因中变异的分布也是群体特异性的。在 TYR 的突变等位基因中，c.929_930insC 等位基因是最常见的等位基因，频率为 19.97%（271/1,357），其次是 c.896G>A（239/1,357），c.832C>T（134/1,357）和其他等位基因，如**图 2D**所示。p.T373L，c.1037-7T>A 和 c.1A>G 是欧洲人群中最常见的等位基因（Lasseaux 等人，在日本人群中，c.929_930insC,p.P431L 和 p.R77Q 是最普遍的等位基因（Okamura 和 Suzuki，

2020）。该图中最常见的 OCA2 等位基因是 p.R136X（31/396），其次是 c.1182+1G>A（22/396）和 p.A481T（21/396）。该队列中 SLC45A2 最常见的等位基因是 p.D160H（111/246）。

在一些外显子和一些变异上聚集的突变变异的分布在不同人群中显示出奠基者效应。在中国 OCA-1 患者中，总 TYR 突变等位基因的 82.54%（1,120/1,357）聚集在外显子 1 和 2 上（**图 2e**），这是中国人群中 TYR 突变的多发区（魏等人，2010）。在欧洲人群中，63.5%的 TYR 等位基因位于外显子 1 和 4 中（Lasseaux 等人，2018）（**图 2f**）。SLC45A2 中的 p.D160H 突变是中国 OCA-4 患者中最常见的突变等位基因，这可能是由于奠基者效应。在日本和韩国 OCA-4 患者中，具有奠基者效应的等位基因是 p.D157N（Inagaki 等人，2005）。总 HPS1 突变等位基因的 34.55%（19/55）位于 HPS1 基因的外显子 11 和 19 上，这表明这些外显子是中国人群中 HPS1 变异的多发区（刘等人，2021）。

对不同人群中白化病基因的遗传筛查表明，按等位基因频率对非致病变异或病理突变的定义是群体特异性的。具有致病性或良性证据的几个常见等位基因总结在**补充表 S5** 中。 有趣的是，我们只发现了一名被诊断患有转移性黑色素瘤的 OCA-1 患者，患者#410，这表明中国白化病伴恶性黑色素瘤的发病率非常低（1/1,146）。

综上所述，我们在这里报道了 199 种不同的新型白化病致病等位基因，这扩大了白化病数据库的等位基因库。疾病基因和等位基因的群体特异性分布对于白化病的精准诊断、携带者筛查、产前诊断和遗传咨询非常重要。

数据可用性声明

本研究期间未生成或分析任何数据集。

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配图描述

图 1：在我们的白化病患者基因分型中实施的诊断策略的流程图。

EM，电子显微镜；

MLPA，多路连接依赖性探针扩增；

NGS，下一代测序；

qPCR，实时荧光定量 PCR。

图 2：不同人群中白化病基因变异的频谱分布。

（a）本研究中不同白化病类型的分布情况。

（b）欧洲人群中白化病类型的患病率（Lasseaux 等人，2018）。

（c）日本人口中白化病类型的患病率（冈村和铃木，2020 年）。

（d）本研究中 TYR 中常见变异的分布情况。

（e）中国人群中 TYR 基因的突变热点。

（f）欧洲人群中 TYR 基因的突变热点（Lasseaux 等人，2018）。
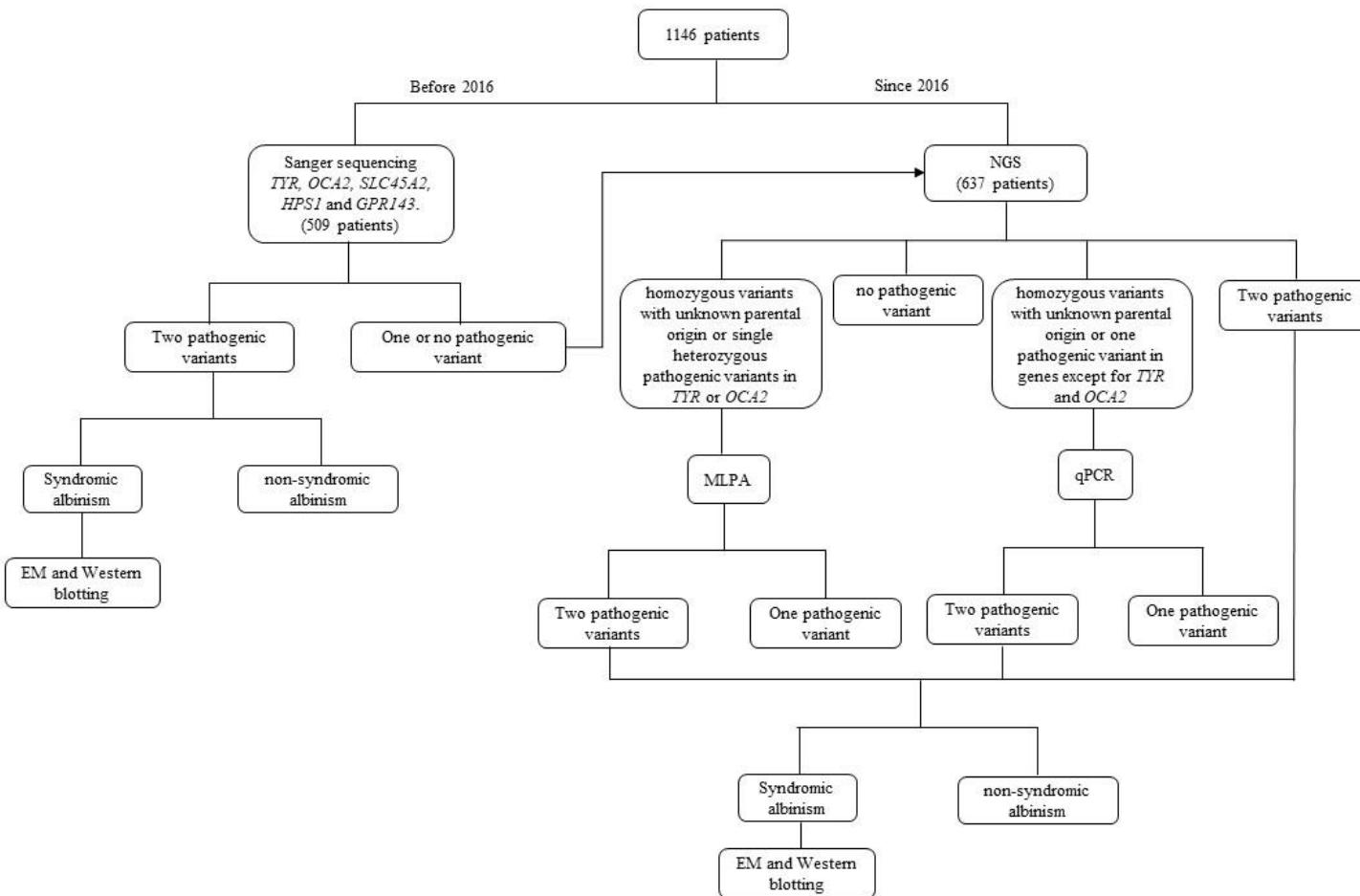
图 1：诊断策略流程图
108x60mm（300 x 300 DPI）
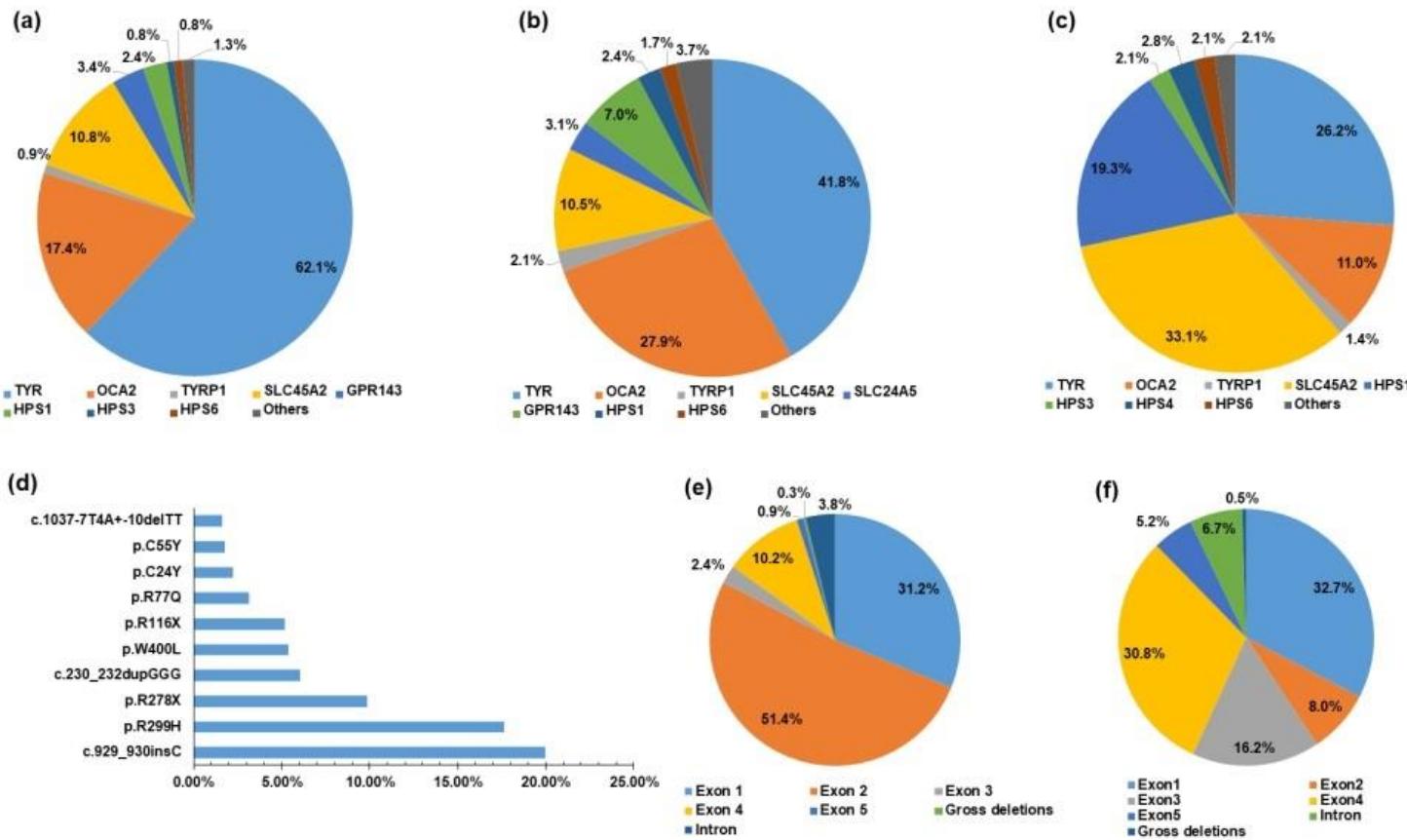
图 2：变体的频谱分布
160x96mm（300 x 300 DPI）

补充材料

I. 补充材料和方法

研究对象

从 2008 年 6 月至 2020 年 12 月，我们招募了 1,146 名来自中国人群的无关患者，并被皮肤科专家和眼科专家临床诊断为白化病，其中包括 858 例未报告病例和 288 例先前报告的患者（王等人，2009；魏等，2009；魏等，2010；林等，2011；魏等，2011；魏等，2013a；魏等，2013b；林等，2014；魏等，2015；魏等，2016；魏等，2017；魏等，2019；张等人，2019a；张等人，2019b；刘等人，2021a；刘等人，2021b）。该队列的平均年龄约为 10 岁，从出生 3 天到 78 岁不等，男性：女性为 1:0.75 岁。患者来自除西藏以外的中国大陆各省，除 20 名其他民族患者外，多为汉族。只有 3 名患者（0.26%，3/1,146）有近亲结婚家族史。本研究经首都医科大学北京同仁医院、北京儿童医院生物伦理学委员会机构评审委员会批准。这项研究是根据《赫尔辛基原则宣言》进行的。参与本研究的所有受试者或儿童的父母或监护人签署了书面知情同意书。患者#1041 和#1052 的父母同意发布图 S1 中的图像。

白化病诊断标准

OCA1A，OCA1B，OCA2 根据临床特征进行临床诊断（魏等人，2016；魏等人，2019）。这些包括皮肤病学表型（皮肤颜色，出生时和咨询时的头发颜色），眼科表型（眼睛颜色，半透明虹膜，存在视力障碍，畏光，眼球震颤和中央凹发育不全），以及支持合并形式的白化病的症状（出血倾向，肉芽肿性结肠炎，肺纤维化，感染倾向）。本研究中招募的患者都有眼球震颤的症状和至少一种白化病的其他眼部特征（半透明虹膜，中央凹发育不全）。

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通过全贴装电子显微镜检查确认 HPS 患者不存在血小板致密颗粒，并通过蛋白质印迹确认 HPS 蛋白不稳定（魏等人，2016；魏等人，2019）。患者的父母在同意后参加了这项研究。临床特征、变异的致病性、分离分析中的隐性转导等位基因或显性从头突变以及功能测定是确认白化病亚型分子诊断的四个关键组成部分。

Sanger 法测序

在 2016 年之前，通过直接 Sanger 测序分析了 509 名患者，以检测一个或多个常见白化病基因（TYR，OCA2，TYRP1，SLC45A2，HPS1 或 GPR143）的整个编码外显子和外显子/内含子侧翼区域（魏等人，2010；魏等人，2011）。使用常规蛋白酶 K/SDS 方法从血液样品中提取总基因组 DNA。所有引物均采用标准 PCR 扩增程序，退火温度为 58-59℃。引物序列可根据要求提供。

外显子捕获和测序

自 2016 年以来，下一代测序（NGS）在 637 名患者的基因检测中实施（魏等人，2016；刘等人，2021a）。在 trio -WES（全外显子组测序）中，使用 Agilent Sure Select 人全外显子 V6 试剂盒富集含外显子的片段，并使用 Illumina 高通量测序平台检测突变。Sanger 测序用于验证所有候选致病变异及其来自其父母的起源。

多重连接依赖性探针扩增（MLPA）和实时定量 PCR（qPCR）

对于那些由 NGS，MLPA 或 qPCR 牵涉的拷贝数变体，进一步用于检测可能的大片段杂合性缺失（魏等人，2016；张等人，2019b）。MLPA 用于 20 名在 TYR 或 OCA2 中鉴定出亲本来源不明的纯合子变异或 TYR 或 OCA2 中单个

杂合致病变异的患者。qPCR 用于检测三名在 HPS1 或 SLC45A2 中具有一种致病变异的患者的杂合度大缺失。

整片血小板的电镜观察和血小板 HPS 蛋白的免疫印迹

利用电子显微镜（EM）观察血小板致密颗粒。先前已经描述了对整片血小板进行 EM 检查的详细程序（魏等人，2016；魏等人，2019）。分离并裂解来自 2mL 外周血的血小板。蛋白质印迹用于检测 HPS 蛋白的稳态水平，并具有前面描述的详细程序（魏等人，2016；魏等人，2019）。

生物信息学分析

GRCh37/UCSChg19 被用作参考基因组来比较和注释变异。对于尚未在文献中报道或包含在 HGMD 数据库中的新变体，通过遵循美国医学遗传学和基因组学学院（ACMG）的指南来评估致病性（Richards 等人，2015）。

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II．附图图例

图 S1：确认 OCA-6 和 HPS-1 诊断的典型病例。

（a-c）一名 1 岁女孩（患者#1041）被临床诊断为 OCA2（a）。SLC24A5 基因的 Sanger 测序直方图显示复合杂合子（b）。整片血小板电子显微镜检查显示，与她的父母相比，血小板致密颗粒数量正常（c）。（d-f）一名 2 个

月大的女孩（患者#1052）被临床诊断为 OCA1（d）。HPS1 基因的 Sanger 测序直方图显示复合杂合子（e）。整片血小板电子显微镜检查显示，与她的父母相比，没有血小板致密颗粒（f）。患者#1041 和#1052 的父母同意发布这些图像。

III．补充表格
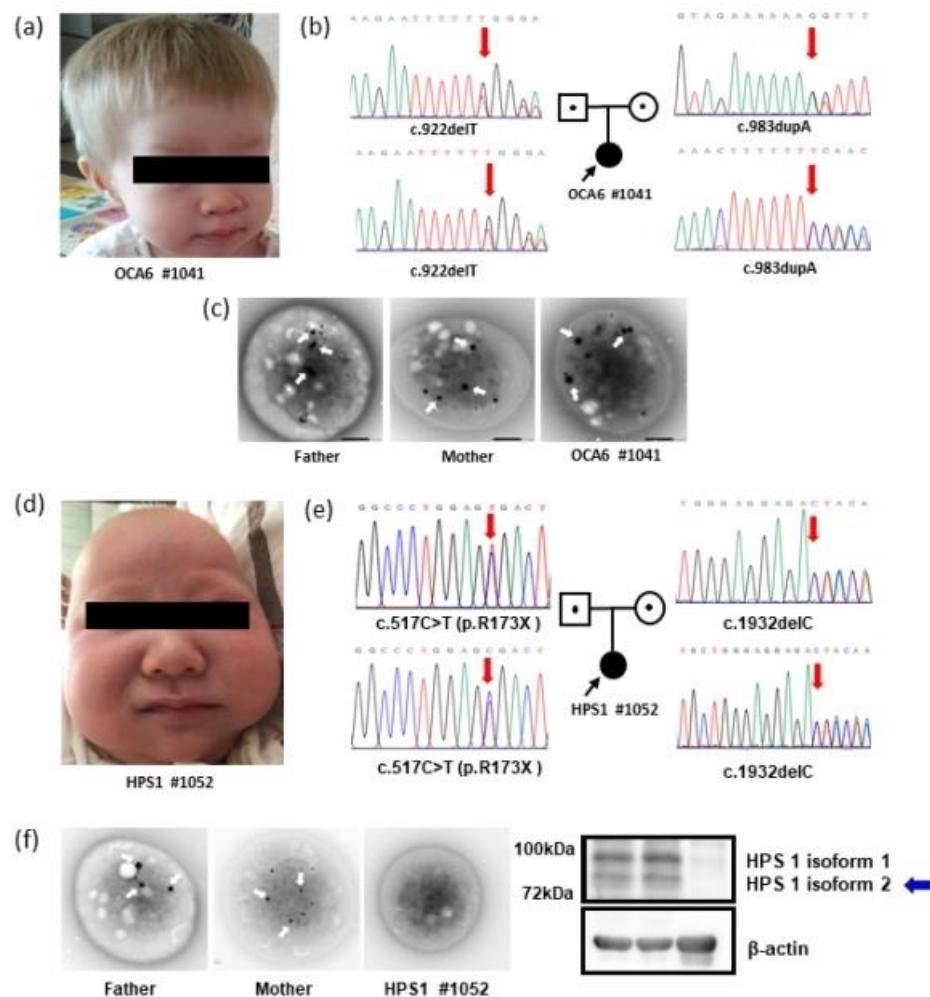
图 S1：代表性案例
108x60mm（300 x 300 DPI)

补充表 S1。858 例中国白化病患者的遗传变异。

Patient	Alleles	Gene	Exon	Variant 1 c.	Variant 1 p.	Gene	Exon	Variant 2 c.	Variant 2 p.	Sequencing
1	2	TYR	1	c.230_232dupGGG	p.R77_E78insG	TYR	1	c.230_232dupGGG	p.R77_E78insG	Sanger
2	2	TYR	1	c.229C>G	p.R77G	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
3	2	TYR	1	c.346C>T	p.R116X	TYR	2	c.832C>T	p.R278X	Sanger
4	2	TYR	1	c.115T>C	p.W39R	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
5	2	TYR	1	c.425A>T	p.K142M	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
6	2	TYR	1	c.655G>A	p.E219K	TYR	2	c.896G>A	p.R299H	Sanger
7	2	TYR	1	c.655G>A	p.E219K	TYR	2	c.896G>A	p.R299H	Sanger
8	2	TYR	1	c.164G>A	p.C55Y	TYR	4	c.1199G>T	p.W400L	Sanger
9	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.896G>A	p.R299H	Sanger
10	2	TYR	1	c.157G>T	p.G53C	TYR	2	c.832C>T	p.R278X	Sanger
11	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
12	2	TYR	1	c.230_232dupGGG	p.R77_E78insG	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
13	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	4	c.1199G>T	p.W400L	Sanger
14	2	TYR	1	c.230_232dupGGG	p.R77_E78insG	TYR	4	c.1234C>G	p.P412L	Sanger
15	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
16	2	TYR	1	c.346C>T	p.R116X	TYR	1	c.346C>T	p.R116X	Sanger
17	2	TYR	1	c.164G>A	p.C55Y	TYR	2	c.832C>T	p.R278X	Sanger
18	2	TYR	1	c.164G>A	p.C55Y	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
19	2	TYR	3	c.1147G>A	p.D383N	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
20	2	TYR	1	c.230_232dupGGG	p.R77_E78insG	TYR	2	c.896G>A	p.R299H	Sanger
21	2	TYR	2	c.832C>T	p.R278X	TYR	2	c.896G>A	p.R299H	Sanger
22	2	TYR	1	c.819G>T	p.Q273H	TYR	2	c.867C>A	p.C289X	Sanger
23	2	TYR	1	c.230_232dupGGG	p.R77_E78insG	TYR	2	c.896G>A	p.R299H	Sanger
24	2	TYR	1	c.71G>A	p.C24Y	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
25	2	TYR	2	c.832C>T	p.R278X	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
26	2	TYR	1	c.164G>A	p.C55Y	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
27	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
28	2	TYR	1	c.107G>A	p.C36T	TYR	2	c.832C>T	p.R278X	Sanger
29	2	TYR	1	c.164G>A	p.C55Y	TYR	2	c.812_815delCTT	----	Sanger

30	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.896G>A	p.R299H	Sanger
31	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
32	2	TYR	1	c.605A>G	p.H202R	TYR	2	c.896G>A	p.R299H	Sanger
33	2	TYR	1	c.538C>A	p.H180N	TYR	4	c.1265G>A	p.R422Q	Sanger
34	2	TYR	1	c.230_232dupGGG	p.R77_E78insG	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
35	2	TYR	1	c.741C>A	p.C247X	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
36	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	3	c.1071delC	----	Sanger
37	2	TYR	1	c.815G>A	p.W272X	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
38	2	TYR	1	c.230_232dupGGG	p.R77_E78insG	TYR	1	c.746A>G	p.D249G	Sanger
39	2	TYR	4	c.1265G>A	p.R422Q	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
40	2	TYR	1	c.346C>T	p.R116X	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
41	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.832C>T	p.R278X	Sanger
42	2	TYR	2	c.832C>T	p.R278X	TYR	3	c.1082G>T	p.S361I	Sanger
43	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	5	c.1451T>G	p.V484G	Sanger
44	2	TYR	2	c.832C>T	p.R278X	TYR	4	c.1199G>T	p.W400L	Sanger
45	2	TYR	2	c.832C>T	p.R278X	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
46	2	TYR	2	c.832C>T	p.R278X	TYR	2	c.896G>A	p.R299H	Sanger
47	2	TYR	1	c.230G>A	p.R77Q	TYR	4	c.1277T>A	p.M426K	Sanger
48	2	TYR	1	c.346C>T	p.R116X	TYR	2	c.896G>A	p.R299H	Sanger
49	2	TYR	1	c.164G>A	p.C55Y	TYR	2	c.896G>A	p.R299H	Sanger
50	2	TYR	1	c.655G>A	p.E219K	TYR	2	c.896G>A	p.R299H	Sanger
51	2	TYR	1	c.346C>T	p.R116X	TYR	2	c.297C>G	p.N99K	Sanger
52	2	TYR	Int2	c.1037-7T4A+-10delTT	----	TYR	4	c.1199G>T	p.W400L	Sanger
53	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.896G>A	p.R299H	Sanger
54	2	TYR	1	c.229C>T	p.R77W	TYR	Int2	c.1037-7T4A+-10delTT	----	Sanger
55	2	TYR	1	c.346C>T	p.R116X	TYR	2	c.895C>A	p.R299S	Sanger
56	2	TYR	2	c.832C>T	p.R278X	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
57	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.896G>A	p.R299H	Sanger
58	2	TYR	2	c.832C>T	p.R278X	TYR	2	c.832C>T	p.R278X	Sanger
59	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
60	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger

61	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.896G>A	p.R299H	Sanger
62	2	TYR	2	c.832C>T	p.R278X	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
63	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	2	c.896G>A	p.R299H	Sanger
64	2	TYR	4	c.1265G>A	p.R422Q	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
65	2	TYR	1	c.346C>T	p.R116X	TYR	2	c.896G>A	p.R299H	Sanger
66	2	TYR	1	c.346C>T	p.R116X	TYR	1	c.346C>T	p.R116X	Sanger
67	2	TYR	2	c.832C>T	p.R278X	TYR	1	c.636A>T	p.R212S	Sanger
68	2	TYR	4	c.1200G>A	p.W400X	TYR	2	c.896G>A	p.R299H	Sanger
69	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
70	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.896G>A	p.R299H	Sanger
71	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.896G>A	p.R299H	Sanger
72	2	TYR	1	c.346C>T	p.R116X	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
73	2	TYR	2	c.832C>T	p.R278X	TYR	Int1	c.820-3C>G	----	Sanger
74	2	TYR	Int2	c.1037-7T4A+-10delTT	----	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
75	2	TYR	1	c.230G>A	p.R77Q	TYR	2	c.896G>A	p.R299H	Sanger
76	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	4	c.1199G>T	p.W400L	Sanger
77	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
78	2	TYR	1	c.346C>T	p.R116X	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
79	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
80	2	TYR	1	c.650G>A	p.R217Q	TYR	1	c.650G>A	p.R217Q	Sanger
81	2	TYR	1	c.230_232dupGGG	p.R77_E78insG	TYR	1	c.650G>A	p.R217Q	Sanger
82	2	TYR	2	c.832C>T	p.R278X	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
83	2	TYR	1	c.230_232dupGGG	p.R77_E78insG	TYR	2	c.895C>A	p.R299S	Sanger
84	2	TYR	2	c.896G>A	p.R299H	TYR	5	c.1380insT	----	Sanger
85	2	TYR	2	c.832C>T	p.R278X	TYR	4	c.1199G>T	p.W400L	Sanger
86	2	TYR	Int2	c.1037-7T4A+-10delTT	----	TYR	4	c.1199G>T	p.W400L	Sanger
87	2	TYR	1	c.229C>T	p.R77W	TYR	1	c.593T>C	p.I198T	Sanger
88	2	TYR	2	c.895C>A	p.R299S	TYR	2	c.895C>A	p.R299S	Sanger
89	2	TYR	2	c.832C>T	p.R278X	TYR	int2	c.1037-2A>G	----	Sanger
90	2	TYR	1	c.116G>A	p.W39X	TYR	2	c.896G>A	p.R299H	Sanger
91	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger

92	2	TYR	1	c.230_232dupGGG	p.R77_E78insG	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
93	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
94	2	TYR	4	c.1265G>A	p.R422Q	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
95	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.896G>A	p.R299H	Sanger
96	2	TYR	1	c.758G>A	p.G253E	TYR	2	c.832C>T	p.R278X	Sanger
97	2	TYR	1	c.230G>A	p.R77Q	TYR	1	c.758G>A	p.G253E	Sanger
98	2	TYR	Int2	c.1037-7T4A+-10delTT	----	TYR	4	c.1199G>T	p.W400L	Sanger
99	2	TYR	1	c.230G>A	p.R77Q	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
100	2	TYR	1	c.593T>G	p.I198S	TYR	2	c.896G>A	p.R299H	Sanger
101	2	TYR	2	c.832C>T	p.R278X	TYR	1	c.221_222delTG	----	Sanger
102	2	TYR	1	c.230_232dupGGG	p.R77_E78insG	TYR	1	c.425A>T	p.K142M	Sanger
103	2	TYR	Int2	c.1037-7T4A+-10delTT	----	TYR	1	c.230_232dupGGG	p.R77_E78insG	Sanger
104	2	TYR	1	c.346C>T	p.R116X	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
105	2	TYR	2	c.896G>A	p.R299H	TYR	4	c.1348insGG	----	Sanger
106	2	TYR	2	c.895C>A	p.R299S	TYR	4	c.1199G>T	p.W400L	Sanger
107	2	TYR	1	c.71G>A	p.C24Y	TYR	4	c.1265T>A	p.M426K	Sanger
108	2	TYR	1	c.346C>T	p.R116X	TYR	1	c.22delT	----	Sanger
109	2	TYR	2	c.832C>T	p.R278X	TYR	2	c.896G>A	p.R299H	Sanger
110	2	TYR	2	c.832C>T	p.R278X	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
111	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.896G>A	p.R299H	Sanger
112	2	TYR	1	c.655G>A	p.E219K	TYR	1	c.230_232dupGGG	p.R77_E78insG	Sanger
113	2	TYR	1	c.346C>T	p.R116X	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
114	2	TYR	2	c.896G>A	p.R299H	TYR	1	c.56G>A	p.H19R	Sanger
115	2	TYR	1	c.707G>C	p.W236S	TYR	2	c.832C>T	p.R278X	Sanger
116	2	TYR	1	c.230_232dupGGG	p.R77_E78insG	TYR	1	c.71G>A	p.C24Y	Sanger
117	2	TYR	1	c.606T>G	p.H202Q	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
118	2	TYR	1	c.283T>C	p.F95L	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
119	2	TYR	4	c.629G>A	p.W210X	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
120	2	TYR	2	c.896G>A	p.R299H	TYR	Int2	c.1037-7T4A+-10delTT	----	Sanger
121	2	TYR	1	c.298T>C	p.C100R	TYR	1	c.346C>T	p.R116X	Sanger
122	2	TYR	4	c.1199G>T	p.W400L	TYR	Int2	c.1037-7T4A+-10delTT	----	Sanger

123	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
124	2	TYR	2	c.896G>A	p.R299H	TYR	4	c.1193A>G	p.E398G	Sanger
125	2	TYR	1	c.706T>C	p.W236R	TYR	1	c.706T>C	p.W236R	Sanger
126	2	TYR	4	c.1199G>T	p.W400L	TYR	2	c.1022G>A	p.R341K	Sanger
127	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
128	2	TYR	4	c.1995C>T	p.Q399X	TYR	Int2	c.1037-7T>A	----	NGS
129	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	2	c.832C>T	p.R278X	NGS
130	2	TYR	3	c.1151C>A	p.P384H	TYR	1	c.593T>C	p.I198T	NGS
131	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	4	c.1204C>T	p.R402X	NGS
132	2	TYR	1	c.816G>A	p.W272X	TYR	2	c.896G>A	p.R299H	NGS
133	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	1	c.701C>T	p.P234L	NGS
134	2	TYR	1	c.230_232dupGGG	p.R77_E78insG	TYR	2	c.929_930insC	p.R311Kfs*7	NGS
135	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	2	c.929_930insC	p.R311Kfs*7	NGS
136	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	2	c.832C>T	p.R278X	NGS
137	2	TYR	1	c.230G>A	p.R77Q	TYR	2	c.929_930insC	p.R311Kfs*7	NGS
138	2	TYR	4	c.1199G>T	p.W400L	TYR	1	c.346C>T	p.R116X	NGS
139	2	TYR	2	c.739T>C	p.C247R	TYR	1	c.346C>T	p.R116X	NGS
140	2	TYR	Int2	c.1037-7T>A	----	TYR	1	c.346C>T	p.R116X	NGS
141	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	4	c.1217C>T	p.P406L	NGS
142	2	TYR	1	c.230_232dupGGG	p.R77_E78insG	TYR	1	c.755T>A	p.M252K	NGS
143	2	TYR	1	c.230G>A	p.R77Q	TYR	1	c.455C>A	p.P152H	NGS
144	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	2	c.896G>A	p.R299H	NGS
145	2	TYR	2	c.832C>T	p.R278X	TYR	2	c.896G>A	p.R299H	NGS
146	2	TYR	2	c.832C>T	p.R278X	TYR	Int2	c.1037-7T>A	----	NGS
147	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	4	c.1275C>G	p.Y425X	NGS
148	2	TYR	1	c.758G>A	p.G253E	TYR	2	c.896G>A	p.R299H	NGS
149	2	TYR	1	c.346C>T	p.R116X	TYR	2	c.896G>A	p.R299H	NGS
150	2	TYR	2	c.896G>A	p.R299H	TYR	4	c.1334T>C	p.L445P	NGS
151	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	Int2	c.1037-7T>A	----	NGS
152	2	TYR	1	c.758G>A	p.G253E	TYR	Int2	c.1037-7T>A	----	NGS
153	2	TYR	1	c.71G>A	p.C24Y	TYR	1	c.164G>A	p.C55Y	NGS

154	2	TYR	1	c.755T>A	p.M252K	TYR	3	c.1168C>G	p.H390D	NGS
155	2	TYR	1	c.230G>A	p.R77Q	TYR	4	c.1263C>G	p.N421K	NGS
156	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.929_930insC	p.R311Kfs*7	NGS
157	2	TYR	1	c.216delA	p.V74Wfs*46	TYR	1	c.216delA	p.V74Wfs*46	NGS
158	2	TYR	2	c.827G>A	p.C276Y	TYR	2	c.896G>A	p.R299H	NGS
159	2	TYR	4	c.1346A>G	p.Y449C	TYR	1	c.561_562ins 25bp	p.G190Cfs*12	NGS
160	2	TYR	2	c.832C>T	p.R278X	TYR	2	c.929_930insC	p.R311Kfs*7	NGS
161	2	TYR	1	c.703T>C	p.Y235H	TYR	2	c.895C>A	p.R299S	NGS
162	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	1	c.230_232dupGGG	p.R77_E78insG	NGS
163	2	TYR	1	c.230G>A	p.R77Q	TYR	2	c.832C>T	p.R278X	NGS
164	2	TYR	1	c.230_232dupGGG	p.R77_E78insG	TYR	2	c.832C>T	p.R278X	NGS
165	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.929_930insC	p.R311Kfs*7	NGS
166	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	4	c.1199G>T	p.W400L	NGS
167	2	TYR	2	c.896G>A	p.R299H	TYR	4	c.1199G>T	p.W400L	NGS
168	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	3	c.1136G>T	p.G379V	NGS
169	2	TYR	4	c.1279delG	p.V427Ffs*58	TYR	2	c.896G>A	p.R299H	NGS
170	2	TYR	2	c.895C>T	p.R299C	TYR	1	c.655G>A	p.E219K	NGS
171	2	TYR	2	c.832C>T	p.R278X	TYR	1	c.655G>A	p.E219K	NGS
172	2	TYR	1	c.346C>T	p.R116X	TYR	1	c.346C>T	p.R116X	NGS
173	2	TYR	1	c.164G>A	p.C55Y	TYR	1	c.230G>A	p.R77Q	NGS
174	2	TYR	1	c.346C>T	p.R116X	TYR	1	c.115T>C	p.W39R	NGS
175	2	TYR	2	c.832C>T	p.R278X	TYR	2	c.896G>A	p.R299H	NGS
176	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	4	c.1231T>C	p.Y411H	NGS
177	2	TYR	1	c.346C>T	p.R116X	TYR	5	c.1425G>A	p.W475X	Sanger
178	2	TYR	1	c.346C>T	p.R116X	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
179	2	TYR	1	c.107G>C	p.C36S	TYR	Int2	c.1037-7T>A	----	NGS
180	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	4	c.1205G>A	p.R402Q	NGS
181	2	TYR	2	c.832C>T	p.R278X	TYR	Int2	c.1037-7T4A+-10delTT	----	NGS
182	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	2	c.929_930insC	p.R311Kfs*7	NGS
183	2	TYR	2	c.896G>A	p.R299H	TYR	3	c.1162C>T	p.L388F	NGS
184	2	TYR	1	c.70T>C	p.C24R	TYR	Int2	c.1037-7T4A+-10delTT	----	NGS

185	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.929_930insC	p.R311Kfs*7	NGS
186	2	TYR	2	c.832C>T	p.R278X	TYR	3	c.1082G>T	p.S361I	NGS
187	2	TYR	1	c.230G>A	p.R77Q	TYR	1	c.230_232dupGGG	p.R77_E78insG	NGS
188	2	TYR	1	c.230_232dupGGG	p.R77_E78insG	TYR	2	c.1022G>A	p.R341K	NGS
189	2	TYR	2	c.896G>A	p.R299H	TYR	4	c.1199G>T	p.W400L	NGS
190	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.995T>C	p.M332T	NGS
191	2	TYR	1	c.758G>A	p.G253E	TYR	2	c.896G>A	p.R299H	NGS
192	2	TYR	1	c.346C>T	p.R116X	TYR	2	c.896G>A	p.R299H	NGS
193	2	TYR	1	c.230_232dupGGG	p.R77_E78insG	TYR	1	c.230_232dupGGG	p.R77_E78insG	NGS
194	2	TYR	1	c.230_232dupGGG	p.R77_E78insG	TYR	2	c.896G>A	p.R299H	NGS
195	2	TYR	3	c.1130T>A	p.V377E	TYR	4	c.1247C>G	p.A416G	NGS
196	2	TYR	2	c.895C>A	p.R299S	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
197	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.929_930insC	p.R311Kfs*7	NGS
198	2	TYR	1	c.819G>T	p.Q273H	TYR	Int2	c.1037-7T4A+-10delTT	----	NGS
199	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	Int2	c.1037-7T4A+-10delTT	----	NGS
200	2	TYR	1	c.230G>A	p.R77Q	TYR	4	c.1275C>G	p.Y425X	NGS
201	2	TYR	2	c.896G>A	p.R299H	TYR	4	c.1199G>T	p.W400L	NGS
202	2	TYR	1	c.230_232dupGGG	p.R77_E78insG	TYR	2	c.832C>T	p.R278X	NGS
203	2	TYR	2	c.896G>A	p.R299H	TYR	4	c.1199G>T	p.W400L	Sanger
204	2	TYR	1	c.230_232dupGGG	p.R77_E78insG	TYR	1	c.593T>C	p.I198T	NGS
205	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	4	c.1265G>A	p.R422Q	NGS
206	2	TYR	2	c.895C>A	p.R299S	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
207	2	TYR	2	c.832C>T	p.R278X	TYR	2	c.880G>A	p.E294K	NGS
208	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.929_930insC	p.R311Kfs*7	NGS
209	2	TYR	1	c.599T>C	p.F200S	TYR	2	c.896G>A	p.R299H	Sanger
210	2	TYR	1	c.455C>A	p.P152H	TYR	2	c.1031T>G	p.L344R	Sanger
211	2	TYR	2	c.832C>T	p.R278X	TYR	2	c.965T>C	p.L322P	Sanger
212	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
213	2	TYR	1	c.230_232dupGGG	p.R77_E78insG	TYR	2	c.896G>A	p.R299H	Sanger
214	2	TYR	1	c.230_232dupGGG	p.R77_E78insG	TYR	4	c.1265G>A	p.R422Q	Sanger
215	2	TYR	1	c.635G>A	p.R212K	TYR	4	c.1199G>T	p.W400L	Sanger

216	2	TYR	1	c.56A>G	p.H19R	TYR	1	c.230G>A	p.R77Q	Sanger
217	2	TYR	1	c.56A>G	p.H19R	TYR	1	c.230G>A	p.R77Q	Sanger
218	2	TYR	1	c.346C>T	p.R116X	TYR	2	c.896G>A	p.R299H	Sanger
219	2	TYR	1	c.346C>T	p.R116X	TYR	1	c.71G>A	p.C24Y	Sanger
220	2	TYR	3	c.1168C>G	p.H390D	TYR	4	c.1199G>T	p.W400L	Sanger
221	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
222	2	TYR	1	c.346C>T	p.R116X	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
223	2	TYR	2	c.832C>T	p.R278X	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
224	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.896G>A	p.R299H	Sanger
225	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.896G>A	p.R299H	Sanger
226	2	TYR	1	c.230_232dupGGG	p.R77_E78insG	TYR	2	c.832C>T	p.R278X	Sanger
227	2	TYR	1	c.425A>T	p.K142M	TYR	1	c.635G>A	p.R212K	Sanger
228	2	TYR	1	c.71G>A	p.C24Y	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
229	2	TYR	Int2	c.1037-7T>A+-10delTT	----	TYR	3	c.1037G>A	p.G346E	Sanger
230	2	TYR	1	c.230G>A	p.R77Q	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
231	2	TYR	1	c.758G>A	p.G253E	TYR	Int1	c.820-3C>G	----	Sanger
232	2	TYR	2	c.895C>A	p.R299S	TYR	4	c.1265G>A	p.R422Q	Sanger
233	2	TYR	1	c.230_232dupGGG	p.R77_E78insG	TYR	3	c.1089A>G	p.H364R	Sanger
234	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
235	2	TYR	2	c.832C>T	p.R278X	TYR	2	c.896G>A	p.R299H	Sanger
236	2	TYR	2	c.895C>T	p.R299C	TYR	2	c.929_930insC	p.R311Kfs*7	NGS
237	2	TYR	1	c.346C>T	p.R116X	TYR	2	c.896G>A	p.R299H	NGS
238	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	4	c.1265G>A	p.R422Q	NGS
239	2	TYR	2	c.832C>T	p.R278X	TYR	4	c.1199G>T	p.W400L	Sanger
240	2	TYR	2	c.896G>A	p.R299H	TYR	3	c.1146C>A	p.N382K	NGS
241	2	TYR	1	c.17delT	p.L6Cfs*25	TYR	2	c.895C>A	p.R299S	Sanger
242	2	TYR	1	c.230G>A	p.R77Q	TYR	2	c.896G>A	p.R299H	NGS
243	2	TYR	1	c.346C>T	p.R116X	TYR	1	c.230_232dupGGG	p.R77_E78insG	Sanger
244	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
245	2	TYR	2	c.896G>A	p.R299H	TYR	1	c.265T>A	p.C89S	Sanger
246	2	TYR	2	c.896G>A	p.R299H	TYR	1	c.758G>A	p.G253E	NGS

247	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
248	1	TYR	1	c.346C>T	p.R116X	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
249	2	TYR	2	c.832C>T	p.R278X	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
250	2	TYR	4	c.1265G>A	p.R422Q	TYR	4	c.1323_1325delATC	p.S442del	Sanger
251	2	TYR	1	c.425A>T	p.K142M	TYR	4	c.1265G>A	p.R422Q	Sanger
252	2	TYR	1	c.230_232dupGGG	p.R77_E78insG	TYR	1	c.230_232dupGGG	p.R77_E78insG	Sanger
253	2	TYR	1	c.346C>T	p.R116X	TYR	Int2	c.1037-7T>A	- - - -	Sanger
254	2	TYR	1	c.658C>T	p.Q220X	TYR	2	c.929_930insC	p.R311Kfs*7	NGS
255	2	TYR	1	c.346C>T	p.R116X	TYR	1	c.115T>C	p.W39R	Sanger
256	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	Int2	c.1037-7T>A	- - - -	WES
257	2	TYR	2	c.832C>T	p.R278X	TYR	2	c.929_930insC	p.R311Kfs*7	Sanger
258	2	TYR	1	c.230G>A	p.R77Q	TYR	2	c.896G>A	p.R299H	Sanger
259	2	TYR	1	c.71G>A	p.C24Y	TYR	1	c.230_232dupGGG	p.R77_E78insG	Sanger
260	2	TYR	2	c.832C>T	p.R278X	TYR	2	c.896G>A	p.R299H	NGS
261	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	2	c.929_930insC	p.R311Kfs*7	NGS
262	2	TYR	2	c.832C>T	p.R278X	TYR	4	c.1199G>T	p.W400L	NGS
263	2	TYR	2	c.832C>T	p.R278X	TYR	1	c.56A>G	p.H19R	NGS
264	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	1	c.265T>A	p.C89S	NGS
265	2	TYR	1	c.425A>T	p.K142M	TYR	1	- - - -	p.A204E	Sanger
266	2	TYR	2	c.896G>A	p.R299H	TYR	Int2	c.1037-7T4A+-10delTT	- - - -	NGS
267	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	2	c.929_930insC	p.R311Kfs*7	NGS
268	2	TYR	1	c.758G>A	p.G253E	TYR	4	c.1265G>A	p.R422Q	NGS
269	2	TYR	1	c.230_232dupGGG	p.R77_E78insG	TYR	1	c.230G>A	p.R77Q	NGS
270	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.896G>A	p.R299H	NGS
271	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	2	c.832C>T	p.R278X	NGS
272	2	TYR	1	c.230_232dupGGG	p.R77_E78insG	TYR	2	c.896G>A	p.R299H	NGS
273	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	2	c.896G>A	p.R299H	NGS
274	2	TYR	2	c.925_926insC	p.T309TfsX9	TYR	1	c.230_232dupGGG	p.R77_E78insG	WES
275	2	TYR	3	c.1082G>T	p.S361I	TYR	Int1	c.820-3C>G	- - - -	WES
276	2	TYR	1	c.56A>G	p.H19R	TYR	2	c.929_930insC	p.R311Kfs*7	WES
277	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.896G>A	p.R299H	WES

278	2	TYR	1	c.164G>A	p.C55Y	TYR	2	c.896G>A	p.R299H	WES
279	2	TYR	1	c.706T>C	p.W236R	TYR	2	c.896G>A	p.R299H	WES
280	2	TYR	2	c.832C>T	p.R278X	TYR	2	c.896G>A	p.R299H	WES
281	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	2	c.929_930insC	p.R311Kfs*7	WES
282	2	TYR	1	c.17delT	p.L6Cfs*25	TYR	2	c.832C>T	p.R278X	WES
283	2	TYR	1	c.346C>T	p.R116X	TYR	2	c.929_930insC	p.R311Kfs*7	WES
284	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.896G>A	p.R299H	WES
285	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.929_930insC	p.R311Kfs*7	WES
286	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.929_930insC	p.R311Kfs*7	WES
287	2	TYR	1	c.346C>T	p.R116X	TYR	3	c.1147G>A	p.D383N	WES
288	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.929_930insC	p.R311Kfs*7	WES
289	2	TYR	2	c.832C>T	p.R278X	TYR	2	c.929_930insC	p.R311Kfs*7	WES
290	2	TYR	1	c.707G>C	p.W236S	TYR	2	c.929_930insC	p.R311Kfs*7	WES
291	2	TYR	1	c.230G>A	p.R77Q	TYR	2	c.832C>T	p.R278X	WES
292	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	Int2	c.1037-2A>T	----	WES
293	2	TYR	1	c.230G>A	p.R77Q	TYR	2	c.929_930insC	p.R311Kfs*7	WES
294	2	TYR	2	c.880G>A	p.E294K	TYR	2	c.929_930insC	p.R311Kfs*7	WES
295	2	TYR	1	c.425A>T	p.K142M	TYR	2	c.929_930insC	p.R311Kfs*7	WES
296	2	TYR	1	c.703T>C	p.Y235H	TYR	2	c.929_930insC	p.R311Kfs*7	WES
297	2	TYR	1	c.758G>A	p.G253E	TYR	2	c.896G>A	p.R299H	WES
298	2	TYR	1	c.164G>A	p.C55Y	TYR	2	c.896G>A	p.R299H	WES
299	2	TYR	1	c.24C>A	p.C8X	TYR	2	c.895C>T	p.R299C	WES
300	2	TYR	2	c.895C>T	p.R299C	TYR	2	c.929_930insC	p.R311Kfs*7	WES
301	2	TYR	1	c.230_232dupGGG	p.R77_E78insG	TYR	2	c.832C>T	p.R278X	WES
302	2	TYR	2	c.895C>A	p.R299S	TYR	2	c.896G>A	p.R299H	WES
303	2	TYR	1	c.240G>T	p.W80C	TYR	1	c.706T>C	p.W236R	WES
304	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	4	c.1199G>T	p.W400L	WES
305	2	TYR	1	c.650G>C	p.R217P	TYR	4	c.1199G>T	p.W400L	WES
306	2	TYR	2	c.896G>A	p.R299H	TYR	4	c.1275C>G	p.Y425X	WES
307	2	TYR	1	c.229C>G	p.R77G	TYR	4	c.1265G>A	p.R422Q	WES
308	2	TYR	2	c.896G>A	p.R299H	TYR	4	c.1199G>T	p.W400L	WES

309	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.896G>A	p.R299H	WES
310	2	TYR	2	c.832C>T	p.R278X	TYR	2	c.896G>A	p.R299H	WES
311	2	TYR	2	c.832C>T	p.R278X	TYR	2	c.896G>A	p.R299H	WES
312	2	TYR	1	c.346C>T	p.R116X	TYR	2	c.929_930insC	p.R311Kfs*7	WES
313	2	TYR	1	c.71G>A	p.C24Y	TYR	2	c.929_930insC	p.R311Kfs*7	WES
314	2	TYR	1	c.547G>A	p.V183M	TYR	2	c.929_930insC	p.R311Kfs*7	WES
315	2	TYR	1	c.632A>G	p.H211R	TYR	2	c.896G>A	p.R299H	WES
316	2	TYR	1	c.757G>T	p.G253X	TYR	2	c.832C>T	p.R278X	WES
317	2	TYR	Int1	c.820-3C>G	----	TYR	2	c.929_930insC	p.R311Kfs*7	WES
318	2	TYR	1	c.230_232dupGGG	p.R77_E78insG	TYR	2	c.929_930insC	p.R311Kfs*7	WES
319	2	TYR	2	c.832C>T	p.R278X	TYR	2	c.929_930insC	p.R311Kfs*7	WES
320	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	2	c.929_930insC	p.R311Kfs*7	WES
321	2	TYR	Int2	c.1037-7T>A	----	TYR	2	c.929_930insC	p.R311Kfs*7	WES
322	2	TYR	2	c.832C>T	p.R278X	TYR	2	c.832C>T	p.R278X	WES
323	2	TYR	2	c.832C>T	p.R278X	TYR	2	c.832C>T	p.R278X	WES
324	2	TYR	1	c.230G>A	p.R77Q	TYR	2	c.832C>T	p.R278X	WES
325	2	TYR	1	c.71G>A	p.C24Y	TYR	1	c.346C>T	p.R116X	WES
326	2	TYR	2	c.832C>T	p.R278X	TYR	2	c.929_930insC	p.R311Kfs*7	WES
327	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	2	c.929_930insC	p.R311Kfs*7	WES
328	2	TYR	4	c.1204C>T	p.R402X	TYR	2	c.929_930insC	p.R311Kfs*7	WES
329	2	TYR	1	c.635G>A	p.R212K	TYR	2	c.832C>T	p.R278X	WES
330	2	TYR	1	c.230G>A	p.R77Q	TYR	4	c.1199G>T	p.W400L	WES
331	2	TYR	1	c.655G>A	p.E219K	TYR	2	c.929_930insC	p.R311Kfs*7	WES
332	2	TYR	2	c.836T>A	p.L279X	TYR	2	c.929_930insC	p.R311Kfs*7	WES
333	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.896G>A	p.R299H	WES
334	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	2	c.929_930insC	p.R311Kfs*7	WES
335	2	TYR	5	c.1454G>A	p.G485E	TYR	5	c.1454G>A	p.G485E	WES
336	2	TYR	1	c.230G>A	p.R77Q	TYR	1	c.230_232dupGGG	p.R77_E78insG	WES
337	2	TYR	1	c.71G>A	p.C24Y	TYR	1	c.17delT	p.L6Cfs*2 5	WES
338	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.929_930insC	p.R311Kfs*7	WES
339	2	TYR	Int1	c.820-3C>G	----	TYR	2	c.896G>A	p.R299H	WES

340	2	TYR	2	c.832C>T	p.R278X	TYR	2	c.896G>A	p.R299H	WES
341	2	TYR	1	c.346C>T	p.R116X	TYR	2	c.929_930insC	p.R311Kfs*7	WES
342	2	TYR	2	c.896G>A	p.R299H	TYR	3	c.1130T>A	p.V377E	WES
343	2	TYR	2	c.832C>T	p.R278X	TYR	2	c.929_930insC	p.R311Kfs*7	WES
344	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.896G>A	p.R299H	WES
345	2	TYR	1	c.71G>A	p.C24Y	TYR	2	c.929_930insC	p.R311Kfs*7	WES
346	2	TYR	1	c.346C>T	p.R116X	TYR	2	c.896G>A	p.R299H	WES
347	2	TYR	1	c.425A>T	p.K142M	TYR	2	c.929_930insC	p.R311Kfs*7	WES
348	2	TYR	2	c.895C>T	p.R299C	TYR	2	c.896G>A	p.R299H	WES
349	2	TYR	2	c.832C>T	p.R278X	TYR	2	c.929_930insC	p.R311Kfs*7	WES
350	2	TYR	1	c.346C>T	p.R116X	TYR	2	c.929_930insC	p.R311Kfs*7	WES
351	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	4	c.1199G>T	p.W400L	WES
352	2	TYR	1	c.230_232dupGGG	p.R77_E78insG	TYR	2	c.929_930insC	p.R311Kfs*7	WES
353	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.929_930insC	p.R311Kfs*7	WES
354	2	TYR	1	c.230_232dupGGG	p.R77_E78insG	TYR	1	c.230_232dupGGG	p.R77_E78insG	WES
355	2	TYR	3	c.1184G>A	p.S395N	TYR	4	c.1199G>T	p.W400L	WES
356	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	2	c.929_930insC	p.R311Kfs*7	WES
357	2	TYR	1	c.346C>T	p.R116X	TYR	2	c.832C>T	p.R278X	WES
358	2	TYR	2	c.896G>A	p.R299H	TYR	3	c.1130T>A	p.V377E	WES
359	2	TYR	2	c.832C>T	p.R278X	TYR	2	c.896G>A	p.R299H	WES
360	2	TYR	2	c.895C>T	p.R299C	TYR	2	c.929_930insC	p.R311Kfs*7	WES
361	2	TYR	1	c.230G>A	p.R77Q	TYR	2	c.929_930insC	p.R311Kfs*7	WES
362	2	TYR	1	c.655G>A	p.E219K	TYR	2	c.832C>T	p.R278X	WES
363	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	2	c.929_930insC	p.R311Kfs*7	WES
364	2	TYR	1	c.230_232dupGGG	p.R77_E78insG	TYR	1	c.425A>T	p.K142M	WES
365	2	TYR	2	c.832C>T	p.R278X	TYR	4	c.1199G>T	p.W400L	WES
366	2	TYR	4	c.1288_1291dupATAC	p.F431Hfs*8	TYR	4	c.1288_1291dupATAC	p.F431Hfs*8	WES
367	2	TYR	2	c.896G>A	p.R299H	TYR	5	c.1425G>A	p.W475X	WES
368	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	2	c.929_930insC	p.R311Kfs*7	WES
369	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	Int2	c.1037-7T>A	----	WES
370	2	TYR	1	c.71G>A	p.C24Y	TYR	1	c.164G>A	p.C55Y	WES

371	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.896G>A	p.R299H	WES
372	2	TYR	1	c.230_232dupGGG	p.R77_E78insG	TYR	2	c.929_930insC	p.R311Kfs*7	WES
373	2	TYR	1	c.56A>G	p.H19R	TYR	2	c.896G>A	p.R299H	WES
374	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	Int2	c.1037-7T>A	----	WES
375	2	TYR	1	c.346C>T	p.R116X	TYR	2	c.896G>A	p.R299H	WES
376	2	TYR	1	c.632A>G	p.H211R	TYR	2	c.895C>T	p.R299C	WES
377	2	TYR	1	c.230_232dupGGG	p.R77_E78insG	TYR	2	c.929_930insC	p.R311Kfs*7	WES
378	2	TYR	1	c.230_232dupGGG	p.R77_E78insG	TYR	2	c.929_930insC	p.R311Kfs*7	WES
379	2	TYR	2	c.865T>C	p.C289R	TYR	2	c.865T>C	p.C289R	WES
380	2	TYR	2	c.832C>T	p.R278X	TYR	5	c.1534C>T	p.Q512X	WES
381	2	TYR	2	c.832C>T	p.R278X	TYR	2	c.865T>C	p.C289R	WES
382	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.929_930insC	p.R311Kfs*7	WES
383	2	TYR	2	c.896G>A	p.R299H	TYR	4	c.1199G>T	p.W400L	WES
384	2	TYR	Int1	c.820-1G>C	----	TYR	2	c.929_930insC	p.R311Kfs*7	WES
385	2	TYR	1	c.655G>A	p.E219K	TYR	3	c.1080_1091del12	p.S361_N364del	WES
386	2	TYR	1	c.164G>A	p.C55Y	TYR	Int2	c.1037-7T>A	----	WES
387	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.896G>A	p.R299H	WES
388	2	TYR	2	c.896G>A	p.R299H	TYR	5	c.1379_1380delTT	p.F460Sfs*5	WES
389	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	5	c.1425G>A	p.W475X	WES
390	2	TYR	1	c.71G>A	p.C24Y	TYR	1	c.346C>T	p.R116X	WES
391	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.1031T>G	p.L344R	WES
392	2	TYR	1	c.71G>A	p.C24Y	TYR	2	c.929_930insC	p.R311Kfs*7	WES
393	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	2	c.929_930insC	p.R311Kfs*7	WES
394	2	TYR	1	c.758G>A	p.G253E	TYR	2	c.832C>T	p.R278X	WES
395	2	TYR	1	c.655G>A	p.E219K	TYR	2	c.896G>A	p.R299H	WES
396	2	TYR	4	c.1199G>T	p.W400L	TYR	Int4	c.1366+3A>T	----	WES
397	2	TYR	1	c.229C>T	p.R77W	TYR	2	c.832C>T	p.R278X	WES
398	2	TYR	2	c.832C>T	p.R278X	TYR	2	c.929_930insC	p.R311Kfs*7	WES
399	2	TYR	4	c.1195C>T	p.Q399X	TYR	4	c.1283C>T	p.P428L	WES
400	2	TYR	1	c.758G>A	p.G253E	TYR	2	c.929_930insC	p.R311Kfs*7	WES
401	2	TYR	1	c.230_232dupGGG	p.R77_E78insG	TYR	2	c.896G>A	p.R299H	WES

402	2	TYR	1	c.164G>A	p.C55Y	TYR	2	c.929_930insC	p.R311Kfs*7	WES
403	2	TYR	1	c.230_232dupGGG	p.R77_E78insG	TYR	4	c.1199G>T	p.W400L	WES
404	2	TYR	2	c.832C>T	p.R278X	TYR	2	c.937_939dupCCC	p.P313dup	WES
405	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	2	c.929_930insC	p.R311Kfs*7	WES
406	2	TYR	1	c.230G>A	p.R77Q	TYR	4	c.1199G>T	p.W400L	WES
407	2	TYR	4	c.1199G>T	p.W400L	TYR	1	c.230_232dupGGG	p.R77_E78insG	WES
408	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.929_930insC	p.R311Kfs*7	WES
409	2	TYR	1	c.346C>T	p.R116X	TYR	1	c.346C>T	p.R116X	WES
410	2	TYR	2	c.832C>T	p.R278X	TYR	2	c.896G>A	p.R299H	WES
411	2	TYR	1	c.230G>A	p.R77Q	TYR	1	c.425A>T	p.K142M	WES
412	2	TYR	1	c.230G>A	p.R77Q	TYR	2	c.929_930insC	p.R311Kfs*7	WES
413	2	TYR	1	c.425A>T	p.K142M	TYR	2	c.929_930insC	p.R311Kfs*7	WES
414	2	TYR	2	c.896G>A	p.R299H	TYR	3	c.1109T>C	p.M370T	WES
415	2	TYR	2	c.832C>T	p.R278X	TYR	4	c.1195C>T	p.Q399X	WES
416	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	2	c.929_930insC	p.R311Kfs*7	WES
417	2	TYR	2	c.832C>T	p.R278X	TYR	2	c.896G>A	p.R299H	WES
418	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	4	c.1199G>T	p.W400L	WES
419	2	TYR	1	c.230_232dupGGG	p.R77_E78insG	TYR	2	c.896G>A	p.R299H	WES
420	2	TYR	1	c.346C>T	p.R116X	TYR	1	c.346C>T	p.R116X	WES
421	2	TYR	2	c.895C>T	p.R299C	TYR	2	c.896G>A	p.R299H	WES
422	2	TYR	1	c.230_232dupGGG	p.R77_E78insG	TYR	4	c.1199G>T	p.W400L	WES
423	2	TYR	1	c.346C>T	p.R116X	TYR	2	c.832C>T	p.R278X	WES
424	2	TYR	1	c.230_232dupGGG	p.R77_E78insG	TYR	4	c.1199G>T	p.W400L	WES
425	2	TYR	1	c.346C>T	p.R116X	TYR	1	c.346C>T	p.R116X	WES
426	2	TYR	2	c.896G>A	p.R299H	TYR	4	c.1199G>T	p.W400L	WES
427	2	TYR	1	c.230G>A	p.R77Q	TYR	1	c.230G>A	p.R77Q	WES
428	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.929_930insC	p.R311Kfs*7	WES
429	2	TYR	2	c.895C>T	p.R299C	TYR	2	c.929_930insC	p.R311Kfs*7	WES
430	2	TYR	1	c.164G>A	p.C55Y	TYR	2	c.896G>A	p.R299H	WES
431	2	TYR	2	c.895C>A	p.R299S	TYR	2	c.896G>A	p.R299H	WES
432	2	TYR	2	c.832C>T	p.R278X	TYR	2	c.832C>T	p.R278X	WES

433	2	TYR	2	c.896G>A	p.R299H	TYR	Int4	c.1366+3A>T	----	WES
434	2	TYR	2	c.832C>T	p.R278X	TYR	2	c.832C>T	p.R278X	WES
435	2	TYR	4	c.1199G>T	p.W400L	TYR	4	c.1199G>T	p.W400L	WES
436	2	TYR	2	c.832C>T	p.R278X	TYR	2	c.929_930insC	p.R311Kfs*7	WES
437	2	TYR	2	c.896G>A	p.R299H	TYR	3	c.1130T>A	p.V377E	WES
438	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.929_930insC	p.R311Kfs*7	WES
439	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	2	c.929_930insC	p.R311Kfs*7	WES
440	2	TYR	2	c.896G>A	p.R299H	TYR	Int2	c.1037-7T>A	----	WES
441	2	TYR	2	c.832C>T	p.R278X	TYR	2	c.865T>C	p.C289R	WES
442	2	TYR	1	c.655G>A	p.E219K	TYR	2	c.896G>A	p.R299H	WES
443	2	TYR	Int4	c.1366+3A>T	----	TYR	Int4	c.1366+3A>T	----	WES
444	2	TYR	1	c.158G>A	p.G53D	TYR	2	c.896G>A	p.R299H	WES
445	2	TYR	1	c.155G>T	p.R52I	TYR	2	c.896G>A	p.R299H	WES
446	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	4	c.1255G>A	p.G419R	WES
447	2	TYR	1	c.819G>T	p.Q273H	TYR	4	c.1199G>T	p.W400L	WES
448	2	TYR	1	c.230_232dupGGG	p.R77_E78insG	TYR	2	c.929_930insC	p.R311Kfs*7	WES
449	2	TYR	1	c.346C>T	p.R116X	TYR	2	c.929_930insC	p.R311Kfs*7	WES
450	2	TYR	1	c.757G>A	p.G253R	TYR	2	c.929_930insC	p.R311Kfs*7	WES
451	2	TYR	2	c.832C>T	p.R278X	TYR	2	c.896G>A	p.R299H	WES
452	2	TYR	1	c.346C>T	p.R116X	TYR	4	c.1199G>T	p.W400L	WES
453	2	TYR	1	c.230_232dupGGG	p.R77_E78insG	TYR	1	c.230_232dupGGG	p.R77_E78insG	WES
454	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	1-4	Ex.1-4del	----	WES+MLPA
455	2	TYR	3	c.1184+5G>A	----	TYR	3	c.1184+5G>A	----	WES
456	2	TYR	4	c.1265G>A	p.R422Q	TYR	2	c.929_930insC	p.R311Kfs*7	WES
457	2	TYR	1	c.71G>A	p.C24Y	TYR	1	c.346C>T	p.R116X	WES
458	2	TYR	1	c.472C>T	pQ158X	TYR	2	c.896G>A	p.R299H	WES
459	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.902C>G	p.P301R	WES
460	2	TYR	2	c.832C>T	p.R278X	TYR	2	c.896G>A	p.R299H	WES
461	2	TYR	4	c.1199G>T	p.W400L	TYR	4	c.1199G>T	p.W400L	WES
462	2	TYR	4	c.1199G>T	p.W400L	TYR	4	c.1199G>T	p.W400L	WES
463	2	TYR	4	c.1195C>T	p.Q399X	TYR	4	c.1199G>T	p.W400L	WES

464	2	TYR	2	c.832C>T	p.R278X	TYR	2	c.896G>A	p.R299H	WES
465	2	TYR	1	c.230G>A	p.R77Q	TYR	1	c.346C>T	p.R116X	WES
466	2	TYR	1	c.715C>T	p.R239W	TYR	2	c.929_930insC	p.R311Kfs*7	WES
467	2	TYR	1	c.230G>A	p.R77Q	TYR	1	c.758G>A	p.G253E	WES
468	2	TYR	1	c.425A>T	p.K142M	TYR	1	c.425A>T	p.K142M	WES
469	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.929_930insC	p.R311Kfs*7	WES
470	2	TYR	1	c.230G>A	p.R77Q	TYR	1	c.655G>A	p.E219K	WES
471	2	TYR	1	c.346C>T	p.R116X	TYR	2	c.896G>A	p.R299H	WES
472	2	TYR	1	c.230G>A	p.R77Q	TYR	2	c.896G>A	p.R299H	WES
473	2	TYR	1	c.755T>A	p.M252K	TYR	2	c.929_930insC	p.R311Kfs*7	WES
474	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	4	c.1199G>T	p.W400L	WES
475	2	TYR	2	c.832C>T	p.R278X	TYR	2	c.896G>A	p.R299H	WES
476	2	TYR	2	c.832C>T	p.R278X	TYR	2	c.929_930insC	p.R311Kfs*7	WES
477	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.929_930insC	p.R311Kfs*7	WES
478	2	TYR	1	c.230G>A	p.R77Q	TYR	4	c.1199G>T	p.W400L	WES
479	2	TYR	1	c.164G>A	p.C55Y	TYR	4	c.1265G>A	p.R422Q	WES
480	2	TYR	1	c.230_232dupGGG	p.R77_E78insG	TYR	2	c.896G>A	p.R299H	WES
481	2	TYR	1	c.425A>T	p.K142M	TYR	4	c.1199G>T	p.W400L	WES
482	2	TYR	1	c.230_232dupGGG	p.R77_E78insG	TYR	2	c.895C>A	p.R299S	WES
483	2	TYR	2	c.832C>T	p.R278X	TYR	2	c.895C>A	p.R299S	WES
484	2	TYR	1	c.559_560ins25	p.G190Cfs*12	TYR	2	c.895C>A	p.R299S	WES
485	2	TYR	1	c.819G>T	p.Q273H	TYR	2	c.832C>T	p.R278X	WES
486	2	TYR	1	c.230_232dupGGG	p.R77_E78insG	TYR	2	c.937_939dupCCC	p.P313dup	WES
487	2	TYR	1	c.542A>G	p.Y181C	TYR	1	c.542A>G	p.Y181C	WES
488	2	TYR	4	c.1199G>T	p.W400L	TYR	4	c.1199G>T	p.W400L	WES
489	2	TYR	1	c.70T>C	p.C24R	TYR	1	c.70T>C	p.C24R	WES
490	2	TYR	1	c.157G>A	p.GI53S	TYR	1	c.157G>A	p.G53S	WES
491	2	TYR	4	c.1199G>T	p.W400L	TYR	4	c.1199G>T	p.W400L	WES
492	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.896G>A	p.R299H	WES
493	2	TYR	1	c.230_232dupGGG	p.R77_E78insG	TYR	2	c.929_930insC	p.R311Kfs*7	WES
494	2	TYR	1	c.741C>A	p.C247X	TYR	4	c.1199G>T	p.W400L	WES

495	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.929_930insC	p.R311Kfs*7	WES
496	2	TYR	1	c.230_232dupGGG	p.R77_E78insG	TYR	2	c.896G>A	p.R299H	WES
497	2	TYR	1	c.819G>T	p.Q273H	TYR	4	c.1193A>G	p.E398G	WES
498	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.929_930insC	p.R311Kfs*7	WES
499	2	TYR	1	c.324G>A	p.W108X	TYR	2	c.929_930insC	p.R311Kfs*7	WES
500	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	4	c.1199G>T	p.W400L	WES
501	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.929_930insC	p.R311Kfs*7	WES
502	2	TYR	2	c.896G>A	p.R299H	TYR	Int2	c.1037-7T>A	----	WES
503	2	TYR	1	c.346C>T	p.R116X	TYR	2	c.896G>A	p.R299H	WES
504	2	TYR	1	c.115T>C	p.W39R	TYR	2	c.929_930insC	p.R311Kfs*7	WES
505	2	TYR	1	c.230_232dupGGG	p.R77_E78insG	TYR	2	c.929_930insC	p.R311Kfs*7	WES
506	2	TYR	4	c.1199G>T	p.W400L	TYR	4	c.1204C>T	p.R402X	WES
507	2	TYR	1	c.230G>A	p.R77Q	TYR	1	c.346C>T	p.R116X	WES
508	2	TYR	1	c.230_232dupGGG	p.R77_E78insG	TYR	2	c.929_930insC	p.R311Kfs*7	WES
509	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.929_930insC	p.R311Kfs*7	WES
510	2	TYR	Int1	c.820-3C>G	----	TYR	4	c.1199G>T	p.W400L	WES
511	2	TYR	2	c.895C>T	p.R299C	TYR	2	c.929_930insC	p.R311Kfs*7	WES
512	2	TYR	1	c.230_232dupGGG	p.R77_E78insG	TYR	1	c.230_232dupGGG	p.R77_E78insG	WES
513	2	TYR	1	c.758G>A	p.G253E	TYR	2	c.976C>T	p.Q326X	WES
514	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	4	c.1292C>T	p.P431L	WES
515	2	TYR	1	c.230_232dupGGG	p.R77_E78insG	TYR	2	c.1022G>A	p.R341K	WES
516	2	TYR	1	c.164G>A	p.C55Y	TYR	1	c.706T>C	p.W236R	WES
517	2	TYR	2	c.896G>A	p.R299H	TYR	2	c.929_930insC	p.R311Kfs*7	WES
518	2	TYR	1	c.115T>C	p.W39R	TYR	4	c.1204C>T	p.R402X	WES
519	2	TYR	1	c.346C>T	p.R116X	TYR	2	c.832C>T	p.R278X	WES
520	2	TYR	1	c.71G>A	p.C24Y	TYR	1	c.819G>T	p.Q273H	WES
521	2	TYR	2	c.896G>A	p.R299H	TYR	3	c.1043C>A	p.A348D	WES
522	2	TYR	2	c.929_930insC	p.R311Kfs*7	TYR	2	c.929_930insC	p.R311Kfs*7	WES
523	1	TYR	2	c.896G>A	p.R299H					WES
524	1	TYR	1	c.24C>A	p.C8X					WES
525	1	TYR	2	c.896G>A	p.R299H					WES

526	1	TYR	1	c.164G>A	p.C55Y					Sanger
527	1	TYR	2	c.832C>T	p.R278X					Sanger
528	1	TYR	2	c.896G>A	p.R299H					Sanger
529	1	TYR	2	c.929_930insC	p.R311Kfs*7					Sanger
530	1	TYR	4	c.1199G>T	p.W400L					Sanger
531	1	TYR	4	c.1199G>T	p.W400L					Sanger
532		TYR	4	c.1193A>G	p.E398G					Sanger
533		TYR	4	c.1265G>A	p.R422Q					Sanger
692	2	OCA2	14	c.1426A>G	p.N476D	OCA2	14	c.1426A>G	p.N476D	Sanger
693	2	OCA2	4	c.406C>T	p.R136X	OCA2	15	c.1636G>A	p.E546K	Sanger
694	2	OCA2	11	c.1160C>T	p.T387M	OCA2	10	c.980dupT	----	Sanger
695	2	OCA2	6	c.593C>T	p.P198L	OCA2	15	c.1504G>A	p.G502S	NGS
696	2	OCA2	14	c.1441G>A	p.A481T	OCA2	13	c.1297G>T	p.A433S	Sanger
697	2	OCA2	9	c.1001C>T	p.A334V	OCA2	13	c.1327delGTCACCAC	----	Sanger
698	2	OCA2	19	c.2051T>G	p.F684C	OCA2	19	c.2074A>T	p.M692L	Sanger
699	2	OCA2	13	c.1363A>G	p.R455G	OCA2	18	c.1888T>A	p.L630M	Sanger
700	2	OCA2	10	c.1079C>T	p.S360F	OCA2	10	c.1079C>T	p.S360F	Sanger
701	2	OCA2	Int22	c.2339-2A>C	----	OCA2	21	c.2158C>T	p.R720C	Sanger
702	2	OCA2	23	c.2344G >A	p.G782R	OCA2	14	c.1441G>A	p.A481T	NGS
703	2	OCA2	Int7	c.808-3C>G	----	OCA2	14	c.1426A>G	p.N476D	NGS
704	2	OCA2	Int7	c.808-3C>G	----	OCA2	22	c.2323G>C	p.G775R	NGS
705	2	OCA2	14	c.1441G>A	p.A481T	OCA2	7	c.776delC	----	Sanger
706	2	OCA2	21	c.2221A>C	p.N741H	OCA2	13	c.1349C>T	p.T450M	Sanger
707	2	OCA2	6	c.593C>T	p.P198L	OCA2	23	c.2363C>T	p.S788T	Sanger
708	2	OCA2	13	c.1255C>T	p.R419W	OCA2	13	c.1255C>T	p.R419W	Sanger
709	2	OCA2	4	c.406C>T	p.R136X	OCA2	4	c.493C>T	p.R165X	Sanger
710	2	OCA2	6	c.593C>T	p.P198L	OCA2	6	c.593C>T	p.P198L	Sanger
711	2	OCA2	17	c.1832T>C	p.L611P	OCA2	Int11	c.1182+1G>A	----	NGS
712	2	OCA2	Int19	c.2080-2A>G	----	OCA2	12	c.1220T>G	p.F407C	NGS
713	2	OCA2	14	c.1444A>G	p.T482A	OCA2	Int7	c.808-3C>G	----	NGS
714	2	OCA2	13	c.1255C>T	p.R419W	OCA2	7	c.791G>A	p.W264S	Sanger

715	2	OCA2	22	c.2327C>A	p.A776D	OCA2	11	c.1177G>A	----	Sanger
716	2	OCA2	2	c.168delC	----	OCA2	10	c.1058C>T	p.T353I	Sanger
717	2	OCA2	14	c.1447G>T	p.A483S	OCA2	14	c.1448C>T	p.A483V	Sanger
718	2	OCA2	10	c.1079C>T	p.S360F	OCA2	11	c.1160C>T	p.T387M	Sanger
719	2	OCA2	14	c.1430T>C	p.I477T	OCA2	23	c.2363C>T	p.S788T	Sanger
720	2	OCA2	3	c.247C>T	p.Q83X	OCA2	13	c.1275G>T	p.M425I	Sanger
721	2	OCA2	14	c.1426A>G	p.N476D	OCA2	2	c.1832T>C	p.L611P	Sanger
722	2	OCA2	Int22	c.2239-2A>C	----	OCA2	22	c.2251G>A	p.V751M	Sanger
723	2	OCA2	2	c.196delC	----	OCA2	13	c.1255C>T	p.R419W	Sanger
724	2	OCA2	12	c.1211C>T	p.T404M	OCA2	14	c.1441G>A	p.A481T	Sanger
725	2	OCA2	23	c.2360C>T	p.A787V	OCA2	9	c.849G>T	p.S283R	Sanger
726	2	OCA2	Int7	c.807+1G>T	----	OCA2	Int7	c.807+1G>T	----	WES
727	2	OCA2	14	c.1441G>A	p.A481T	OCA2	Int11	c.1182+1G>A	----	NGS
728	2	OCA2	Int11	c.1182+1G>A	splice-5	OCA2	22	c.2248C>A	p.P750T	NGS
729	2	OCA2	14	c.1441G>A	p.A481T	OCA2	7	c.727C>T	p.R243C	NGS
730	2	OCA2	23	c.2363C>T	p.S788L	OCA2	4	c.406C>T	p.R136X	NGS
731	2	OCA2	9	c.913C>T	p.R305W	OCA2	9	c.1001C>T	p.A334V	NGS
732	2	OCA2	Int11	c.1182+1G>A	splice-5	OCA2	Int5	c.573+5G>A	----	NGS
733	2	OCA2	11	c.1160C>T	p.T387M	OCA2	21	c.2228C>T	p.P743L	NGS
734	2	OCA2	4	c.406C>T	p.R136X	OCA2	4	c.406C>T	p.R136X	NGS
735	2	OCA2	20	c.2080G>A	p.A694T	OCA2	23	c.2359G>A	p.A787T	NGS
736	2	OCA2	17	c.1832T>C	p.L611P	OCA2	17	c.1832T>C	p.L611P	NGS
737	2	OCA2	14	c.1441G>A	p.A481T	OCA2	22	c.2323G>A	p.G775S	NGS
738	2	OCA2	14	c.1441G>A	p.A481T	OCA2	Int11	c.1182+1G>A	----	NGS
739	2	OCA2	15	c.1526C>T	p.T509I	OCA2	24	c.2438G>T	p.G813V	NGS
740	2	OCA2	4	c.406C>T	p.R136X	OCA2	24	c.2491G>C	p.A831P	NGS
741	2	OCA2	13	c.1255C>T	p.R419W	OCA2	13	c.1255C>T	p.R419W	NGS
742	2	OCA2	13	c.1349C>T	p.T450M	OCA2	13	c.1349C>T	p.T450M	NGS
743	2	OCA2	3	c.247C>T	p.Q83X	OCA2	23	c.2344G>A	p.G782R	NGS
744	2	OCA2	13	c.1255C>T	p.R419W	OCA2	Int23	c.2432+1G>A	----	NGS
745	2	OCA2	12	c.1210A>G	p.T404A	OCA2	13	c.1288T>C	p.C430R	NGS

746	2	OCA2	13	c.1262G>A	p.R421Q	OCA2	13	c.1363A>G	p.R455G	NGS
747	2	OCA2	9	c.980dupT	----	OCA2	13	c.1255C>T	p.R419W	NGS
748	2	OCA2	4	c.406C>T	p.R136X	OCA2	13	c.1255C>T	p.R419W	NGS
749	2	OCA2	7	c.727C>T	p.R243C	OCA2	14	c.1397_1398delAA	----	NGS
750	2	OCA2	11	c.1160C>T	p.T387M	OCA2	Int14	c.1504-1G>C	----	NGS
751	2	OCA2	14	c.1441G>A	p.A481T	OCA2	23	c.2359G>A	p.A787T	NGS
752	2	OCA2	13	c.1358C>T	p.T453I	OCA2	Int14	c.1504-2A>G	----	NGS
753	2	OCA2	14	c.1441G>A	p.A481T	OCA2	4	c.406C>T	p.R136X	NGS
754	2	OCA2	Int6	c.647-2A>G	----	OCA2	2	c.156delC	p.R53Gfs*49	NGS
755	2	OCA2	14	c.1441G>A	p.A481T	OCA2	14	c.1426A>G	p.N476D	NGS
756	2	OCA2	14	c.1441G>A	p.A481T	OCA2	Int11	c.1182+1G>A	----	NGS
757	2	OCA2	16	c.1663C>T	p.R555C	OCA2	9	c.947T>G	p.L316R	NGS
758	2	OCA2	13	c.1349C>T	p.T450M	OCA2	14	c.1441G>A	p.A481T	NGS
759	2	OCA2	4	c.406C>T	p.R136X	OCA2	Int9	c.1045-9T>G	----	NGS
760	2	OCA2	9	c.944C>G	p.P315R	OCA2	Int7	c.808-3C>G	----	NGS
761	2	OCA2	13	c.1255C>T	p.R419W	OCA2	23	c.2359G>A	p.A787T	NGS
762	2	OCA2	3	c.247C>T	p.Q83X	OCA2	11	----	p.E381G	Sanger
763	2	OCA2	Int23	c.2339+1G>A	----	OCA2	Int23	c.2339+1G>A	----	Sanger
764	2	OCA2	13	c.1349C>T	p.T450M	OCA2	13	c.1349C>T	p.T450M	Sanger
765	2	OCA2	Int11	c.1182+1G>A	splice-5	OCA2	22	c.2323G>C	p.G775R	NGS
766	2	OCA2	6	c.805C>T	p.Q269X	OCA2	5	c.587T>C	p.L196P	Sanger
767	2	OCA2	7	c.824C>T	p.T275M	OCA2	21	c.2249C>T	p.P750L	Sanger
768	2	OCA2	9	c.980dupT	----	OCA2	22	c.2251G>A	p.V751M	Sanger
769	2	OCA2	22	c.2323G>A	p.G775S	OCA2	13	c.1363A>G	p.R455G	WES
770	2	OCA2	23	c.2344G >A	p.G782R	OCA2	23	c.2344G>A	p.G782R	Sanger
771	2	OCA2	9	c.849G>T	p.S283R	OCA2	Int11	c.1182+1G>A	----	NGS
772	2	OCA2	18	c.1844A>G	p.H615R	OCA2	10-14	Ex.10-14del	----	NGS+MLPA
773	2	OCA2	21	c.2155C>T	p.Q719X	OCA2	Int21	c.2245-6C>G	----	NGS
774	2	OCA2	14	c.1441G>A	p.A481T	OCA2	14	c.1433G>A	p.G478E	NGS
775	2	OCA2	24	c.2438G>T	p.G813V	OCA2	24	c.2438G>T	p.G813V	NGS
776	2	OCA2	13	c.1327G>A	p.V443I	OCA2	13	c.1349C>T	p.T450M	NGS

777	2	OCA2	Int11	c.1182+1G>A	splice-5	OCA2	5	c.535A>G	p.K179E	NGS
778	2	OCA2	14	c.1465A>T	p.N489Y	OCA2	13	c.1265G>T	p.R119L	NGS
779	2	OCA2	4	c.478delG	----	OCA2	21	c.2228C>T	p.P743L	NGS
780	2	OCA2	13	c.1327G>A	p.V443I	OCA2	19	c.2021T>C	p.L674P	NGS
781	2	OCA2	Int11	c.1182+1G>A	splice-5	OCA2	14	c.1441G>A	p.A481T	NGS
782	2	OCA2	24	c.2491G>C	p.A831P	OCA2	Int18	c.1951+1G>C	----	WES
783	2	OCA2	9	c.950delT	p.L317X	OCA2	9	c.950delT	p.L317X	WES
784	2	OCA2	4	c.406C>T	p.R136X	OCA2	4	c.406C>T	p.R136X	WES
785	2	OCA2	13	c.1349C>T	p.T450M	OCA2	3	c.247C>T	p.Q83X	WES
786	2	OCA2	20	c.2093T>G	p.L698R	OCA2	2	c.157delA	p.AR53Gfs*49	WES
787	2	OCA2	15	c.1560_1562delCCT	p.L521del	OCA2	13	c.1255C>T	p.R419W	WES
788	2	OCA2	23	c.2344G >A	p.G782R	OCA2	10	c.1064C>A	p.A355E	WES
789	2	OCA2	8	c.863_886del24	p.M288_L295del	OCA2	6	c.593C>T	p.P198L	WES
790	2	OCA2	14	c.1426A>G	p.N476D	OCA2	4	c.406C>T	p.R136X	WES
791	2	OCA2	Int20	c.2140-2A>G	----	OCA2	6	c.632C>T	p.P211L	WES
792	2	OCA2	Int11	c.1182+1G>A	splice-5	OCA2	Int11	c.1182+1G>A	----	WES
793	2	OCA2	17	c.1832T>C	p.L611P	OCA2	Int7	c.808-3C>G	----	WES
794	2	OCA2	23	c.2359G>A	p.A787T	OCA2	4	c.406C>T	p.R136X	WES
795	2	OCA2	14	c.1426A>G	p.N476D	OCA2	Int7	c.808-3C>G	----	WES
796	2	OCA2	21	c.2228C>T	p.P743L	OCA2	13	c.1349C>T	p.T450M	WES
797	2	OCA2	11	c.1178G>T	p.G393V	OCA2	4	c.406C>T	p.R136X	WES
798	2	OCA2	23	c.2363C>T	p.S788L	OCA2	4	c.406C>T	p.R136X	WES
799	2	OCA2	12	c.1211C>T	p.T404M	OCA2	10	c.1079C>T	p.S360F	WES
800	2	OCA2	14	c.1426A>G	p.N476D	OCA2	14	c.1426A>G	p.N476D	WES
801	2	OCA2	23	c.2359G>A	p.A787T	OCA2	Int7	c.808-3C>G	----	WES
802	2	OCA2	Int22	c.2339-2A>C	----	OCA2	4	c.406C>T	p.R136X	WES
803	2	OCA2	Int11	c.1182+1G>A	splice-5	OCA2	Int11	c.1182+1G>A	----	WES
804	2	OCA2	14	c.1444A>G	p.T482A	OCA2	14	c.1426A>G	p.N476D	WES
805	2	OCA2	14	c.1405_1406delinsC	p.I469Lfs*4	OCA2	Int11	c.1182+1G>A	----	WES
806	2	OCA2	21	c.2228C>T	p.P743L	OCA2	18	c.1884_1885delAG	p.L630Gfs*19	WES
807	2	OCA2	23	c.2363C>T	p.S788L	OCA2	10	c.980dupT	----	WES

808	2	OCA2	Int11	c.1182+1G>A	splice-5	OCA2	Int11	c.1182+1G>A	- - - -	WES
809	2	OCA2	13	c.1278delinsTATCAT	p.M428Ifs*27	OCA2	9	c.913C>T	p.R305W	WES
810	2	OCA2	Int21	c.2245-6C>G	- - - -	OCA2	13	c.1349C>T	p.T450M	WES
811	2	OCA2	10	c.1054A>G	p.R352G	OCA2	9	c.1001C>T	p.A334V	WES
812	2	OCA2	13	c.1349C>T	p.T450M	OCA2	4	c.406C>T	p.R136X	WES
813	2	OCA2	23	c.2363C>T	p.S788L	OCA2	23	c.2359G>A	p.A787T	WES
814	2	OCA2	13	c.1349C>T	p.T450M	OCA2	8	c.889delA	p.R297Efs*21	WES
815	2	OCA2	15	c.1596dupG	p.N533Efs*6	OCA2	13	c.1278delinsTATCAT	p.M428Ifs*27	WES
816	2	OCA2	23	c.2359G>A	p.A787T	OCA2	4	c.406C>T	p.R136X	WES
817	2	OCA2	21	c.2180T>C	p.L727P	OCA2	13	c.1349C>T	p.T450M	WES
818	2	OCA2	Int7	c.808-3C>G	- - - -	OCA2	Int7	c.808-3C>G	- - - -	WES
819	2	OCA2	14	c.1426A>G	p.N476D	OCA2	6	c.593C>T	p.P198L	WES
820	2	OCA2	23	c.2359G>A	p.A787T	OCA2	13	c.1255C>T	p.R419W	WES
821	2	OCA2	22	c.2323G>A	p.G775S	OCA2	4	c.406C>T	p.R136X	WES
822	2	OCA2	Int11	c.1182+1G>A	splice-5	OCA2	9	c.1001C>T	p.A334V	WES
823	2	OCA2	19	c.2030T>G	p.V677G	OCA2	14	c.1426A>G	p.N476D	WES
824	2	OCA2	4	c.406C>T	p.R136X	OCA2	16-21	Ex.16-21del	- - - -	WES+MLPA
825	2	OCA2	Int11	c.1182+1G>A	splice-5	OCA2	2-11	Ex.2-11del	- - - -	WES+MLPA
826	2	OCA2	4	c.493C>T	p.R165X	OCA2	3-22	Ex.3-22del	- - - -	WES+MLPA
827	2	OCA2	Int7	c.808-3C>G	- - - -	OCA2	2-7	Ex.2-7del	- - - -	WES+MLPA
828	2	OCA2	14	c.1426A>G	p.N476D	OCA2	8	c.863_886del24	p.M288_L295del	WES
829	2	OCA2	24	c.2491G>C	p.A831P	OCA2	Int7	c.807+1G>T	- - - -	WES
830	2	OCA2	4	c.406C>T	p.R136X	OCA2	2	c.168delC	p.Q58Rfs*44	WES
831	2	OCA2	23	c.2359G>A	p.A787T	OCA2	1-24	Ex.1-24del	- - - -	WES+MLPA
832	2	OCA2	14	c.1444A>G	p.T482A	OCA2	6	c.632C>T	p.P211L	WES
833	2	OCA2	16	c.1700A>T	p.E567V	OCA2	4	c.406C>T	p.R136X	WES
834	2	OCA2	14	c.1441G>A	p.A481T	OCA2	Int8	c.808-1G>C	- - - -	WES
835	2	OCA2	17	c.1832T>C	p.L611P	OCA2	Int7	c.808-3C>G	- - - -	WES
836	2	OCA2	13	c.1349C>T	p.T450M	OCA2	10-14	Ex.10-14del	- - - -	WES+MLPA
837	2	OCA2	Int23	c.2433-6T>A	- - - -	OCA2	23	c.2339G>A	p.G780D	WES
838	2	OCA2	22	c.2323G>A	p.G775S	OCA2	4	c.406C>T	p.R136X	WES

839	2	OCA2	22	c.2323G>A	p.G775S	OCA2	13	c.1255C>T	p.R419W	WES
840	2	OCA2	24	c.2495A>C	p.H832P	OCA2	10	c.980dupT	- - - -	WES
841	2	OCA2	23	c.2359G>A	p.A787T	OCA2	Int11	c.1182+1G>A	- - - -	WES
842	2	OCA2	23	c.2363C>T	p.S788L	OCA2	22	c.2323G>C	p.G775R	WES
843	2	OCA2	13	c.1363A>G	p.R455G	OCA2	Int11	c.1182+1G>A	- - - -	WES
844	2	OCA2	23	c.2344G >A	p.G782R	OCA2	23	c.2344G>A	p.G782R	WES
845	2	OCA2	22	c.2323G>C	p.G775R	OCA2	22	c.2323G>C	p.G775R	WES
846	2	OCA2	13	c.1349C>T	p.T450M	OCA2	4	c.406C>T	p.R136X	WES
847	2	OCA2	21	c.2228C>T	p.P743L	OCA2	14	c.1426A>G	p.N476D	WES
848	2	OCA2	24	c.2438G>A	p.G813D	OCA2	13	c.1349C>T	p.T450M	WES
849	2	OCA2	14	c.1426A>G	p.N476D	OCA2	13	c.1255C>T	p.R419W	WES
850	2	OCA2	14	c.1367T>C	p.L456S	OCA2	Int7	c.808-3C>G	- - - -	WES
851	2	OCA2	15	c.1560_1562delCCT	p.L521del	OCA2	15	c.1560_1562delCCT	p.L521del	WES
852	2	OCA2	16	c.1714C>T	p.R572C	OCA2	10	c.980dupT	- - - -	WES
853	2	OCA2	13	c.1327G>A	p.V443I	OCA2	4	c.406C>T	p.R136X	WES
854	2	OCA2	19	c.1964T>A	p.I655N	OCA2	16	c.1732A>G	p.K578E	WES
855	2	OCA2	23	c.2359G>A	p.A787T	OCA2	23	c.2359G>A	p.A787T	WES
856	2	OCA2	17	c.1832T>C	p.L611P	OCA2	13	c.1349C>T	p.T450M	WES
857	1	OCA2	16	c.1664G>A	p.R555H					NGS
858	1	OCA2	11	c.1182G>A	p.M394I					WES
859	1	OCA2	4	c.493C>T	p.R165X					WES
860	1	OCA2		c.406C>T	p.R136X					WES
861	1	OCA2	Int9	c.1045-9T>G	- - - -					WES
862	1	OCA2	13	c.1255C>T	p.R419W					Sanger
863	1	OCA2	21	c.2170G>C	p.A724P					Sanger
864	1	OCA2	23	c.2360C>T	p.A787V					Sanger
865	1	OCA2	22	c.2327C>A	p.A776D					Sanger
866	1	OCA2	22	c.2327C>A	p.A776D					Sanger
867	1	OCA2	10	c.1086_1094del9	- - - -					Sanger
901	2	TYRP1	6	c.1120C>T	p.R374X	TYRP1	Int7	c.1408+135G>C	- - - -	Sanger
902	2	TYRP1	6	c.1214C>A	p.T405N	TYRP1	7	c.1333dupG	- - - -	Sanger

903	2	TYRP1	2	c.260G>A	p.R87Q	TYRP1	Int5	c.1262-46_1262-13del34	- - - -	Sanger
904	2	TYRP1	1	c.785C>T	p.T262M	TYRP1	3	c.1138G>T	p.A380S	NGS
905	2	TYRP1	3	c.551T>C	p.I184T	TYRP1	7	c.1332delG	- - - -	NGS
906	2	TYRP1	5	c.1067G>A	p.R356Q	TYRP1	Int7	c.1408+135G>C	- - - -	NGS
907	2	TYRP1	2	c.176C>G	p.S59X	TYRP1	Int7	c.1408+135G>C	- - - -	NGS
908	2	TYRP1	3	c.536T>C	p.F179S	TYRP1	Int4	c.913+2T>C	- - - -	WES
909	2	TYRP1	Int6	c.1262-1_1264dupGAT	- - - -	TYRP1	Int6	c.1262-1_1264dupGAT	- - - - -	WES
910	2	TYRP1	5	c.1066C>T	p.R356X	TYRP1	5	c.1066C>T	p.R356X	WES
911	1	TYRP1	1	c.67_68insC	p.R23Pfs*12					NGS
912	2	SLC45A2	3	c.661A>G	p.S221G	SLC45A2	3	c.661A>G	p.S221G	Sanger
913	2	SLC45A2	2	c.478G>C	p.D160H	SLC45A2	2	c.478G>C	p.D160H	Sanger
914	2	SLC45A2	1	c.152-153delTG	- - - -	SLC45A2	2	c.481G>A	p.G161R	Sanger
915	2	SLC45A2	2	c.478G>C	p.D160H	SLC45A2	2	c.478G>C	p.D160H	Sanger
916	2	SLC45A2	2	c.478G>C	p.D160H	SLC45A2	3	c.563delG	- - - -	Sanger
917	2	SLC45A2	2	c.478G>C	p.D160H	SLC45A2	2	c.478G>C	p.D160H	Sanger
918	2	SLC45A2	2	c.478G>C	p.D160H	SLC45A2	2	c.478G>C	p.D160H	Sanger
919	2	SLC45A2	2	c.478G>C	p.D160H	SLC45A2	2	c.478G>C	p.D160H	Sanger
920	2	SLC45A2	2	c.478G>C	p.D160H	SLC45A2	6	c.1256C>T	p.P419L	Sanger
921	2	SLC45A2	2	c.478G>C	p.D160H	SLC45A2	2	c.478G>C	p.D160H	Sanger
922	2	SLC45A2	2	c.478G>C	p.D160H	SLC45A2	7	c.1519G>C	p.V507L	NGS
923	2	SLC45A2	2	c.478G>C	p.D160H	SLC45A2	7	c.1456G>A	p.A486T	Sanger
924	2	SLC45A2	2	c.478G>C	p.D160H	SLC45A2	2	c.478G>C	p.D160H	Sanger
925	2	SLC45A2	2	c.478G>C	p.D160H	SLC45A2	5	c.1086-1094del 9bp	- - - -	Sanger
926	2	SLC45A2	2	c.478G>C	p.D160H	SLC45A2	4	c.974T>A	p.L325H	Sanger
927	2	SLC45A2	2	c.478G>C	p.D160H	SLC45A2	2	c.478G>C	p.D160H	Sanger
928	2	SLC45A2	2	c.478G>C	p.D160H	SLC45A2	2	c.494C>A	p.A165D	Sanger
929	2	SLC45A2	7	c.1509delC	- - - -	SLC45A2	7	c.1509delC	- - - -	Sanger
930	2	SLC45A2	7	c.1451A>G	p.Q484R	SLC45A2	2	c.478G>C	p.D160H	Sanger
931	2	SLC45A2	2	c.478G>C	p.D160H	SLC45A2	2	c.478G>C	p.D160H	Sanger
932	2	SLC45A2	2	c.478G>C	p.D160H	SLC45A2	2	c.478G>C	p.D160H	NGS
933	2	SLC45A2	2	c.478G>C	p.D160H	SLC45A2	6	c.1256C>T	p.P419L	NGS

934	2	SLC45A2	2	c.478G>C	p.D160H	SLC45A2	5	c.1122G>C	p.L374F	NGS
935	2	SLC45A2	2	c.478G>C	p.D160H	SLC45A2	5	c.1122G>C	p.L374F	NGS
936	2	SLC45A2	2	c.478G>C	p.D160H	SLC45A2	2	c.478G>C	p.D160H	NGS
937	2	SLC45A2	2	c.478G>C	p.D160H	SLC45A2	2	c.478G>C	p.D160H	NGS
938	2	SLC45A2	2	c.547C>T	p.H183Y	SLC45A2	5	c.1122G>C	p.L374F	NGS
939	2	SLC45A2	6	c.1256C>T	p.P419L	SLC45A2	5	c.1122G>C	p.L374F	NGS
940	2	SLC45A2	2	c.478G>C	p.D160H	SLC45A2	2	c.478G>C	p.D160H	NGS
941	2	SLC45A2	7	c.1532C>T	p.A511V	SLC45A2	7	c.1456G>A	p.A486T	WES
942	2	SLC45A2	5	c.1076_1077delAG	----	SLC45A2	5	c.1122G>C	p.L374F	NGS
943	2	SLC45A2	7	c.1519G>C	p.V507L	SLC45A2	7	c.1519G>C	p.V507L	NGS
944	2	SLC45A2	4	c.1020T>G	p.D340E	SLC45A2	5	c.1090G>A	p.E364K	NGS
945	2	SLC45A2	6	c.1186G>A	p.G396R	SLC45A2	7	c.1492G>A	p.V498I	NGS
946	2	SLC45A2	1	c.305G>T	p.R102L	SLC45A2	6	c.1304C>A	p.S435Y	NGS
947	2	SLC45A2	2	c.469G>A	p.D157N	SLC45A2	2	c.478G>C	p.D160H	NGS
948	2	SLC45A2	1	c.275G>A	p.S92N	SLC45A2	3	c.706A>C	p.S236R	NGS
949	2	SLC45A2	1	c.157delG	----	SLC45A2	2	c.478G>C	p.D160H	NGS
950	2	SLC45A2	3	c.775_778dup	p.L260Sfs*17	SLC45A2	2	c.1033-5T>G	----	NGS
951	2	SLC45A2	2	c.478G>C	p.D160H	SLC45A2	2	c.478G>C	p.D160H	Sanger
952	2	SLC45A2	2	c.478G>C	p.D160H	SLC45A2	2	c.478G>C	p.D160H	Sanger
953	2	SLC45A2	2	c.478G>C	p.D160H	SLC45A2	2	c.478G>C	p.D160H	Sanger
954	2	SLC45A2	1	c.452T>C	p.L151S	SLC45A2	3	c.798C>G	p.Y266X	NGS
955	2	SLC45A2	2	c.478G>C	p.D160H	SLC45A2	2	c.478G>C	p.D160H	NGS
956	2	SLC45A2	2	c.478G>C	p.D160H	SLC45A2	5	c.1090G>A	p.E364K	Sanger
957	2	SLC45A2	2	c.478G>C	p.D160H	SLC45A2	2	c.478G>C	p.D160H	Sanger
958	2	SLC45A2	1	c.328G>A	p.G110R	SLC45A2	1	c.276C>G	p.S92R	Sanger
959	2	SLC45A2	2	c.478G>C	p.D160H	SLC45A2	5	c.1154C>A	p.S385Y	Sanger
960	2	SLC45A2	5	c.1102G>A	p.E368K	SLC45A2	5	c.1045C>T	p.G349R	Sanger
961	2	SLC45A2	5	c.1102G>A	p.E368K	SLC45A2	4	c.1016C>G	p.T339R	NGS
962	2	SLC45A2	2	c.478G>C	p.D160H	SLC45A2	7	c.1424A>G	p.D475G	Sanger
963	2	SLC45A2	3	c.814G>A	p.E272K	SLC45A2	3	c.806G>T	p.G269V	NGS
964	2	SLC45A2	2	c.478G>C	p.D160H	SLC45A2	2	c.478G>C	p.D160H	Sanger

965	2	SLC45A2	2	c.478G>C	p.D160H	SLC45A2	6	c.1256C>T	p.P419L	Sanger
966	2	SLC45A2	2	c.478G>C	p.D160H	SLC45A2	6	c.1304C>A	p.S435Y	NGS
967	2	SLC45A2	2	c.478G>C	p.D160H	SLC45A2	7	c.1456G>A	p.A486T	NGS
968	2	SLC45A2	2	c.478G>C	p.D160H	SLC45A2	6	c.1256C>T	p.P419L	NGS
969	2	SLC45A2	2	c.478G>C	p.D160H	SLC45A2	6	c.1318A>G	p.T440A	NGS
970	2	SLC45A2	2	c.478G>C	p.D160H	SLC45A2	2	c.478G>C	p.D160H	NGS
971	2	SLC45A2	2	c.478G>C	p.D160H	SLC45A2	7	c.1456G>A	p.A486T	WES
972	2	SLC45A2	5	c.1045G>A	p.G349R	SLC45A2	2	c.478delG	p.K160Rfs*14	WES
973	2	SLC45A2	2	c.478G>C	p.D160H	SLC45A2	2	c.478G>C	p.D160H	WES
974	2	SLC45A2	2	c.478G>C	p.D160H	SLC45A2	2	c.478G>C	p.D160H	WES
975	2	SLC45A2	5	c.1045G>A	p.G349R	SLC45A2	1	c.152_153delTG	p.V51Gfs*82	WES
976	2	SLC45A2	2	c.478G>C	p.D160H	SLC45A2	2	c.478G>C	p.D160H	WES
977	2	SLC45A2	4	c.1008_1009insCTGCTCAAAA	p.F337Lfs*20	SLC45A2	5	c.1045G>A	p.G349R	WES
978	2	SLC45A2	2	c.459_470del12	p.A155_F158del	SLC45A2	1	c.137A>G	p.E46G	WES
979	2	SLC45A2	2	c.478G>C	p.D160H	SLC45A2	1	c.143_145delGCT	p.C48del	WES
980	2	SLC45A2	Int3	c.888+1G>A	----	SLC45A2	2	c.469G>A	p.D157N	WES
981	2	SLC45A2	7	c.1456G>A	p.A486T	SLC45A2	2	c.478G>C	p.D160H	WES
982	2	SLC45A2	5	c.1102G>A	p.E368K	SLC45A2	5	c.1045G>A	p.G349R	WES
983	2	SLC45A2	1	c.328G>A	p.G110R	SLC45A2	1	c.143_145delGCT	p.C48del	WES
984	2	SLC45A2	7	c.1532C>T	p.A511V	SLC45A2	2	c.478G>C	p.D160H	WES
985	2	SLC45A2	2	c.478G>C	p.D160H	SLC45A2	2	c.478G>C	p.D160H	WES
986	2	SLC45A2	2	c.478G>C	p.D160H	SLC45A2	2	c.478G>C	p.D160H	WES
987	2	SLC45A2	2	c.478G>C	p.D160H	SLC45A2	2	c.478G>C	p.D160H	WES
988	2	SLC45A2	2	c.478G>C	p.D160H	SLC45A2	1	c.133A>G	p.R45G	WES
989	2	SLC45A2	5	c.1122G>C	p.L374F	SLC45A2	2	c.478G>C	p.D160H	WES
990	2	SLC45A2	1	c.305G>A	p.R102Q	SLC45A2	1	c.305G>A	p.R102Q	WES
991	2	SLC45A2	7	c.1456G>A	p.A486T	SLC45A2	6	c.1256C>T	p.P419L	WES
992	2	SLC45A2	Int4	c.1032+1G>T	----	SLC45A2	2	c.478G>C	p.D160H	WES
993	2	SLC45A2	7	c.1456G>A	p.A486T	SLC45A2	1	c.366T>A	p.N122K	WES
994	2	SLC45A2	2	c.478G>C	p.D160H	SLC45A2	2	c.478G>C	p.D160H	WES
995	2	SLC45A2	5	c.1045G>A	p.G349R	SLC45A2	1	c.143_145delGCT	p.C48del	WES

996	2	SLC45A2	7	c.1456G>A	p.A486T	SLC45A2	2	c.478G>C	p.D160H	WES
997	2	SLC45A2	2	c.478G>C	p.D160H	SLC45A2	1	c.133A>G	p.R45G	WES
998	2	SLC45A2	3	c.869dupA	p.N290Kfs*6	SLC45A2	2	c.478G>C	p.D160H	WES
999	2	SLC45A2	6	c.1304C>A	p.S435Y	SLC45A2	5	c.1045G>A	p.G349R	WES
1000	2	SLC45A2	4	c.1020T>G	p.D340E	SLC45A2	1	c.133A>G	p.R45G	WES
1001	2	SLC45A2	2	c.478G>C	p.D160H	SLC45A2	2	c.478G>C	p.D160H	WES
1002	2	SLC45A2	7	c.1456G>A	p.A486T	SLC45A2	1	c.143_145delGCT	p.C48del	WES
1003	2	SLC45A2	1	c.328G>A	p.G110R	SLC45A2	1	c.328G>A	p.G110R	WES
1004	2	SLC45A2	2	c.478G>C	p.D160H	SLC45A2	2	c.459_470del12	p.A155_F158del	WES
1028	2	SLC45A2	3	c.888G>A	p.Q296Q	SLC45A2	1	Ex.1del	----	WES
1029	1	SLC45A2	2	c.478G>C	p.D160H					Sanger
1030	1	SLC45A2	2	c.478G>C	p.D160H					Sanger
1031	1	SLC45A2	7	c.1456G>A	p.A486T					Sanger
1041	2	SLC24A5	7	c.922delT	p.W306Gfs*13	SLC24A5	7	c.983dupA	p.F329Vfs*74	WES
1042	2	SLC24A5	8	c.1148A>G	p.D383G	SLC24A5	9	c.1361dupT	p.L454Ffs*33	WES
1046	2	HPS1	13	c.1189C>T	p.Q397X	HPS1	5	c.301delA	p.S101Afs*23	NGS
1047	2	HPS1	7	c.517C>T	p.R173X	HPS1	19	c.1932delC	p.L668P	WES
1048	2	HPS1	13	c.1283T>G	p.L428R	HPS1	Int5	c.398+5G>A	----	WES
1049	2	HPS1	19	c.1932delC	p.Y645Tfs*?	HPS1	14	c.1340_1341insT	p.T448Lfs*5	WES
1050	2	HPS1	12	c.1099dupC	p.T368Hfs*85	HPS1	12	c.1099dupC	p.T368Hfs*85	WES
1051	2	HPS1	Int5	c.398+5G>A	----	HPS1	5	c.355_358delCACT	p.H119Lfs*4	WES
1052	2	HPS1	19	c.1932delC	p.Y645Tfs*?	HPS1	7	c.517C>T	p.R173X	WES
1053	2	HPS1	11	c.972dupC	p.M325Hfs*128	HPS1	11	c.972dupC	p.M325Hfs*128	WES
1054	1	HPS1	18	c.1766C>T	p.A589V					WES
1075	2	HPS3	2	c.449T>A	p.V150D	HPS3	10	c.1838C>G	p.S613X	WES
1076	1	HPS3	10	c.1838C>G	p.S613X					WES
1084	2	HPS4	4	c.148C>T	p.Q50X	HPS4	Int5	c.1713+5G>C	----	Sanger
1085	2	HPS4	8	c.649C>T	p.R217X	HPS4	4	c.148C>T	p.Q50X	WES
1091	2	HPS6	1	c.257G>A	p.W86X	HPS6	1	c.2038C>T	p.Q680X	WES
1101	1	GPR143	6	c.251G>A	p.G84D					Sanger
1102	1	GPR143	3	c.943G>T	p.G315X					Sanger

1103	1	GPR143	1	c.223_228dupGCTGCC	p.A75_A76dup					Sanger
1104	1	GPR143	1	c.31_33del	p.C11del					Sanger
1105	1	GPR143	4	c.482C>T	p.A161V					Sanger
1106	1	GPR143	1	c.248T>C	p.L83P					Sanger
1107	1	GPR143	6	c.733C>T	p.R245X					Sanger
1108	1	GPR143	1	c.223_228delGCTGC	p.A75_A76del					Sanger
1109	1	GPR143	6	c.709_711delAGG	p.P237del					Sanger
1110	1	GPR143	5	c.601_602delinsG	p.L204Gfs*14					Sanger
1111	1	GPR143	7	c.817C>T	p.Q273X					Sanger
1112	1	GPR143	2	c.280G>T	p.G96X					Sanger
1113	1	GPR143	7	c.846delA	p.K282Nfs*17					Sanger
1114	1	GPR143	2	c.278delT	p.L93X					Sanger
1115	1	GPR143	1	c.237_239delTCT	p.L80del					Sanger
1116	1	GPR143	6-8	Ex.6-8del	----					Sanger
1117	1	GPR143	4	c.486G>A	p.W162X					WES
1118	1	GPR143	2	c.280G>T	p.G94X					Sanger
1119	1	GPR143	1-4	Ex.1-4del	----					Sanger
1120	1	GPR143	Int2	c.360+2T>A	splice-5					NGS
1121	1	GPR143	1	c.208_218del11	----					NGS
1122	1	GPR143	7	c.778A>G	p.N260D					WES
1123	1	GPR143	5	c.640C>T	p.Q214X					WES
1124	1	GPR143	5	c.623C>A	p.A208E					WES

NGS：下一代测序;WES：全外显子组测序；MLPA：多重连接依赖性探针扩增；qPCR：定量聚合酶链反应；Int：内含子。蛋白质变化中的破折号代表未知的变化。

补充表 S2：白化病亚型在不同人群中的分布频率。

Subtype	Distribution Frequencies		
	Chinese (cases)	European	Japanese
OCA-1	62.1% (666)	41.80%	26.20%
OCA-2	17.4% (187)	27.90%	11.00%
OCA-3	0.9% (10)	2.10%	1.40%
OCA-4	10.9% (116)	10.50%	33.10%
OCA-6	0.5% (5)	3.10%	0.00%
OCA-7	0.0% (0)	0.40%	0.00%
OCA-8	0.0% (0)	0.00%	0.00%
OA-1	3.4% (36)	7.00%	0.00%
FHONDA	0.0% (0)	0.60%	0.00%
HPS-1	2.4% (26)	2.40%	19.30%
HPS-2	0.1% (1)	0.00%	0.70%
HPS-3	0.8% (8)	0.30%	2.10%
HPS-4	0.3% (3)	0.30%	2.80%
HPS-5	0.4% (4)	1.40%	0.70%
HPS-6	0.8% (9)	1.70%	2.10%
HPS-7	0.0% (0)	0.10%	0.00%
HPS-8	0.0% (0)	0.30%	0.00%
HPS-9	0.1% (1)	0.00%	0.70%
HPS-10	0.0% (0)	0.00%	0.00%
HPS-11	0.0% (0)	0.00%	0.00%
CHS-1	0.0% (0)	0.30%	0.00%
Total	100% (1073)	100%	100%
Reference	This study	Lasseaux, et a1 (2018)	Okamura & Suzuki (2020)

CHS：Chediak-Higashi syndrome 综合征；FHONDA：中央凹发育不全，视神经脱位缺陷和前节段发育不良；HPS：Hermansky-Pudlak syndrome 综合征；OCA：眼皮肤白化病；OA：眼白化病。

补充表 S3：10 例中国 OCA-3 患者的临床特征。

Patient	Molecular Diagnosis	Skin color （darken when exposed to sunlight）	Hair color at birth (darken in later age)	Iris color	Nystagmus （improved in later age）	Visual Acuity	Photophobia
901	OCA-3	Fair （Yes）	Golden yellow (Yes)	Brown	Slight (Yes)	Slightly Reduced	No
902	OCA-3	Normal （Yes）	Reddish-ginger (No)	Brownish black	Slight (No)	Slightly Reduced	No
903	OCA-3	Normal （Yes）	Golden yellow （Yes）	Brown	Slight (Yes)	Reduced	Yes
904	OCA-3	Normal （Yes）	Brownish yellow （Yes）	Brown	No	Normal	No
905	OCA-3	Normal （Yes）	Golden yellow （Yes）	Brown	Slight (No)	Reduced	Yes
906	OCA-3	Normal （No）	Golden yellow （Yes）	Brownish black	Slight (Yes)	Reduced	Yes
907	OCA-3	Normal （Yes）	Brownish yellow （No）	Brownish black	No	Normal	No
908	OCA-3	Normal （Yes）	Brownish yellow （No）	Brownish black	Slight (Yes)	Slightly Reduced	No
909	OCA-3	Normal （Yes）	Brownish yellow （No）	Brownish black	No	Normal	No
910	OCA-3	Normal （Yes）	Yellowish white （Yes）	Blue Grey	No	Normal	No

补充表 S4：本研究中确定了 199 个变体。

Gene	Exon	Variant c.	Variant p.	Pathogenic	Number of alleles
TYR	1	c.107G>C	p.C36S	LP	1
TYR	1	c.157G>A	p.G53S	VUS	2
TYR	1	c.158G>A	p.G53D	LP	1
TYR	1	c.240G>T	p.W80C	LP	1
TYR	1	c.297C>G	p.N99K	LP	1
TYR	1	c.298T>C	p.C100R	LP	1
TYR	1	c.472C>T	p.Q158X	P	1
TYR	1	c.547G>A	p.V183M	LP	1
TYR	1	c.593T>G	p.I198S	LP	1
TYR	1	c.599T>C	p.F200S	LP	1
TYR	1	c.650G>C	p.R217P	LP	1
TYR	1	c.658C>T	p.Q220X	P	1
TYR	1	c.701C>T	p.P234L	LP	1
TYR	1	c.755T>A	p.M252K	LP	3
TYR	1	c.757G>T	p.G253X	P	1
TYR	2	c.836T>A	p.L279X	P	1
TYR	2	c.902C>G	p.P301R	LP	1
TYR	2	c.965T>C	p.L322P	LP	1
TYR	2	c.1022G>A	p.R341K	LP	3
TYR	2	c.1031T>G	p.L344R	LP	2
TYR	3	c.1043C>A	p.A348D	LP	1
TYR	3	c.1082G>T	p.S361I	LP	3
TYR	3	c.1130T>A	p.V377E	LP	4
TYR	3	c.1151C>A	p.P384H	LP	1
TYR	3	c.1162C>T	p.L388F	LP	1
TYR	4	c.1200G>A	p.W400X	P	1
TYR	4	c.1247C>G	p.A416G	LP	1

TYR	4	c.1263C>G	p.N421K	LP	1
TYR	4	c.1283C>T	p.P428L	LP	1
TYR	4	c.1334T>C	p.L445P	LP	1
TYR	5	c.1451T>G	p.V484G	LP	1
TYR	5	c.1534C>T	p.Q512X	P	1
TYR	1	c.17delT	p.L6Cfs*25	P	3
TYR	3	c.1071delC	---	P	1
TYR	3	c.1080_1091del 12bp	p.S361_N364del	P	1
TYR	3	c.1184+5G>A	---	VUS	2
TYR	4	c.1279delG	p.V427Ffs*58	P	1
TYR	4	c.1288_1291dupATAC	p.F431Hfs*8	P	2
TYR	4	c.1323_1325delATC	p.S442del	P	1
TYR	4	c.1348insGG	---	P	1
TYR	5	c.1380insT	---	P	1
TYR	1	c.221_222delTG	---	P	1
TYR	1	c.22delT	---	P	1
TYR	1	c.812_815delCTT	---	P	1
TYR	Int1	c.820-1G>C	---	P	1
TYR	2	c.925_926insC	p.T309TfsX9	P	1
TYR	2	c.937_939dupCCC	p.P313dup	P	2
TYR	1-4	Ex.1-4del	---	P	1
TYR	1-5	Ex.1-5del	---	P	1
TYR	2-3	Ex.2-3del	---	P	2
TYR	1	c.629G>A	p.W210X	P	1
TYR	1	---	p.A204E	LP	1
OCA2	5	c.587T>C	p.L196P	LP	1
OCA2	7	c.791G>A	p.W264S	LP	1
OCA2	7	c.805C>T	p.Q269X	P	1
OCA2	9	c.944C>G	p.P315R	LP	1

OCA2	9	c.947T>G	p.L316R	LP	1
OCA2	10	c.1054A>G	p.R352G	LP	1
OCA2	10	c.1058C>T	p.T353I	LP	1
OCA2	10	c.1086_1094delAGCACTGGC	---	P	1
OCA2	11	c.1177G>A	---	LP	1
OCA2	11	c.1178G>T	p.G393V	LP	1
OCA2	12	c.1210A>G	p.T404A	LP	1
OCA2	13	c.1262G>A	p.R421Q	LP	1
OCA2	13	c.1265G>T	p.R119L	VUS	1
OCA2	13	c.1275G>T	p.M425I	LP	1
OCA2	13	c.1288T>C	p.C430R	LP	1
OCA2	13	c.1297G>T	p.A433S	LP	1
OCA2	13	c.1358C>T	p.T453I	LP	1
OCA2	14	c.1367T>C	p.L456S	LP	1
OCA2	14	c.1430T>C	p.I477T	LP	1
OCA2	14	c.1433G>A	p.G478E	LP	1
OCA2	14	c.1444A>G	p.T482A	LP	3
OCA2	14	c.1447G>T	p.A483S	VUS	1
OCA2	14	c.1448C>T	p.A483V	VUS	1
OCA2	14	c.1465A>T	p.N489Y	LP	1
OCA2	15	c.1526C>T	p.T509I	LP	1
OCA2	15	c.1636G>A	p.E546K	LP	1
OCA2	16	c.1664G>A	p.R555H	LP	1
OCA2	16	c.1700A>T	p.E567V	LP	1
OCA2	16	c.1732A>G	p.K578E	VUS	1
OCA2	18	c.1888T>A	p.L630M	LP	1
OCA2	19	c.1964T>A	p.I655N	VUS	2
OCA2	19	c.2021T>C	p.L674P	LP	1
OCA2	19	c.2074A>T	p.M692L	LP	1

OCA2	20	c.2093T>G	p.L698R	LP	1
OCA2	21	c.2155C>T	p.Q719X	P	1
OCA2	21	c.2221A>C	p.N741H	LP	1
OCA2	22	c.2248C>A	p.P750T	LP	1
OCA2	22	c.2249C>T	p.P750L	LP	1
OCA2	22	c.2251G>A	p.V751M	LP	2
OCA2	24	c.2438G>T	p.G813V	VUS	3
OCA2	24	c.2438G>A	p.G813D	VUS	1
OCA2	Int23	c.2433-6T>A	---	P	1
OCA2	13	c.1278delinsTATCAT	p.M428Ifs*27	P	2
OCA2	13	c.1327delGTCACCAC	---	P	1
OCA2	14	c.1397_1398delAA	---	P	1
OCA2	14	c.1405_1406delinsC	p.I469Lfs*4	P	1
OCA2	Int14	c.1504-1G>C	---	P	1
OCA2	2	c.156delC	p.R53Gfs*49	P	1
OCA2	15	c.1596dupG	p.N533Efs*6	P	1
OCA2	18	c.1884_1885delAG	p.L630Gfs*19	P	1
OCA2	Int18	c.1951+1G>C	---		1
OCA2	2	c.196delC	---		1
OCA2	Int23	c.2339+1G>A	---		2
OCA2	23	c.2350_2377del 26bp	---	P	1
OCA2	4	c.478delG	---	P	1
OCA2	Int5	c.573+5G>A	---	LP	1
OCA2	Int6	c.647-2A>G	---	LP	1
OCA2	7	c.776delC	---	P	1
OCA2	Int7	c.807+1G>T	---	P	2
OCA2	Int8	c.808-1G>C	---	P	1
OCA2	8	c.889delA	p.R297Efs*21	P	1
OCA2	9	c.950delT	---	P	2

OCA2	10-14	Ex.10-14del	---	P	2
OCA2	16-21	Ex.16-21del	---	P	1
OCA2	18-21	Ex.18-21del	---	P	1
OCA2	20-22	Ex.20-22del	---	P	1
OCA2	2-11	Ex.2-11del	---	P	1
OCA2	2-18	Ex.2-18del	---	P	1
OCA2	3-22	Ex.3-22del	---	P	1
OCA2	2-7	Ex.2-7del	---	P	1
OCA2	6-7	Ex.6-7del	---	P	1
TYRP1	2	c.176C>G	p.S59X	P	1
TYRP1	2	c.260G>A	p.R87Q	LP	1
TYRP1	3	c.536T>C	p.F179S	LP	1
TYRP1	3	c.551T>C	p.I184T	LP	1
TYRP1	6	c.1138G>T	p.A380S	LP	1
TYRP1	Int6	c.1262-46_1262-13del 34bp	---	P	1
TYRP1	Int6	c.1262-1_1264dupGAT	---	VUS	2
TYRP1	7	c.1332delG	---	P	1
TYRP1	7	c.1333dupG	---	P	1
TYRP1	Int7	c.1408+135G>C	---	LP	3
TYRP1	2	c.67_68insC	p.R23Pfs*12	P	1
TYRP1	Int4	c.913+2T>C	---	P	1
SLC45A2	1	c.137A>G	p.E46G	LP	1
SLC45A2	1	c.275G>A	p.S92N	LP	1
SLC45A2	1	c.276C>G	p.S92R	LP	1
SLC45A2	1	c.305G>A	p.R102Q	LP	2
SLC45A2	1	c.305G>T	p.R102L	LP	1
SLC45A2	1	c.366T>A	p.N122K	LP	1
SLC45A2	2	c.481G>A	p.G161R	LP	1
SLC45A2	2	c.494C>A	p.A165D	LP	1

SLC45A2	2	c.547C>T	p.H183Y	LP	1
SLC45A2	3	c.661A>G	p.S221G	VUS	2
SLC45A2	3	c.706A>C	p.S236R	VUS	1
SLC45A2	3	c.806G>T	p.G269V	LP	1
SLC45A2	4	c.974T>A	p.L325H	LP	1
SLC45A2	4	c.1016C>G	p.T339R	LP	1
SLC45A2	4	c.1020T>G	p.D340E	LP	2
SLC45A2	5	c.1045C>T	p.G349R	LP	1
SLC45A2	5	c.1090G>A	p.E364K	LP	2
SLC45A2	5	c.1154C>A	p.S385Y	LP	1
SLC45A2	6	c.1186G>A	p.G396R	VUS	1
SLC45A2	7	c.1424A>G	p.D475G	LP	1
SLC45A2	7	c.1451A>G	p.Q484R	LP	1
SLC45A2	7	c.1492G>A	p.V498I	VUS	1
SLC45A2	4	c.1008_1009insCTGCTCAAAA	p.F337Lfs*20	P	1
SLC45A2	Int4	c.1033-5T>G	---	LP	2
SLC45A2	5	c.1086_1094del 9bp	---	P	1
SLC45A2	7	c.1509delC	---	P	2
SLC45A2	1	c.157delG	---	P	1
SLC45A2	2	c.478delG	p.K160Rfs*14	P	1
SLC45A2	3	c.563delG	---	P	1
SLC45A2	3	c.661_663delTTC	p.F221del	P	1
SLC45A2	3	c.775_778dup	p.L260Sfs*17	P	1
SLC45A2	Int3	c.888+1G>A	---	LP	1
SLC45A2	1	Ex.1del	---	P	1
SLC24A5	7	c.922delT	p.W306Gfs*13	P	1
SLC24A5	7	c.983dupA	p.F329Vfs*74	P	1
SLC24A5	8	c.1148A>G	p.D383G	P	1
GPR143	2	c.280G>T	p.G96X	P	2

GPR143	4	c.482C>T	p.A161V	VUS	1
GPR143	4	c.486G>A	p.W162X	P	1
GPR143	6	c.688A>G	p.I230V	VUS	1
GPR143	7	c.778A>G	p.N260D	LP	1
GPR143	7	c.817C>T	p.Q273X	P	1
GPR143	1	c.237_239delTCT	p.L80del	P	1
GPR143	Int1	c.250+1G>A	- - -	P	1
GPR143	2	c.278delT	p.L93X	P	1
GPR143	1	c.31_33del	p.C11del	P	1
GPR143	Int2	c.360+2T>A	splice-5	P	1
GPR143	3	c.415delG	p.V139Wfs*5	P	1
GPR143	5	c.560dupG	p.G187Gfs*38	P	1
GPR143	5	c.601_602delinsG	p.L204Gfs*14	P	1
GPR143	6	c.709_711delAGG	p.P237del	P	1
GPR143	7	c.846delA	p.K282Nfs*17	P	1
GPR143	1-4	Ex.1-4del	- - -	P	1
GPR143	6-8	Ex.6-8del	- - -	P	1
GPR143	3	c.943G>T	p.G315X	P	1
HPS1	13	c.1189C>T	p.Q397X	P	1
HPS1	13	c.1283T>G	p.L428R	LP	1
HPS1	18	c.1766C>T	p.A589V	VUS	1
HPS1	12	c.1099dupC	p.T368Hfs*85	P	2
HPS1	14	c.1340_1341insT	p.T448Lfs*5	P	1
HPS1	5	c.301delA	p.S101Afs*23	P	1
HPS1	5	c.355_358delCACT	p.H119Lfs*4	P	1
HPS3	2	c.449T>A	p.V150D	LP	1
HPS6	1	c.257G>A	p.W86X	P	1

P：致病性；LP：可能致病；VUS：意义不确定的变体。Int：内含子。

补充表 S5。群体特异性致病性或可能的致病性等位基因。

等位基因	致病性（P）或可能致病性（LP）	良性（B）或可能良性（LB）
TYR p.S192Y	P ／ LP 与中国 OCA-1 患者中的另一个 TYR 病理等位基因共存时（魏等人，2015）。克林瓦尔（ID 3778）中具有不确定意义的变体（VUS）。	dbSNP 中的 SNP（rs1042602），在 GnomaD 中等位基因频率为 0.254211。
TYR p.R402Q	一项针对欧洲人的研究表明，在被明确诊断为 OCA-1 的患者中，有 46.33%（139/300）携带这种变异（Lasseaux 等人，2018）。该等位基因的频率在该队列中要低得多（0.15%，1/666），这表明它是中文中的 P ／ LP 变体.三个变体 p.R402Q，p.R422Q 和 p.P406L 是先前研究中报告的温度敏感变体，称为温度敏感 OCA1（OCA1TS）（Spritz 等人，1997）。我们在该队列中鉴定出 20 个 OCA1TS，均显示轻度眼部和皮肤色素减退，13/20 患者的发色随季节变化显着，夏季呈棕黄色或金黄色，冬季呈棕黑色。	这种变异在高加索人中非常普遍，频率为 0.278，但在非洲裔美国人中要低得多，在亚洲人群中极为罕见（Oetting 等人，2009）。
OCA2 A481T	p.A481T 在黑色素生成中保留了约 70% 的功能活性（Sviderskaya 等人，1997）。在高加索人中，其杂合子状态的致病性仅在一例中报告（Hutton 和 Spritz，2008）。在我们的研究中，发现 19 名患者携带 A481T 变体和另一种病理变体，这表明该变体是中国轻度白化病的 P ／ LP。	等位基因频率在东北亚最高，日本等位基因频率为 0.12（Suzuki 等人，2003）。已经表明，纯合 A481T 个体与正常人群之间的色素沉着没有显着差异。
OCA2 p.H615R	它在欧洲和西非人群中非常罕见（Edwards 等人，2010）。	这种等位基因在大多数东亚人群中非常普遍，并且与汉族北部的皮肤美白有关（汉族人中 50% 的 G 等位基因）。一名患者（患者#772）是 p.H615R 和 Ex.10-14del 的复合杂合子，表现为轻度白化病。然而，患者的父亲是纯合子为 p.H615R，没有出现白化病表型，认为其在中国具有致病性。
SLC45A2 p.L374F	在我们的研究中，共有 6 名患者是该变异的复合杂合子，他们都具有轻度的 OCA 临床表现，表明该变异可被视为轻度白化病的 P ／ LP。	该基因的突变与不同祖先群体的关联研究中的轻度色素沉着表型有关，该表型已被报道为 dbSNP 中的 SNP（rs16891982），在 ClinVar 中被归类为 B 等位基因（ID 19789）。

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