The Modified Shields Classification and 12 Families with Defined *DSPP* Mutations

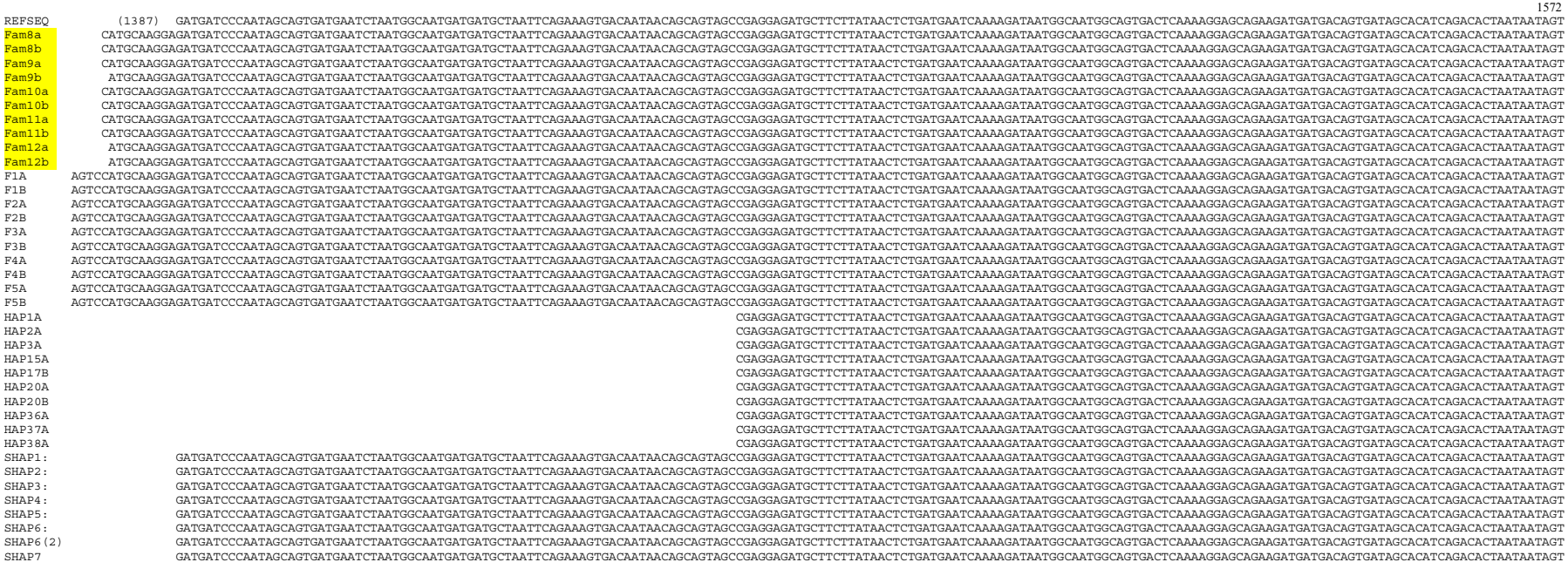
James P. Simmer[1*], Hong Zhang[1], Sophie J.H. Moon[1], Lori A-J. Donnelly[2], Yuan-Ling Lee[3], Figen Seymen[4],Mine Koruyucu[5], Hui-Chen Chan[6], Kevin Y. Lee[6], Suwei Wu[6], Chia-Lan Hsiang[6], Anthony T.P. Tsai[6], Rebecca L. Slayton[7], Melissa Morrow[8], Shih-Kai Wang[9], Edward D. Shields[10], and Jan C.-C. Hu[1]

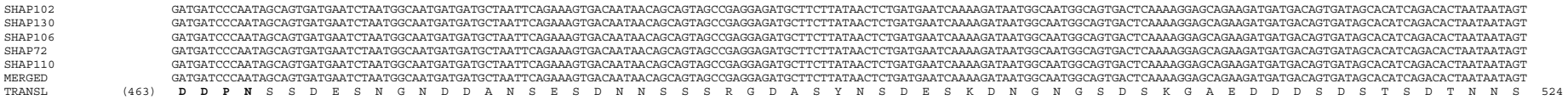
1. Biologic and Materials Sciences & Prosthodontics, University of Michigan School of Dentistry, 1011 N University Ave. Ann Arbor, Michigan, USA.
2. Department of Oral and Maxillofacial Surgery, Adams School of Dentistry, University of North Carolina at Chapel Hill, 149 Brauer Hall, CB #7450 Chapel Hill, NC 27599.
3. Graduate Institute of Clinical Dentistry, National Taiwan University, No.1, Chang-de St., Zhongzheng Dist., Taipei City 100, Taiwan R.O.C.
4. Department of Pedodontics, Faculty of Dentistry, Altinbas University, Istanbul, Turkey
5. Department of Pedodontics, Faculty of Dentistry, Istanbul University, Istanbul, Turkey.
6. Taipei Municipal WanFang Hospital, Xinglong Rd 111, Taipei, Taiwan.
7. Department of Pediatric Dentistry, University of Washington School of Dentistry. 1959 NE Pacific St., B-307 Seattle, WA 98195-6365.
8. Department of Orthodontic and Pediatric Dentistry, University of Michigan School of Dentistry, 1011 N University Ave. Ann Arbor, Michigan, USA.
9. Department of Dentistry, National Taiwan University School of Dentistry, No. 1, Changde St., Zhongzheng Dist., Taipei City 100, Taiwan.
10. 2161 Pardee Road, Neebing, Ontario, CA P7L0G7

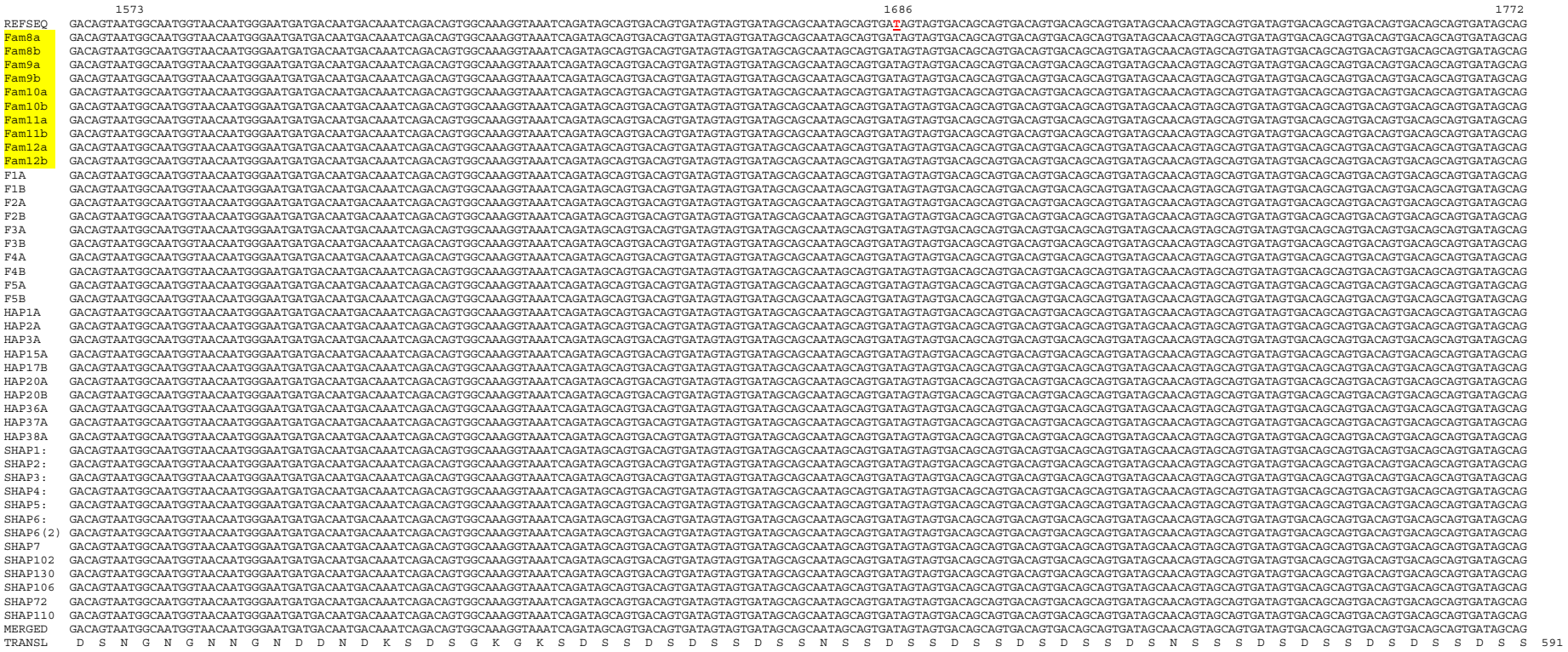
Supplemental Data File

Table S1. Alignment of DPP coding region of *DSPP* showing allelic variants and disease-causing mutations

Table S1. Alignment of DPP coding region of *DSPP* showing allelic variants and disease-causing mutations. DPP sequences exhibit novel patterns of insertions and deletions (indels), necessitating the use of this type of alignment to properly compare patient data to the DSPP reference sequencer ("REFSEQ" is the NCBI *DSPP* reference sequence NM_014208.3). "Fam8a, Fam8b, Fam9a, Fam9b, Fam10a, Fam10b, Fam12a and Fam12b" are DPP sequences determined by SMART sequencing that show the mutated and native alleles of an affected member from Families 8 through 11 in this study. Ten DPP sequences (F1A through F5B) are from the 5 patients with inherited dentin defects previously characterized by SMART sequencing [1] Wild-type DPP haplotypes were downloaded from NCBI PopSets 162077127 and 162077085 [2]. These PopSets contain DPP haplotype sequences from 2 different sizes of cloned DPP polymerase chain reaction products [3] and are labeled "HAP#". Haplotypes labeled "SHAP#" were characterized in China and published, but were not submitted to GenBank [4]. However, the locations of all indels were clearly described with respect to the reference sequence. The alignments were made manually, trying to minimize the number of genetic events that would have been required to generate the observed allelic differences in DPP sequences. Only a single previously published DPP sequence for each indel pattern was retained in the final alignment. "MERGED" is a hypothetical *DSPP* haplotype that contains the sequences of all indels in the alignment, while "TRANSL" is the translation of the "MERGED" sequence. Notes provide the locations and phenotypes of mutations associated with inherited dentin defects. Blue highlight indicates a mutation that was manifested as type II dentin dysplasia. Green highlight indicates a mutation that was manifested as dentinogenesis imperfecta. Numbering of the mutation positions was based on the *DSPP* gene reference sequence NG_012151.1, starting with nucleotide 1, the *DSPP* mRNA reference sequence NM_004771.3, starting from the A of the ATG translation initiation codon, and the protein reference sequence NP_055023.2, starting with the Met[1] at the begining of the signal peptide sequence. The nomenclature used for all disease-causing *DSPP* sequence variations were verified using Mutalyzer 2.0.32 at https://mutalyzer.nl/

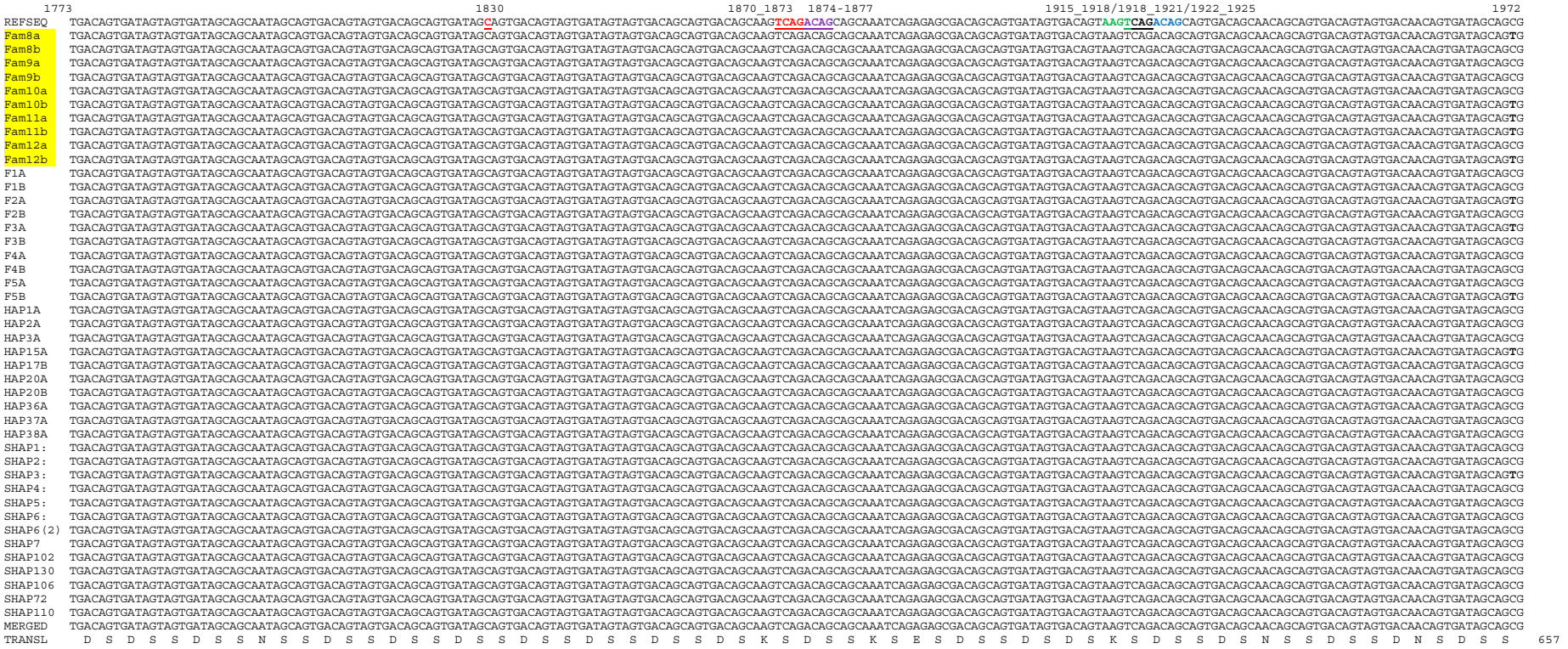






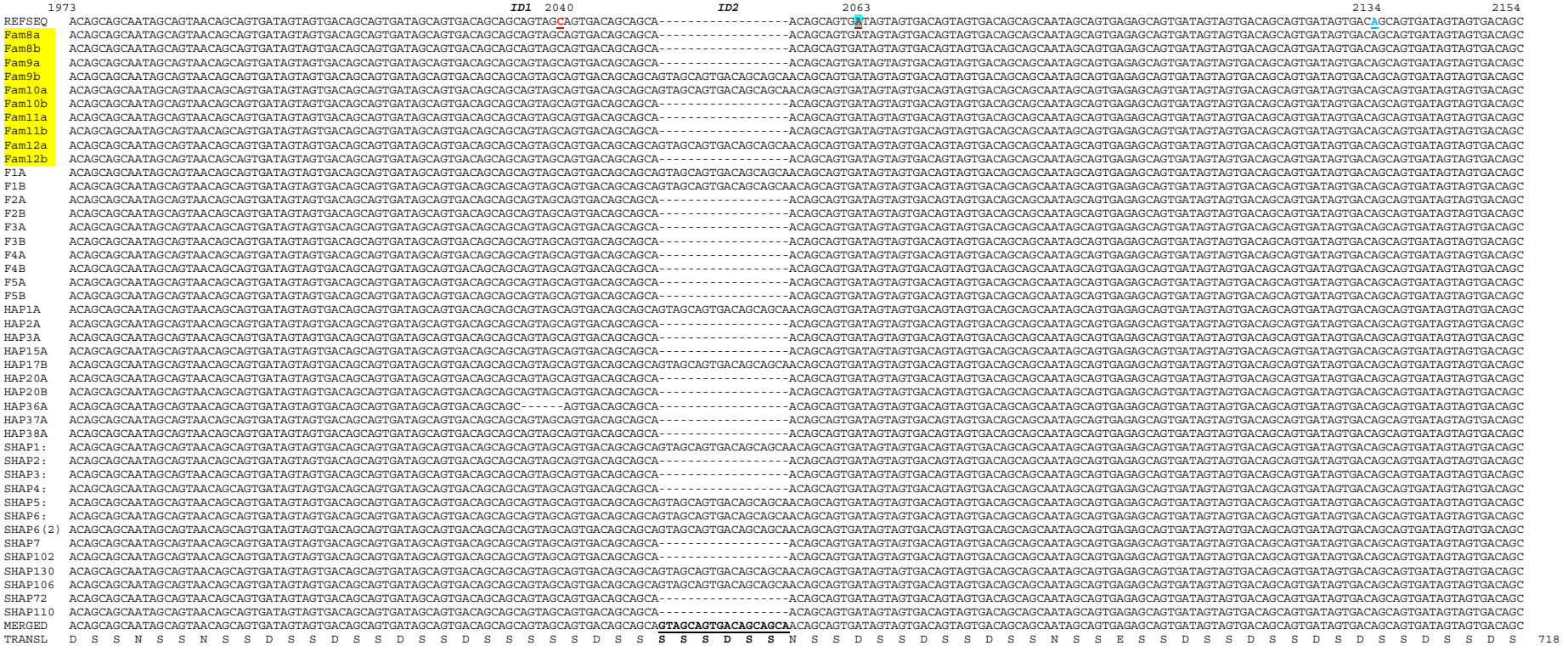
Mutations:

1. g.10820delT; c.1686delT; p.(Asp562Glufs*752) [5]



Mutations:

2. g.10964delC; c.1830delC; p.(Ser610Argfs*704) [5]
3. g.11004_11007delTCAG; c.1870_1873delTCAG; p.(Ser624Thrfs*689) [2]
4. g.11008_11011delACAG; c.1874_1877delACAG; p.(Asp625Alafs*688) [6]
5. g.11049_11052delAAGT; c.1915_1918delAAGT; p.(Lys639Glnfs*674) [1,7]
6. g.11052_11055delTCAG; c.1918_1921delTCAG; p.(Ser640Thrfs*673) [1,2,5]
7. g.11056_11059delACAG; c.1922_1925delACAG; p.(Asp641Alafs*672) [5]



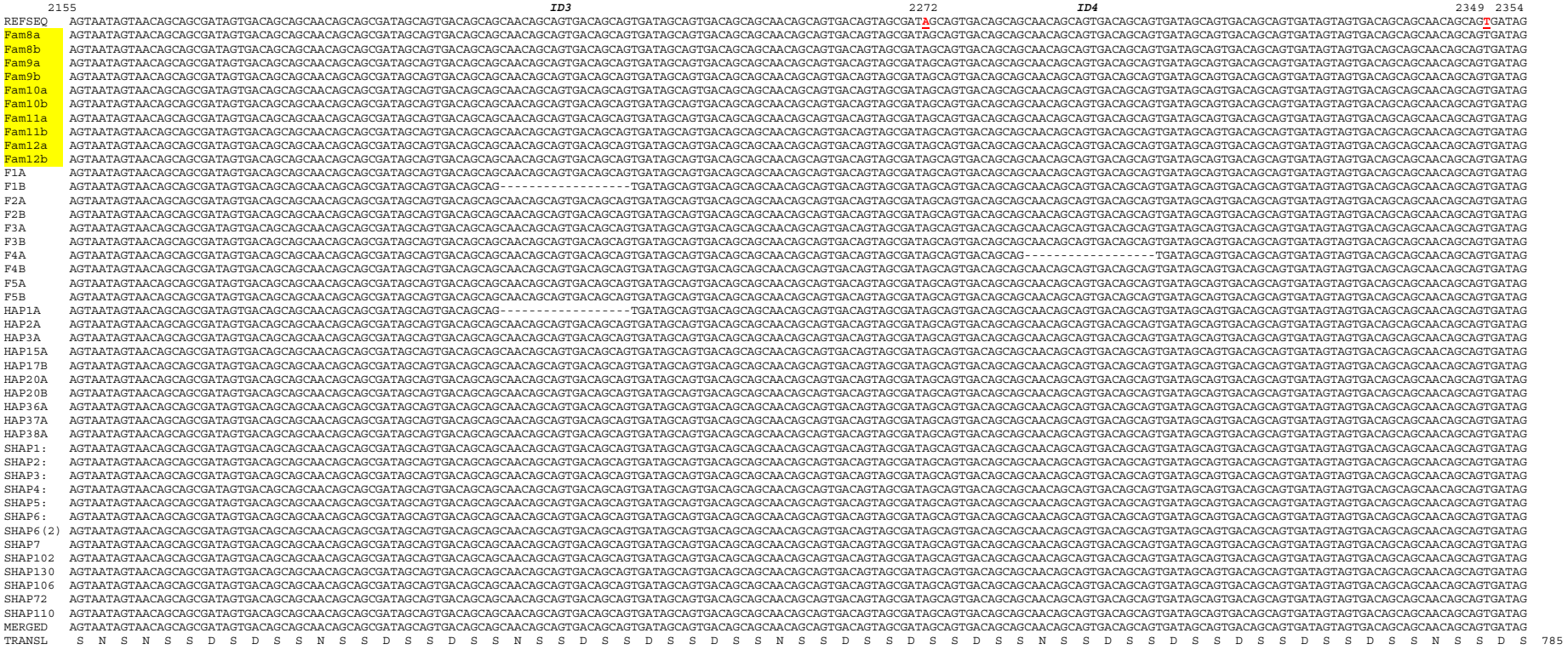
Notes:

ID1: NM_014208.3:c.2035_2040del AGTAGC.

ID2: NM_014208.3:c.2053_2054insGTAGCAGTGACAGCAGCA.

Mutations:

8. g.11174delC; c.2040delC; p.(Ser680Argfs*634) [4]
9. g.11197delA; c.2063delA; p.(Asp688Valfs*626) [5]
10. g.11268delA; c.2134delA; p.(Ser712Alafs*602) [1,8]



Notes:

ID3: NM_014208.3:c.2214_2231delCAACAGCAGTGACAGCAG.
ID4: NM_014208.3:c.2286_2303delCAACAGCAGTGACAGCAG.

Mutations:

11. g.11406delA; c.2272delA; p.(Ser758Alafs*556) [2]
12. g.11483delT; c.2349delT; p.(Ser783Argfs*531) [5]

Notes:

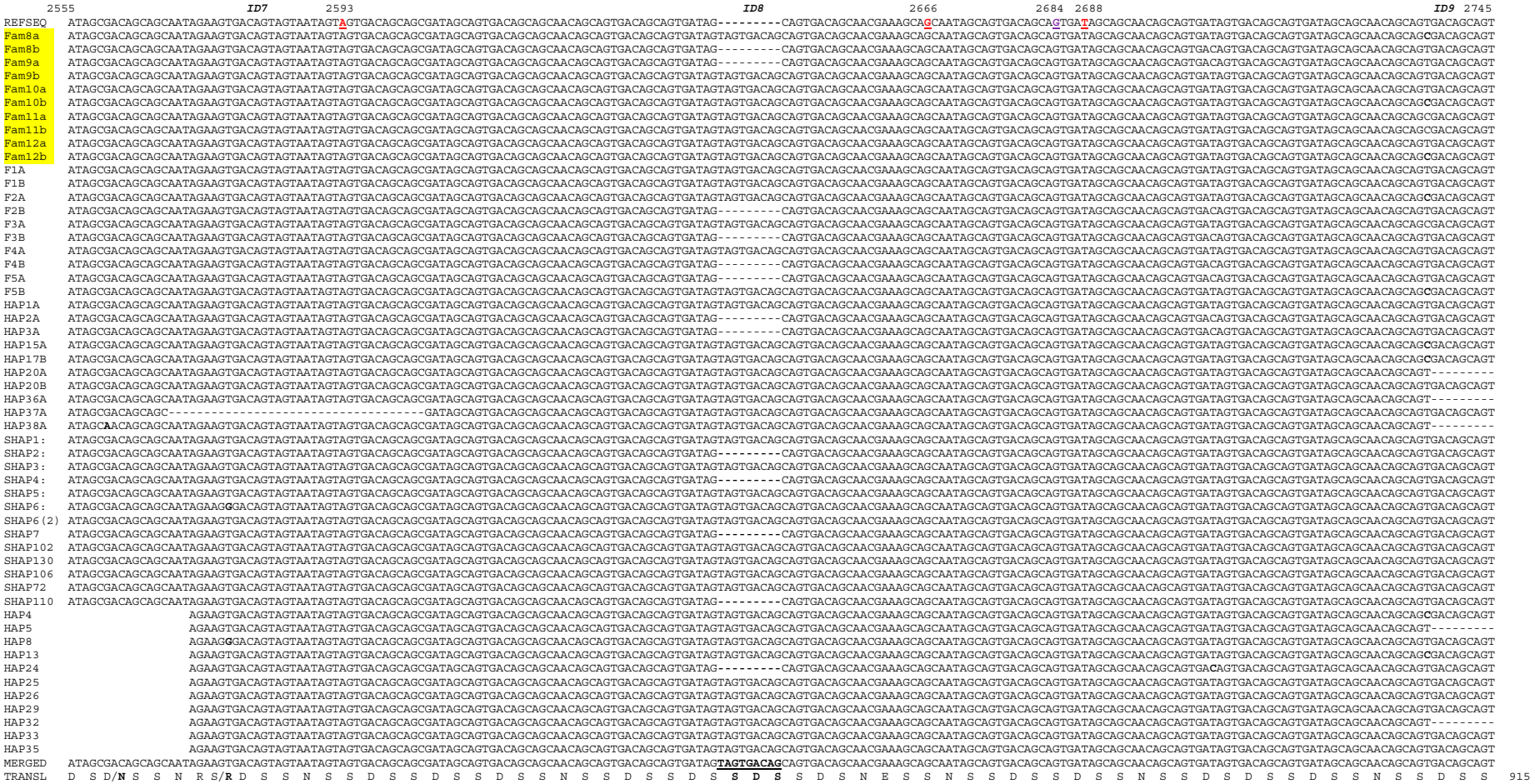
SNP: c.2535C>A or p.Ser845Arg; c.2535C>A; c.2548G>A (p.Gly850Ser).

ID5: NM_014208.3:c.2507_2509delGCA.

ID6: NM_014208.3:c.2509_2526delAACAGCAGTGATAGCAGC.

Mutations:

13. g.11659delG; c.2525delG; p.(Ser842Thrfs*472); Fam 8&9 [2]



Notes:

c.2571T is the beginning of the Hap3 to Hap38 sequences.

SNPs: c.2560G>A (p.Asp854Asn); c.2577T>G (p.Ser859Arg); c.2706T>C; c.2736T>C.

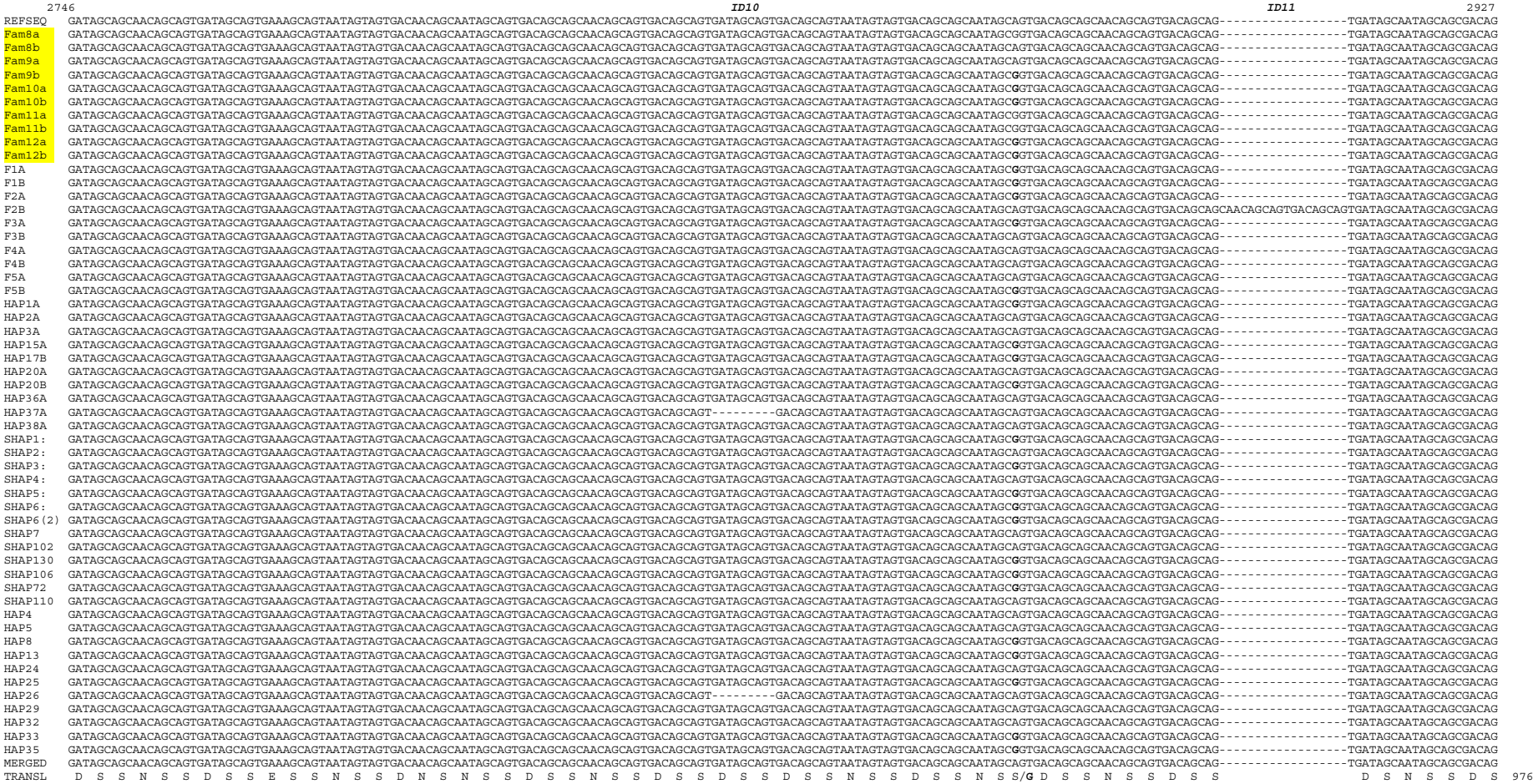
ID7: NM_014208.3:c.2569_2604delAATAGAAGTGACAGTAGTAATAGTAGTGACAGCAGC.

ID8: NM_014208.3:c.2645_2646insTAGTGACAG.

ID9: NM_014208.3:c.2737_2745delGACAGCAGT.

Mutations:

14. g.11727delA; c.2593delA; p.(Ser865Valfs*449)[4]
15. g.11800delG; c.2666delG; p.(Ser889Thrfs*425)[5]
16. g.11818delG; c.2684delG; p.(Ser895Metfs*419)[4,6]
17. g.11822delT; c.2688delT; p.(Asp896Glufs*418)[9]



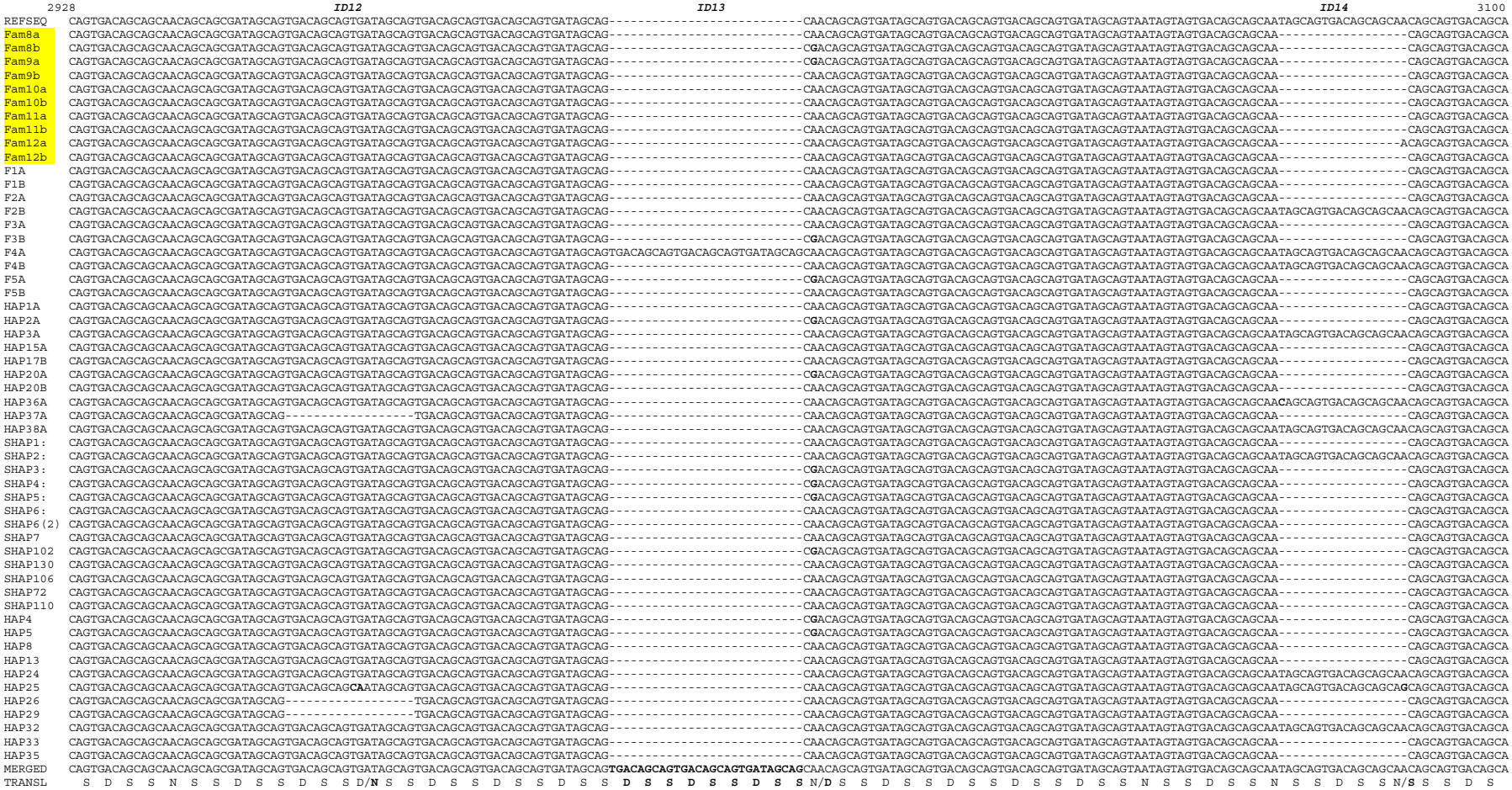
Notes:

SNP: c.2878A>G (p.Ser960Gly).

ID10: NM_014208.3:c.2836_2844delGATAGCAGT.

ID11: NM_014208.3:c.2877_2906dup (Same as designation: NM_014208.3:c.2906_2907insCAACAGCAGTGACAGCAG).

Mutations: No disease-causing frameshifts have been observed in this region.



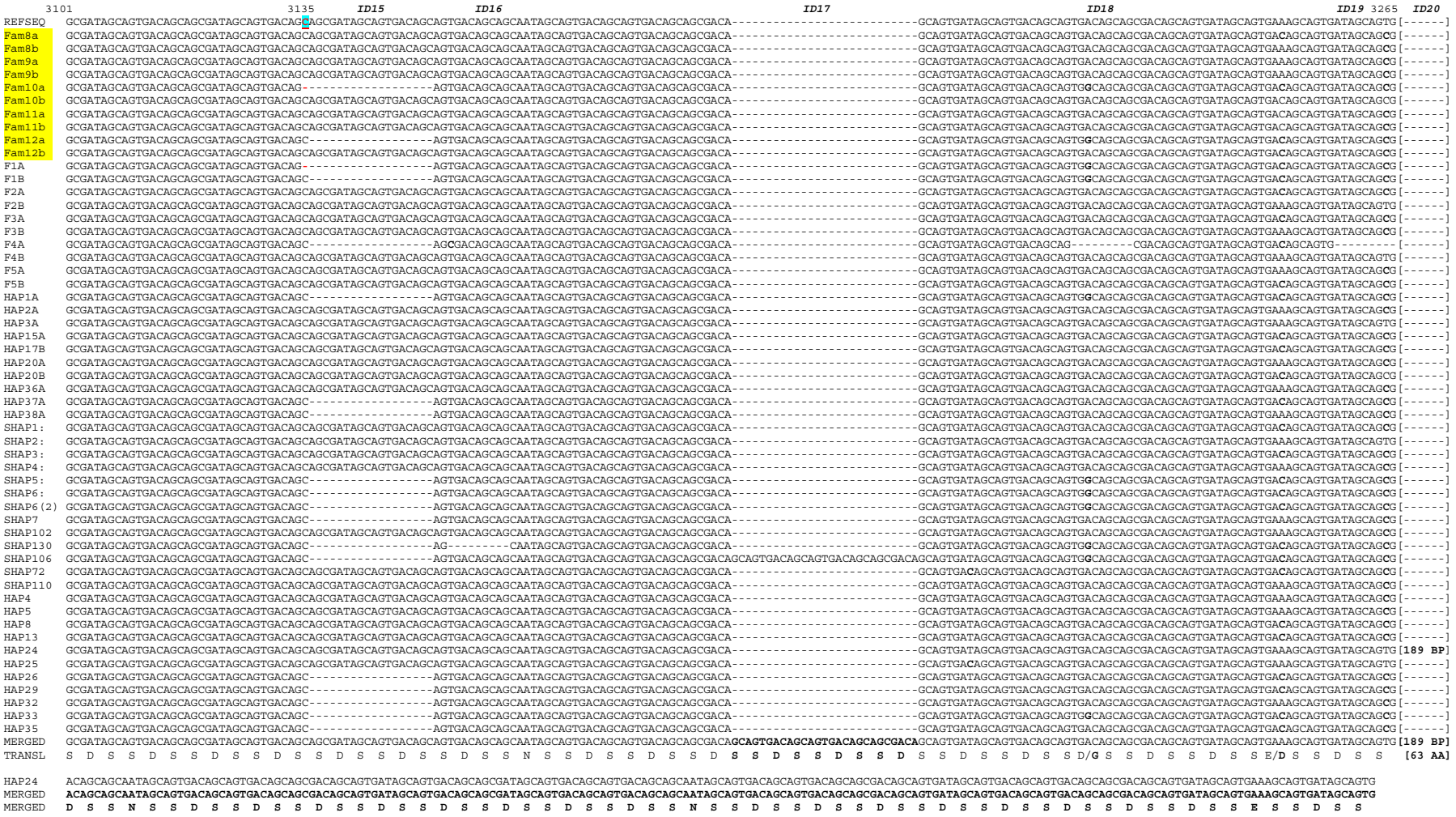
Notes:

SNPs: c.2967T>C; c.2968G>A (p.Asp990Asn); c.3004A>G (p.Asn1002Asp); c.3069T>C; c.3085A>G (p.Asn1029Asp); c.3086A>G (p.Asn1029Ser); c.3087C>T.

ID12: NM_014208.3:c.2958_2975delTGACAGCAGTGATAGCAG.

ID13: NM_014208.3:c.2976_3002dup (Same as designation: NM_014208.3:c.3002_3003insTGACAGCAGTGACAGCAGTGATAGCAG).
ID14: NM_014208.3:c.3069_3086delTAGCAGTGACAGCAGCAA.

Mutations: No disease-causing frameshifts have been observed in this region.



Notes:

The [189 bp] at the end of the alignment for Hap24 refers to the sequence immediately above these notes.

SNPs: multiple haplotypes: c.3221A>G (p.Asp1074Gly); c.3249A>C (p.Glu1083Asp); c.3264T>C.

ID15: NM_014208.3:c.3136_3153delAGCGATAGCAGTGACAGC.

ID16: NM_014208.3:c.3156_3164delTGACAGCAG.

ID17: NM_014208.3:c.3170_3196dup (Same as designation: NM_014208.3:c.3196_3197insGCAGTGACAGCAGTGACAGCAGCGACA).

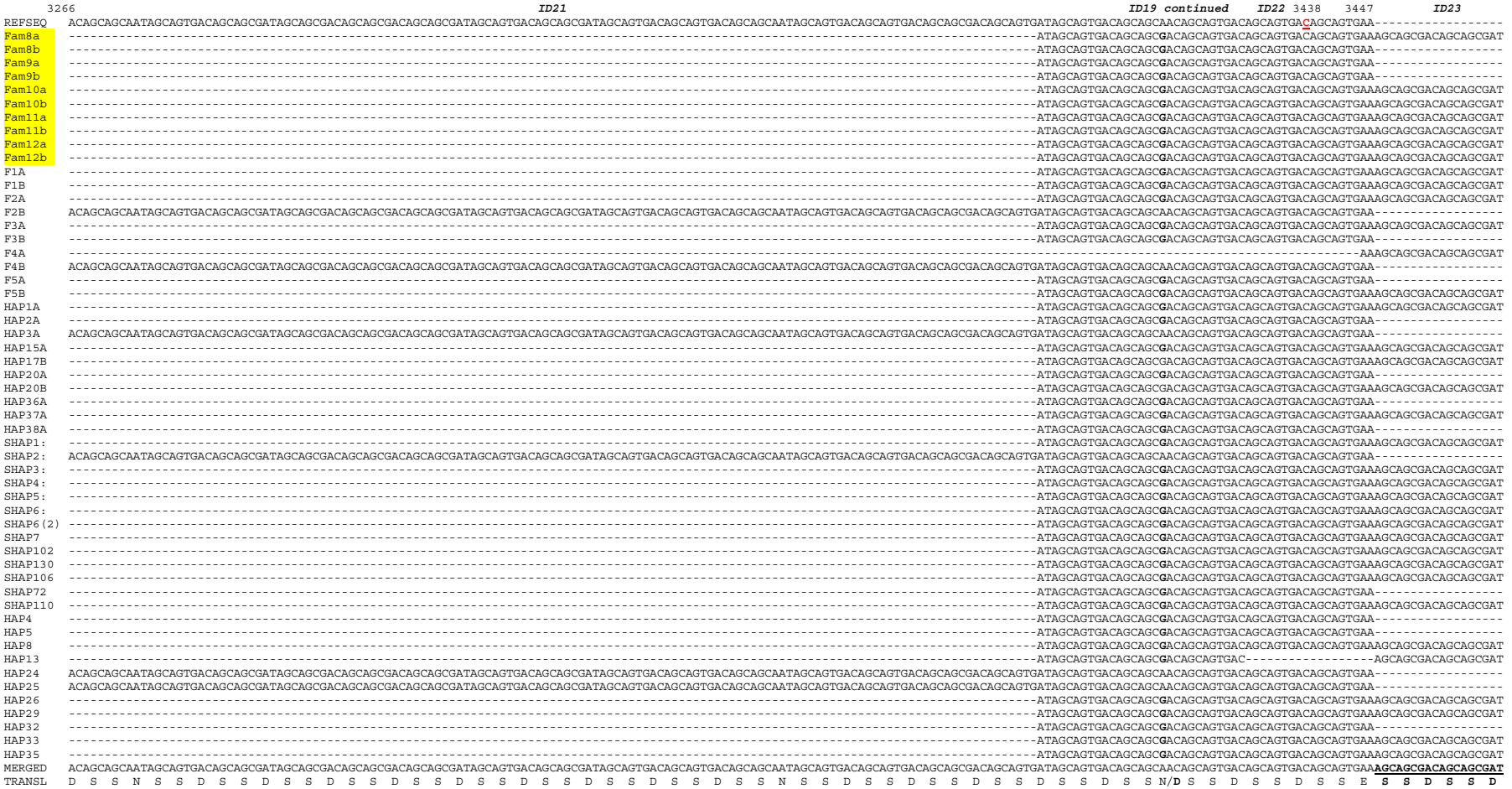
ID18: NM_014208.3:c.3219_3227delTGACAGCAG.

ID19: NM_014208.3:c.3257_3445delATAGCAGTGATAGCAGTGACAGCAGCAACAGCAGTGACAGCAGTGACAGCAGTG.

ID20: NM_014208.3:c.3265_3266insACAGCAGCAATAGCAGTGACAGCAGTGACAGCAGCGACAGCAGTGATAGCAGTGACAGCAGCGATAGCAGTGACAGCAGTGACAG CAGCAATAGCAGTGACAGCAGTGACAGCAGCGACAGCAGTGATAGCAGTGACAGCAGTGACAGCAGCGACAGCAGTGATAGCAGTGAAAGCAGTGATAGCAGT.

Mutations:

18. g.12269delC; c.3135delC; p.(Ser1045Argfs*269); Family 10 [1,10]



Notes:

SNP: c.3418A>G (p.(Asn1140Asp);

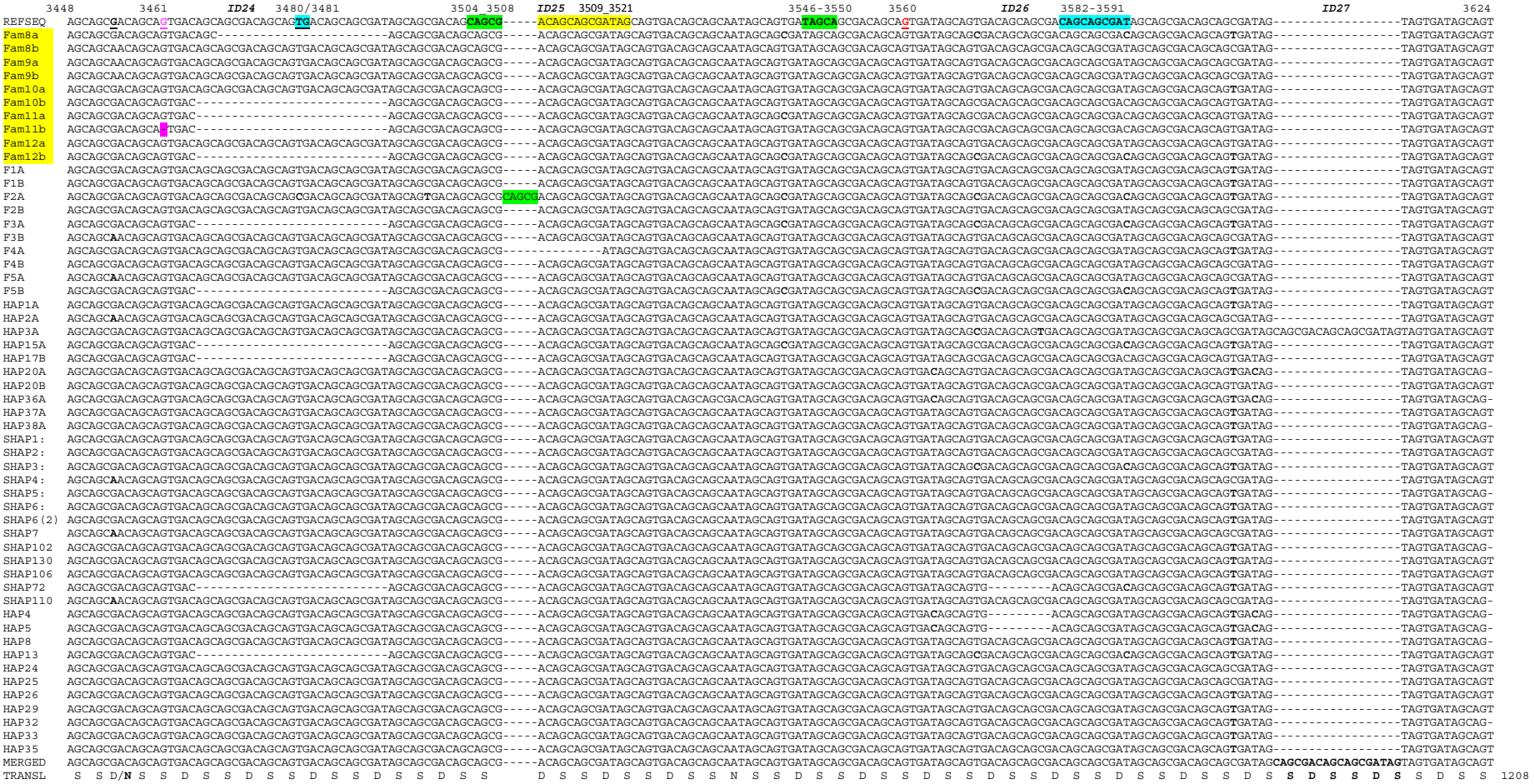
ID21: NM_014208.3:c.3266_3400delACAGCAGCAATAGCAGTGACAGCAGCGATAGCAGCGACAGCAGCGACAGCAGCGATAGC AGTGACAGCAGCGATAGCAGTGACAGCAGTGACAGCAGCAATAGCAGTGACAGCAGTGACAGCAGCGACAGCAGTG.

ID22: NM_014208.3:c.3430_3447delAGCAGTGACAGCAGTGAA.

ID23: NM_014208.3:c.3447_3448insAGCAGCGACAGCAGCGAT.

Mutations:

20. g.12572delC; c.3438delC; p.(Asp1146Glufs*168) [4]



Notes:

Snp8: c.3454G>A; p.D1152N

ID24: NM_014208.3:c.3466_3492delAGCAGCGACAGCAGTGACAGCAGCGAT

ID25: NM_014208.3:c.3509_3517delACAGCAGCG.

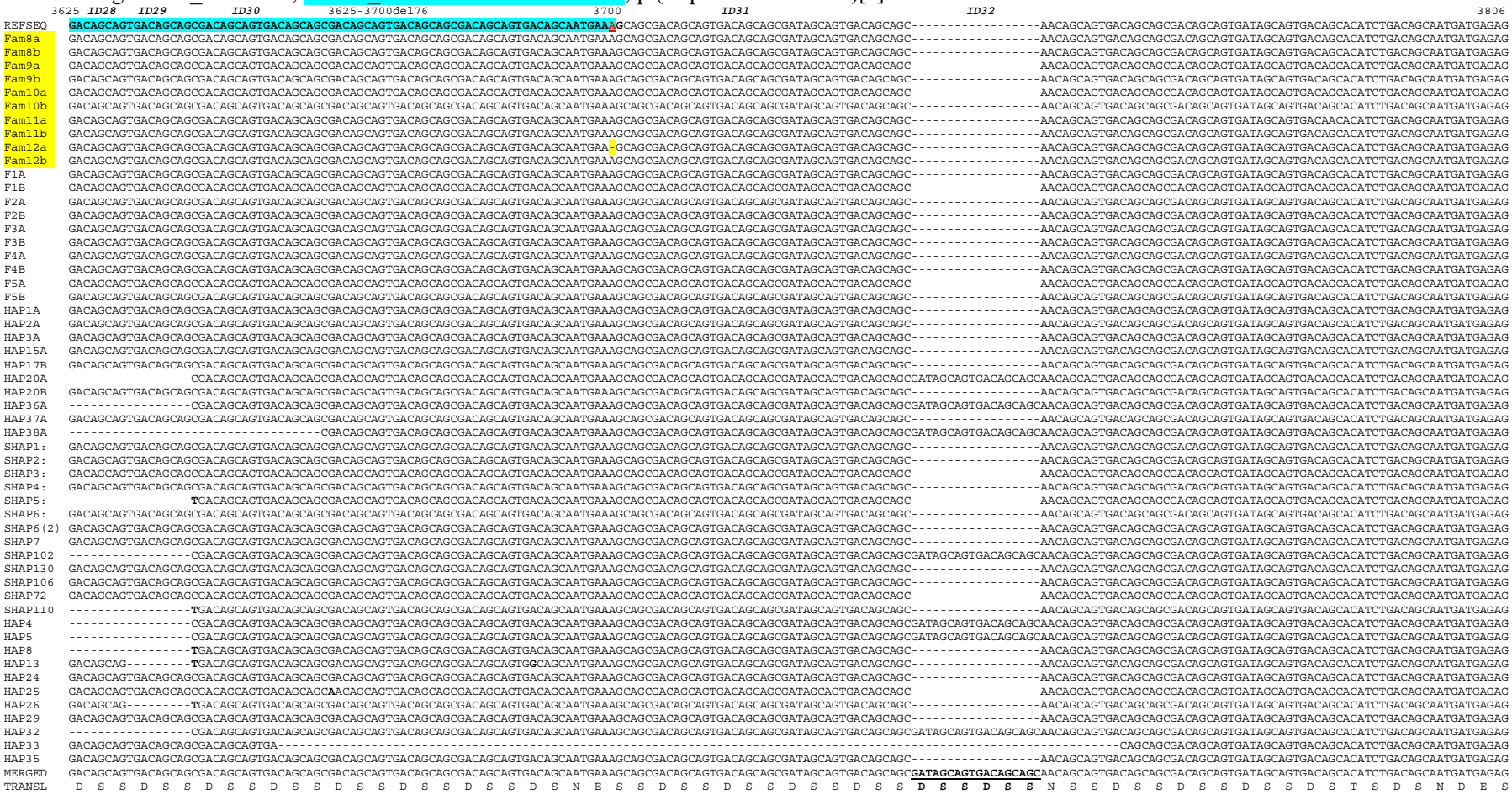
ID26: NM_014208.3:c.3591_3599delTAGCAGCGA.

ID27: NM_014208.3:c.3594_3611dupCAGCGACAGCAGCGATAG.

Mutations: 21. g.12595delG; c.3461delG; p.(Ser1154Metfs*160) [This paper, Family 11]

22. g.12614_12615insCTGCT; c.3480_3481insCTGCT; p.(Asp1161Leufs*155) [8]

23. g.12638_12642dupCAGCG; c.3504_3508dupCAGCG; p.(Asp1170Alafs*146) [1]
24. g.12643_12655del13; c.3509_3521delACAGCAGCGATAG; p.(Asp1170Alafs*140)[6]
25. g.12680_12684delinsG; c.3546_3550delTAGCAinsG; p.(Asp1182Glufs*131)[4]
26. g.12694delG; c.3560delG; p.(Ser1187Metfs*127) [9]
27. g.12716_12725del; c.3582_3591delCAGCAGCGAT; p.(Asp1194Glufs*117)[5]



Notes:

ID28: NM_014208.3:c.3624_3641delTGACAGCAGTGACAGCAG.

ID29: NM_014208.3:c.3633_3641delTGACAGCAG.

ID30: NM_014208.3:c.3624_3659delTGACAGCAGTGACAGCAGCGACAGCAGTGACAGCAG

ID31: NM_014208.3:c.3654_3752delCAGCAGCGACAGCAGTGACAGCAGCGACAGCAGTGACAGCAATGAAAGCAG CGACAGCAGTGACAGCAGCGATAGCAGTGACAGCAGCAACAGCAGTGA.

ID32: NM_014208.3:c.3724_3741dup (same as: NM_014208.3:c.3741_3742insGATAGCAGTGACAGCAGC).

Mutations:

28. g.12810delA; c.3676delA; p.(Ser1226Alafs*88) [11]
29. g.12759_12834del76; c.3625-3700del76; p.(Asp1209Alafs*80) [5]
30. g.12834delA; c.3700delA; p.(Ser1234Alafs*80); [This paper, Family 12]

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F1B       TGACAGCCAGAGCAAGTCTGGTAACGGTAACAACAATGGAAGTGACAGTGACAGTGACAGTGAAGGCAGTGACAGTAACCACTCAACCAGTGATGATTAG
F2A       TGACAGCCAGAGCAAGTCTGGTAACGGTAACAACAATGGAAGTGACAGTGACAGTGACAGTGAAGGCAGTGACAGTAACCACTCAACCAGTGATGATTAG
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F3A       TGACAGCCAGAGCAAGTCTGGTAACGGTAACAACAATGGAAGTGACAGTGACAGTGACAGTGAAGGCAGTGACAGTAACCACTCAACCAGTGATGATTAG
F3B       TGACAGCCAGAGCAAGTCTGGTAACGGTAACAACAATGGAAGTGACAGTGACAGTGACAGTGAAGGCAGTGACAGTAACCACTCAACCAGTGATGATTAG
F4A       TGACAGCCAGAGCAAGTCTGGTAACGGTAACAACAATGGAAGTGACAGTGACAGTGACAGTGAAGGCAGTGACAGTAACCACTCAACCAGTGATGATTAG
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HAP15A    TGACAGCCAGAGCAAGTCTGGTAACGGTAACAACAATGGAAGTGACAGTGACAGTGACAGTGAAGGCAGTGACAGTAACCACTCAACCAGTGATGATTAG
HAP17B    TGACAGCCAGAGCAAGTCTGGTAACGGTAACAACAATGGAAGTGACAGTGACAGTGACAGTGAAGGCAGTGACAGTAACCACTCAACCAGTGATGATTAG
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SHAP6(2)  TGACAGCCAGAGCAAGTCTGGTAACGGTAACAACAATGGAAGTGACAGTGACAGTGACAGTGAAGGCAGTGACAGTAACCACTCAACCAGTGATGATTAG
SHAP7     TGACAGCCAGAGCAAGTCTGGTAACGGTAACAACAATGGAAGTGACAGTGACAGTGACAGTGAAGGCAGTGACAGTAACCACTCAACCAGTGATGATTAG
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SHAP110   TGACAGCCAGAGCAAGTCTGGTAACGGTAACAACAATGGAAGTGACAGTGACAGTGACAGTGAAGGCAGTGACAGTAACCACTCAACCAGTGATGATTAG
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HAP5      TGACAGCCAGAGCAAGTCTGGTAACGGTAACAACAATGGAAGTGACAGTGACAGTGACAGTGAAGGCAGTGACAGTAACCACTCAACCAGTGATGATTAG
HAP8      TGACAGCCAGAGCAAGTCTGGTAACGGTAACAACAATGGAAGTGACAGTGACAGTGACAGTGAAGGCAGTGACAGTAACCACTCAACCAGTGATGATTAG
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HAP24     TGACAGCCAGAGCAAGTCTGGTAACGGTAACAACAATGGAAGTGACAGTGACAGTGACAGTGAAGGCAGTGACAGTAACCACTCAACCAGTGATGATTAG
HAP25     TGACAGCCAGAGCAAGTCTGGTAACGGTAACAACAATGGAAGTGACAGTGACAGTGACAGTGAAGGCAGTGACAGTAACCACTCAACCAGTGATGATTAG
HAP26     TGACAGCCAGAGCAAGTCTGGTAACGGTAACAACAATGGAAGTGACAGTGACAGTGACAGTGAAGGCAGTGACAGTAACCACTCAACCAGTGATGATTAG
HAP29     TGACAGCCAGAGCAAGTCTGGTAACGGTAACAACAATGGAAGTGACAGTGACAGTGACAGTGAAGGCAGTGACAGTAACCACTCAACCAGTGATGATTAG
HAP32     TGACAGCCAGAGCAAGTCTGGTAACGGTAACAACAATGGAAGTGACAGTGACAGTGACAGTGAAGGCAGTGACAGTAACCACTCAACCAGTGATGATTAG
HAP33     TGACAGCCAGAGCAAGTCTGGTAACGGTAACAACAATGGAAGTGACAGTGACAGTGACAGTGAAGGCAGTGACAGTAACCACTCAACCAGTGATGATTAG
HAP35     TGACAGCCAGAGCAAGTCTGGTAACGGTAACAACAATGGAAGTGACAGTGACAGTGACAGTGAAGGCAGTGACAGTAACCACTCAACCAGTGATGATTAG
MERGED    TGACAGCCAGAGCAAGTCTGGTAACGGTAACAACAATGGAAGTGACAGTGACAGTGACAGTGAAGGCAGTGACAGTAACCACTCAACCAGTGATGATTAG
TRANSL      D  S  Q  S  K  S  G  N  G  N  N  N  G  S  D  S  D  S  D  S  E  G  S  D  S  N  H  S  T  S  D  D  *
```

Mutations: No disease-causing frameshifts have been observed in this region.

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