

Mutation database of Japanese congenital factor VII deficiency

| No | exon/intron   | A.A change 1 | A.A change 2 | Mutation        | sex          | clinical Phenotype | PT/reagent*                             | FVII:C /reagent*                    | FVII:Ag      | Reference                                       |
|----|---------------|--------------|--------------|-----------------|--------------|--------------------|---|-------------------------------------|--------------|---|
| 1  | Promoter IVS4 | -96T>C       | IVS4+1G>A    | compound hetero | female       | sever              |   | <1%/Rb                              | 6%           | Nagaizumi K; Br J Haematol 119: 1052-1058, 2002 |
| 2  | Promoter      | -96T>C       |              | hetero          | brother No1  | asyp               |   | 57%                                 | 57%          | Nagaizumi K; Br J Haematol 119: 1052-1058, 2002 |
| 3  | exon 1A       | Lue-26Pro    |              | homo            | male         | asyp               | 13.3 sec                                | 10.7%/h                             | 11%          | Ozawa T; Br J Haematol 101:47-49, 1998          |
| 4  | exon 2 exon 8 | Glu20Lys     | Arg277His    | compound hetero | female       | mild               | 19.1 sec/Rb<br>12.7 sec/rh              | 9%/Rb<br>53%/rh                     | 102%         | 金沢 香: 日本血栓止血誌15:458,2004                        |
| 5  | exon 2        | Glu20Lys     |              | hetero          | female       | mild               | 14.4 sec/R<br>14.5 sec/rh               | 37.5%/Rb<br>30.5%/rh                |              | 金沢 香: 第4回北海道凝固線溶異常研究会、2007                      |
| 6  | exon 2 exon 8 | Glu25Lys     | His348Gln    | compound hetero | male         | asyp               |   | 1%/Rb                               | 21%          | Nagaizumi K; Br J Haematol 119: 1052-1058, 2002 |
| 7  | exon 5        | Tyr68Cys&    | 1bp deletion | compound hetero | female       | sever              |   | <1%/rh                              | <1%          | 篠沢圭子: ;第54回日本臨床検査医学会学術集会 2007                   |
| 8  | exon 4        | Arg79Gln     |              | homo            | male         | asyp               | 16.4 sec/Rb<br>11.0 sec/h<br>35.3 sec/b | 11%/Rb<br>100%/h<br>150/b           | 93%          | Takamiya O; Haemostasis 25: 89-97, 1995         |
| 9  | exon 4        | Arg79Gln     |              | homo            | brother No8  | asyp               |   | 8.6%/Rb<br>100%/h                   | 100%         | Takamiya O; Haemostasis 25: 89-97, 1995         |
| 10 | exon 4        | Arg79Gln     |              | hetero          | children No8 | asyp               |   | 43%/Rb<br>101%/h                    | 89%          | Takamiya O; Haemostasis 25: 89-97, 1995         |
| 11 | exon 4        | Arg79Gln     |              | hetero          | nephew No8   | asyp               |   | 52%/Rb<br>101%/h                    | 82%          | Takamiya O; Haemostasis 25: 89-97, 1995         |
| 12 | exon 4        | Arg79Gln     |              | homo            | female       | asyp               |   | 6%/Rb<br>38%/rh<br>36%/h<br>68%/b   | 65%<br>5%*   | Takamiya O; Clin Chem 44:9, 1998                |
| 13 | exon 4        | Arg79Gln     |              | hetero          | sister No12  | asyp               |   | 44%/Rb<br>95%/rh<br>80%/h<br>120%/b | 105%<br>34%* | Takamiya O; Clin Chem 44:9, 1998                |

|    |                        |             |             |                 |                     |       |             |                                     |              |  |
|----|------------------------|-------------|-------------|-----------------|---------------------|-------|-------------|-------------------------------------|--------------|--|
| 14 | exon 4                 |             |             | hetero          | father No12         | asyp  |             | 38%/Rb<br>95%/rh<br>90%/h<br>110%/b | 100%<br>32%* | Takamiya O: Clin Chem<br>44:9, 1998                    |
| 15 | IVS4                   | IVS4+1G>A   |             | hetero          | brother<br>No1      | asyp  |             | 68%/Rb                              | 57%          | Nagaizumi K; Br J<br>Haematol 119: 1052-<br>1058, 2002 |
| 16 | IVS4                   | IVS4 splice |             | hetero          | mother<br>No21      | asyp  |             | 53%                                 | 45%          | Takamiya O; Br J<br>Haematol 114:369-374,<br>2001      |
| 17 | exon 5                 | Gly97Ser    |             | hetero          | female              | asyp  |             | 43%                                 | 46%          | 未発表(高宮 脩)  |
| 18 | exon 5                 | Arg110Cys   |             | homo            | male                | asyp  |             | 25%/h                               | 28%          | Suto m: Blood Coagul<br>Fibrinolysis 11:415-9,<br>2000 |
| 19 | exon 5                 | Arg110Cys   |             | hetero          | father No18         | asyp  |             | 62%/h                               | 58%          | Suto m: Blood Coagul<br>Fibrinolysis 11:415-9,<br>2000 |
| 20 | exon 5                 | Arg110Cys   |             | hetero          | mother<br>No18      | asyp  |             | 73%/h                               | 79%          | Suto m: Blood Coagul<br>Fibrinolysis 11:415-9,<br>2000 |
| 21 | IVS4 <sub>8</sub> exon | Gln211stop  | IVS4 splice | compound hetero | male                | sever | 24.0 sec/Rb | <1.5%/rh                            | <5%          | Takamiya O; Br J<br>Haematol 114:369-374,<br>2001      |
| 22 | exon 8                 | Gln211stop  |             | hetero          | father No21         | asyp  |             | 47%                                 | 40%          | Takamiya O; Br J<br>Haematol 114:369-374,<br>2001      |
| 23 | exon 8                 | Arg247His   |             | homo            | female              | asyp  | 15.8 sec    | 28%/Rb<br>24%/h                     | 25.9%        | Ohiwa M: Thrombo<br>Haemosta 71:773-7,1994             |
| 24 | exon 8                 | Arg247His   |             | homo            | sister<br>No23      | asyp  | 15.8 sec    | 18.5%/Rb<br>16.5%/h                 | 16.7%        | Ohiwa M: Thrombo<br>Haemosta 71:773-7,1994             |
| 25 | exon 8                 | Arg247His   |             | homo            | sister<br>No23      | asyp  | 14.8 sec    | 25.5%/Rb<br>26.5%/h                 | 27.5%        | Ohiwa M: Thrombo<br>Haemosta 71:773-7,1994             |
| 26 | exon 8                 | Arg247His   |             | hetero          | child 1 No23        | asyp  | 14 sec      | 42%/Rb<br>41%/h                     | 47.4%        | Ohiwa M: Thrombo<br>Haemosta 71:773-7,1994             |
| 27 | exon 8                 | Arg247His   |             | hetero          | child 2 No23        | asyp  | 14 sec      | 52%/Rb<br>50%/h                     | 65.0%        | Ohiwa M: Thrombo<br>Haemosta 71:773-7,1994             |
| 28 | exon 8                 | Arg247His   |             | hetero          | niece No23          | asyp  | 12.9 sec    | 62%/Rb<br>60%/h                     | 67.3%        | Ohiwa M: Thrombo<br>Haemosta 71:773-7,1994             |
| 29 | exon 8                 | Arg247His   |             | hetero          | grandfather<br>No23 | asyp  | 14.1 sec    | 52%/Rb<br>60%/h                     | 69.6%        | Ohiwa M: Thrombo<br>Haemosta 71:773-7,1994             |
| 30 | exon 8                 | Arg247His   |             | hetero          | grandmother<br>No23 | asyp  | 13.8 sec    | 52%/Rb<br>48%/h                     | 65.9%        | Ohiwa M: Thrombo<br>Haemosta 71:773-7,1994             |

|    |       |           |        |                 |                 |          |  |                           |                       |   |
|----|-------|-----------|--------|-----------------|-----------------|----------|--|---------------------------|-----------------------|---|
| 31 | exon8 | Gly283Ser |        | hetero          | female          | mild     |  | 52%/Rb                    | 73%                   | 永泉圭子; 日本血栓止血誌 12(2):133-143,2001                  |
| 32 | exon8 | Arg304Trp |        | homo            | male            | asyp     | 40.8 sec/Rb<br>21.5 sec/ rh<br>48.89sec/b<br>(48.4-58.4) | <5%/Rb<br>16%/rh<br>60%/b | 454ng/ml<br>(350-520) | Matsushita: J Biol Chem<br>269:7355-63, 1994      |
| 33 | exon8 | Gly331Ser |        | homo            | female          | asyp     | 35.4 sec   | 1.2%/rh<br>1.8%/Rb        | 84%                   | Takamiya O: thromb<br>Haemosta 93:414-9,<br>2005  |
| 34 | exon8 | Ser339Cys |        | hetero          | male            | asyp     | 14.4 sec/Rb  | 34%/rh                    | 40%                   | Takamiya O: Clin Lab<br>Haematol.24:233,02        |
| 35 | exon8 | Ser339Cys |        | hetero          | mother<br>No34  | asyp     |  | 36%/rh                    | 42%                   | Takamiya O: Clin Lab<br>Haematol.24:233,02        |
| 36 | exon8 | His348Gln |        | homo            | male            | moderate | 31.5 sec/Rb  | 5.2%/Rb                   | 60ng/ml<br>(350-520)  | Katsumi A: thromb<br>Haemost 83:239-43,<br>2000   |
| 37 | exon8 | His348Gln |        | hetero          | male            | asyp     |  | 23%/Rb                    | 24%                   | 永泉圭子; 日本血栓止血<br>学会誌 12(2):133-<br>143,2001        |
| 38 | exon8 | His348Gln |        | hetero          | female          | asyp     | 14.8 sec   | 44%/Rb                    | 40%                   | 高宮 脩: 日本血栓止血<br>学会誌 9: 252, 1998                  |
| 39 | exon8 | His348Gln |        | hetero          | female          | asyp     | 14.3 sec/Rb  | 56%/Rb                    |                       | 未発表(高宮 脩)   |
| 40 | exon8 | His348Gln | IVS5-1 | compound hetero |                 |          |  |                           |                       | 未発表(高宮 脩)   |
| 41 | exon8 | Gly354Cys |        | homo            | female          | mild     | 14.1 sec   | 5%                        | 7.30%                 | Takamiya O; Br J<br>Haematol 124:336-342,<br>2004 |
| 42 | exon8 | Gly354Cys |        | hetero          | brather<br>No41 | asyp     |  | 56.6%                     | 62%                   | Takamiya O; Br J<br>Haematol 124:336-342,<br>2004 |
| 43 | exon8 | Gly354Cys |        | hetero          | father No41     | asyp     |  | 52.9%                     | 41%                   | Takamiya O; Br J<br>Haematol 124:336-342,<br>2004 |
| 44 | exon8 | Gly354Cys |        | hetero          | mother<br>No41  | asyp     |  | 52%                       | 45.50%                | Takamiya O; Br J<br>Haematol 124:336-342,<br>2004 |
| 45 | exon8 | Thr359Met |        | homo            | female          | sever    | 36.4 sec   | 1.6%h<br>0.8%/Rb          | 2                     | Ozawa T: thromb<br>Haemosta 78:987-9,<br>1997     |
| 46 | exon8 | Thr359Met |        | homo            | female          | sever    |  | <1%/Rb                    | 2%                    | 永泉圭子; 日本血栓止血<br>誌 12(2):133-143,2001              |
| 47 | exon8 | Thr359Met |        | homo            | male            | asyp     | 78.9 sec   | 5%                        | 1%                    | 大倉由希子: 検査血液学<br>会雑誌 6: 377-82                     |
| 48 | exon8 | Thr359Met |        | hetero          | sister<br>No47  | asyp     | 13 sec   | 52%                       | 46%                   | 大倉由希子: 検査血液学<br>会雑誌 6: 377-82                     |
| 49 | exon8 | Thr359Met |        | homo            | male            | asyp     | 30.5 sec/h   | 1.35%/h                   | <1%                   | 宮崎浩二: 日本血栓止血<br>学会誌 16: 98-103, 2005              |

|    |       |            |           |                 |        |  |             |       |       |                              |
|----|-------|------------|-----------|-----------------|--------|--|-------------|-------|-------|------------------------------|
| 50 | exon8 | Thr359Met  |           | homo            | male   | asyp                                   |             | 0.90% | 0.80% | 未発表(高宮 脩)                    |
| 51 | exon8 | Thr359Met  |           | homo            | male   | sever                                  |             | 5%/Rb | <1%   | 未発表(篠沢圭子)                    |
| 52 | exon8 | Thr359Met  |           | homo            | male   | bleeding tendency                      | 31.9 sec    | <3%   |       | 仁井見英樹;第54回日本臨床検査医学会学術集会 2007 |
| 53 | exon8 | Thr359Met  |           | homo            | male   | epistaxis                              | 49.9 sec/Rb | <3%   |       | 仁井見英樹;第54回日本臨床検査医学会学術集会 2007 |
| 54 | exon8 | Arg402Stop |           | hetero          | male   | hematemesis /discharge after operation | 16.4 sec/Rb | 29%   |       | 仁井見英樹;第54回日本臨床検査医学会学術集会 2007 |
| 55 | exon8 | Arg402Stop | Thr359Met | compound hetero | female | mild                                   |             | 4%    |       | 勝田逸朗;第54回日本臨床検査医学会学術集会 2007  |

reagent\*: Rb:rabbit brain/lung TPL, h; human placenta TPL, rh; recombinant human TPL, b; bovine brain TPL

高宮 脩:日本人の先天性VII因子欠乏・異常症の遺伝子変異. 日本血栓止血学会誌 19(1): 64-76, 2008