



Molecular characteristics of Human Endogenous Retrovirus type-W in schizophrenia and bipolar disorder.

Hervé Perron, Nora Hamdani, Raphaël Faucard, Mohamed Lajnef, Stéphane Jamain, Claire Daban-Huard, Samuel Sarrazin, Emmanuel Leguen, Josselin Houenou, Marine Delavest, et al.

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SUPPLEMENTARY INFORMATION

Molecular characteristics of Human Endogenous Retrovirus type-W (HERV-W) in schizophrenia and bipolar disorder.

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I. Complementary Statistical analyses:

Table S1: HERV-W RNA relative expression of the MSRV subtype, all controls

Variables	BP,N=91	SZ,N=45	Controls,N=73	P for all	P BP vs TEM	P BP vs SZ	P SZ vs TEM
	Mean(SD)			P value Kruskal Wallis/Mann Whitney			
RNA	1.62 (4.6)	0.84 (0.5)	0.65 (0.6)	<0.0001	<0.0001	0.01	0.012
DNA	0.61(0.3)	0.55(0.3)	0.77(0.3)	0.0005	0.0016	0.575	0.0003

Table S2: HERV-W relative expression of the MSRV subtype, Controls with negative CRP (C-)

Variables	BP,N=91	SZ,N=45	Controls,N=46	P for all	P BP vs TEM	P BP vs SZ	P SZ vs TEM
	Mean(SD)			P value Kruskal Wallis/Mann Whitney			
RNA	1.62 (4.6)	0.84 (0.5)	0.62 (0.6)	<0.0001	<0.0001	0.01	0.007
DNA	0.60(0.3)	0.55(0.3)	0.77(0.3)	0.0015	0.003	0.575	0.0006

Table S3: HERV_W RNA relative expression and DNA copy numbers of the MSRV subtype. Statistical analyses excluding Bipolar Disorder Patients treated with Valproate.

Variables	BP,N=68	SZ,N=45	Controls,N=73	P for all	P BP vs TEM	P BP vs SZ	P SZ vs TEM
	Mean(SD)			P value Kruskal Wallis/Mann Whitney			
RNA	1.71 (5.3)	0.84 (0.5)	0.65 (0.6)	<0.0001	<0.0001	0.087	0.007
DNA	0.61(0.3)	0.55(0.3)	0.77(0.3)	0.0009	0.006	0.468	0.0003

II. Sequence analyses

Figure S1: Sequence alignments with the HERV-W/MSRV-env specific Probe

Figure S1A: HC RNA

```

MSRVqPCR p 10 20
            TTCTTCAAATGGAGCCCCAGATGCAG
            AAGAAGTTTACCTCGGGTCTACGTC

1. RNA-H12_1 40 50
[ 104 ] TTCTTCAAATGGAGCCCCAGATGCAG>
          |||
MSRVqPCR p TTCTTCAAATGGAGCCCCAGATGCAG

2. RNA-H12_1 40 50
[ 104 ] TTCTTCAAATGGAGCCCCAGATGCAG>
          |||
MSRVqPCR p TTCTTCAAATGGAGCCCCAGATGCAG

3. RNA-H12_1 40 50
[ 104 ] TTCTTCAAATGGAGCCCCAGATGCAG>
          |||
MSRVqPCR p TTCTTCAAATGGAGCCCCAGATGCAG

4. RNA-H12_1 40 50
[ 104 ] TTCTTCAAATGGAGCCCCAGATGCAG>
          |||
MSRVqPCR p TTCTTCAAATGGAGCCCCAGATGCAG

5. RNA-H12_1 40 50
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          |||
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6. RNA-H12_6 40 50
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10. RNA-H16_ 40 50
[ 104 ] TTCTTCAAATGGAGCCCCAGATGCAG>
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12. RNA-H16_ 40 50
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13. RNA-H16_ 40 50
[ 104 ] TTCTTCAAATGGAGCCCCAGATGCAG>
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14. RNA-H1_1 40 50
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          |||
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15. RNA-H1_1 40 50
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16. RNA-H1_2 40 50
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17. RNA-H1_3 40 50
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MSRVqPCR p TTCTTCAAATGGAGCCCCAGATGCAG

18. RNA-H12_ 40 50
[ 100 ] TTCTTCAAATGGAGCCCCAGATGCA>
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20. RNA-H1_8      40      50
[ 100 ] >TTCTTCAAATGGAGCCCCAGATGCA>
          |||
MSRVqPCR p TTCTTCAAATGGAGCCCCAGATGCA

21. RNA-H12_     130      120      110
[ 98 ] <TTCTTCAAATGGAAACCCAGATGCAG
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22. RNA-H12_      40      50
[ 98 ] >TTCTTCAAATGGAACCCAGATGCAG>
          |||
MSRVqPCR p TTCTTCAAATGGAGCCCCAGATGCAG

23. RNA-H12_      40      50
[ 98 ] >TTCTTCAAATGGAACCCAGATGCAG>
          |||
MSRVqPCR p TTCTTCAAATGGAGCCCCAGATGCAG

24. RNA-H16_     130      120      110
[ 98 ] <TTCTTCAAATGGAACCCAGATGCAG
          |||
MSRVqPCR p TTCTTCAAATGGAGCCCCAGATGCAG

25. RNA-H16_     130      120      110
[ 98 ] <TTCTTCAAATGGAACCCAGATGCAG
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26. RNA-H16_      40      50
[ 98 ] >TTCTTCAAATGGAACCCAGATGCAG>
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MSRVqPCR p TTCTTCAAATGGAGCCCCAGATGCAG

27. RNA-H16_      40      50
[ 98 ] >TTCTTCAAATGGAACCCAGATGCAG>
          |||
MSRVqPCR p TTCTTCAAATGGAGCCCCAGATGCAG

28. RNA-H1_1      40      50
[ 98 ] >TTCTTCAAATGGAACCCAGATGCAG>
          |||
MSRVqPCR p TTCTTCAAATGGAGCCCCAGATGCAG

29. RNA-H1_1     130      120      110
[ 98 ] <TTCTTCAAATGGAACCCAGATGCAG
          |||
MSRVqPCR p TTCTTCAAATGGAGCCCCAGATGCAG

30. RNA-H1_1     130      120      110
[ 98 ] <TTCTTCAAATGGAACCCAGATGCAG
          |||
MSRVqPCR p TTCTTCAAATGGAGCCCCAGATGCAG

31. RNA-H1_7      40      50
[ 98 ] >TTCTTCAAATGGAACCCAGATGCAG>
          |||
MSRVqPCR p TTCTTCAAATGGAGCCCCAGATGCAG

32. RNA-H16_     130      120      110
[ 92 ] <TTCTTCAAACGGAACCCAGATGCAG
          |||
MSRVqPCR p TTCTTCAAATGGAGCCCCAGATGCAG

33. RNA-H12_     320      330
[ 88 ] >TTCTTCAAATGGAGCCCCAGA--CAG>
          |||
MSRVqPCR p TTCTTCAAATGGAGCCCCAGATGCAG

```

Figure S1B: HC DNA

```

MSRVqPCR p      10      20
                TTCTTCAAATGGAGCCCCAGATGCAG
                AAGAAGTTTACCTCGGGGTCTACGTC

1. DNA-H12_1      40      50
[ 104 ]          TTCTTCAAATGGAGCCCCAGATGCAG>
                |||
MSRVqPCR p      TTCTTCAAATGGAGCCCCAGATGCAG

2. DNA-H12_5      40      50
[ 104 ]          TTCTTCAAATGGAGCCCCAGATGCAG>
                |||
MSRVqPCR p      TTCTTCAAATGGAGCCCCAGATGCAG

3. DNA-H16_1      40      50
[ 104 ]          TTCTTCAAATGGAGCCCCAGATGCAG>
                |||
MSRVqPCR p      TTCTTCAAATGGAGCCCCAGATGCAG

4. DNA-H16_1      40      50
[ 104 ]          TTCTTCAAATGGAGCCCCAGATGCAG>
                |||
MSRVqPCR p      TTCTTCAAATGGAGCCCCAGATGCAG

5. DNA-H16_1      40      50
[ 104 ]          TTCTTCAAATGGAGCCCCAGATGCAG>
                |||
MSRVqPCR p      TTCTTCAAATGGAGCCCCAGATGCAG

6. DNA-H16_140    50      60
[ 104 ]          TTCTTCAAATGGAGCCCCAGATGCAG>
                |||
MSRVqPCR p      TTCTTCAAATGGAGCCCCAGATGCAG

7. DNA-H16_5      40      50
[ 104 ]          TTCTTCAAATGGAGCCCCAGATGCAG>
                |||
MSRVqPCR p      TTCTTCAAATGGAGCCCCAGATGCAG

8. DNA-H16_8      40      50
[ 104 ]          TTCTTCAAATGGAGCCCCAGATGCAG>
                |||
MSRVqPCR p      TTCTTCAAATGGAGCCCCAGATGCAG

9. DNA-H1_13      40      50
[ 104 ]          TTCTTCAAATGGAGCCCCAGATGCAG>
                |||
MSRVqPCR p      TTCTTCAAATGGAGCCCCAGATGCAG

10. DNA-H1_1      40      50
[ 104 ]          TTCTTCAAATGGAGCCCCAGATGCAG>
                |||
MSRVqPCR p      TTCTTCAAATGGAGCCCCAGATGCAG

11. DNA-H12_130   120     110
[ 98 ]          <TTCTTCAAATGGAGCCCCAGATGCAG
                |||
MSRVqPCR p      TTCTTCAAATGGAGCCCCAGATGCAG

12. DNA-H12_      40      50
[ 98 ]          TTCCTCAAATGGAGCCCCAGATGCAG>
                |||
MSRVqPCR p      TTCTTCAAATGGAGCCCCAGATGCAG

13. DNA-H12_      40      50
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                |||
MSRVqPCR p      TTCTTCAAATGGAGCCCCAGATGCAG

14. DNA-H16_40    50      60
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                |||
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15. DNA-H16_40    50      60
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16. DNA-H16_      40      50
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                |||
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17. DNA-H1_130    120     110
[ 98 ]          <TTCCTCAAATGGAGCCCCAGATGCAG
                |||
MSRVqPCR p      TTCTTCAAATGGAGCCCCAGATGCAG

18. DNA-H1_7      40      50
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22. DNA-H12_      40      50
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MSRVqPCR p TTCTTCAAATGGAGCCCCAGATGCAG

23. DNA-H12_      40      50
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24. DNA-H12_      40      50
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25. DNA-H12_      40      50
[ 92 ] TTCTTCAAATTGAGCCTCAGATGCAG>
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26. DNA-H12_      40      50
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      ||| |||
MSRVqPCR p TTCTTCAAATGGAGCCCCAGATGCAG

27. DNA-H16_ 130      120      110
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28. DNA-H16_40      50      60
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MSRVqPCR p TTCTTCAAATGGAGCCCCAGATGCAG

29. DNA-H16_ 130      120      110
[ 92 ] <TTCTTAAATTGGAGCCCCAGATGCAG
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30. DNA-H16_      40      50
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31. DNA-H16_      40      50
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      ||| |||
MSRVqPCR p TTCTTCAAATGGAGCCCCAGATGCAG

32. DNA-H1_1 130      120      110
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33. DNA-H1_1      40      50
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34. DNA-H1_3 130      120      110
[ 92 ] <TTCTTAAATTGGAGCCCCAGATGCAG
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35. DNA-H1_6      40      50
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36. DNA-H1_9 130      120      110
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Figure S1C: BD RNA

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      10      20
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1. RNA70_10.      40      50
[ 104 ]  TTCTTCAAATGGAGCCCCAGATGCAG>
              |||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

2. RNA70_13.      40      50
[ 104 ]  TTCTTCAAATGGAGCCCCAGATGCAG>
              |||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

3. RNA70_15.      40      50
[ 104 ]  TTCTTCAAATGGAGCCCCAGATGCAG>
              |||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

4. RNA70_16.      40      50
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              |||
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6. RNA71_6.n      40      50
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7. RNA71_9.n      40      50
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MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

8. RNA71_16.      40      50
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9. RNA71_7.n0      50      60
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10. RNA66_1.      40      50
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              |||
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              |||
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14. RNA66_16      40      50
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              |||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

15. RNA66_2.      40      50
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16. RNA66_5.      130      120      110
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18. RNA66_7.      130      120      110
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MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

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      |||
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      |||
MSRVqPCR p TTCTTCAAATGGAGCCCCAGATGCAG

22. RNA70_14     40      50
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      |||
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      |||
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26. RNA70_7.     40      50
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      |||
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      |||
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34. RNA71_15     40      50
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35. RNA71_8.     130     120     110
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36. RNA70_11     320     330
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37. RNA70_2.     40      50
[ 88 ] TTCTTCAAATGGAGCCCCAGA--CAG>
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38. RNA70_8.     320     330
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39. RNA71_4.130   120     110
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      ||||| || |||||
MSRVqPCR p TTCTTCAAATGGAGCCCCAGATGCAG

21. DNA70_13 130      120      110
[ 92 ] <TTCTTAAATTGGAGCCCCAGATGCAG>
      ||||| || |||||
MSRVqPCR p TTCTTCAAATGGAGCCCCAGATGCAG

22. DNA70_16 40      50
[ 92 ] TTCTTAAATTGGAGCCCCAGATGCAG>
      ||||| || |||||
MSRVqPCR p TTCTTCAAATGGAGCCCCAGATGCAG

23. DNA70_4. 130      120      110
[ 92 ] <TTCTTAAATTGGAGCCCCAGATGCAG>
      ||||| || |||||
MSRVqPCR p TTCTTCAAATGGAGCCCCAGATGCAG

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MSRVqPCR p TTCTTCAAATGGAGCCCCAGATGCAG

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      ||||| || |||||
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26. DNA71_11 40      50
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      ||||| || |||||
MSRVqPCR p TTCTTCAAATGGAGCCCCAGATGCAG

27. DNA71_13 40      50
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      ||||| || |||||
MSRVqPCR p TTCTTCAAATGGAGCCCCAGATGCAG

28. DNA71_14 40      50
[ 92 ] TTCTTAAATTGGAGCCCCAGATGCAG>
      ||||| || |||||
MSRVqPCR p TTCTTCAAATGGAGCCCCAGATGCAG

29. DNA71_2. 130      120      110
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      ||||| || |||||
MSRVqPCR p TTCTTCAAATGGAGCCCCAGATGCAG

30. DNA71_3. 40      50
[ 92 ] TTCTTAAATTGGAGCCCCAGATGCAG>
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MSRVqPCR p TTCTTCAAATGGAGCCCCAGATGCAG

31. DNA71_5. 40      50
[ 92 ] TTCTTAAATTGGAGCCCCAGATGCAG>
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MSRVqPCR p TTCTTCAAATGGAGCCCCAGATGCAG

32. DNA71_7. 40      50
[ 92 ] TTCTTAAATTGGAGCCCCAGATGCAG>
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MSRVqPCR p TTCTTCAAATGGAGCCCCAGATGCAG

33. DNA71_8. 40      50
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Figure S1E: SZ RNA

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      10      20
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1. RNA11_10.      40      50
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2. RNA11_11.      40      50
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3. RNA11_12.      40      50
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4. RNA11_14.      40      50
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5. RNA11_15.      40      50
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6. RNA11_2.n      40      50
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8. RNA11_6.n      40      50
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9. RNA11_8.n      40      50
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|||||
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|||||
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|||||
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CR p TTCTTCAAATGGAGCCCCAGATGCAG

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[ 92 ] <TTCTTAAATTGGAGCCCCAGATGCAG
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MSRVqPCR p TTCTTCAAATGGAGCCCCAGATGCAG

21. DNA23_4.      40      50
[ 92 ] TTCTTAAATTGGAGCCCCAGATGCAG>
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MSRVqPCR p TTCTTCAAATGGAGCCCCAGATGCAG

22. DNA23_8. 130      120      110
[ 92 ] <TTCTTAAATTGGAGCCCCAGATGCAG
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MSRVqPCR p TTCTTCAAATGGAGCCCCAGATGCAG

23. DNA32_12      40      50
[ 92 ] TTCTTAAATTGGAGCCCCAGATGCAG>
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MSRVqPCR p TTCTTCAAATGGAGCCCCAGATGCAG

24. DNA32_15 130      120      110
[ 92 ] <TTCTTAAATTGGAGCCCCAGATGCAG
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25. DNA32_2.      40      50
[ 92 ] TTCTTAAATTGGAGCCCCAGATGCAG>
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MSRVqPCR p TTCTTCAAATGGAGCCCCAGATGCAG

26. DNA32_3.      40      50
[ 92 ] TTCTTCAAATTGAGCCTCAGATGCAG>
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MSRVqPCR p TTCTTCAAATGGAGCCCCAGATGCAG

27. DNA32_7.      40      50
[ 92 ] TTCTTAAATTGGAGCCCCAGATGCAG>
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MSRVqPCR p TTCTTCAAATGGAGCCCCAGATGCAG

28. DNA32_8.      40      50
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```

Figure S2: Phylogenetic tree representation of aligned clones with related HERV-W and distant HERV-K env gene sequences:

Figure S2A: RNA and DNA clones from BD

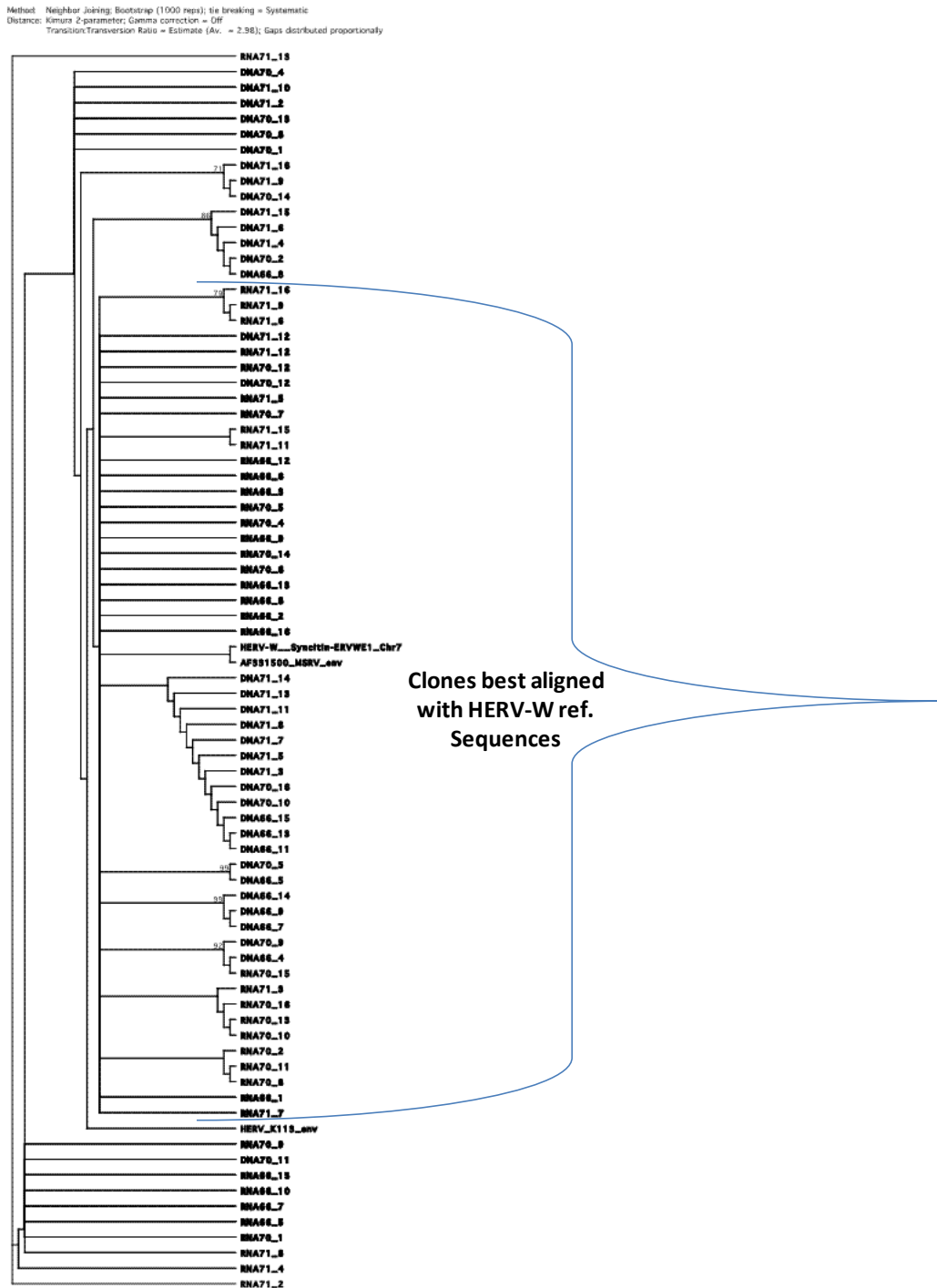


Figure S2B: RNA and DNA clones from SZ

Method: Neighbor Joining; Bootstrap (1000 reps); tie breaking = Systematic
Distance: Kimura 2-parameter; Gamma correction = Off
Transition/Transversion Ratio = Estimate (Av. = 2.75); Gaps distributed proportionally

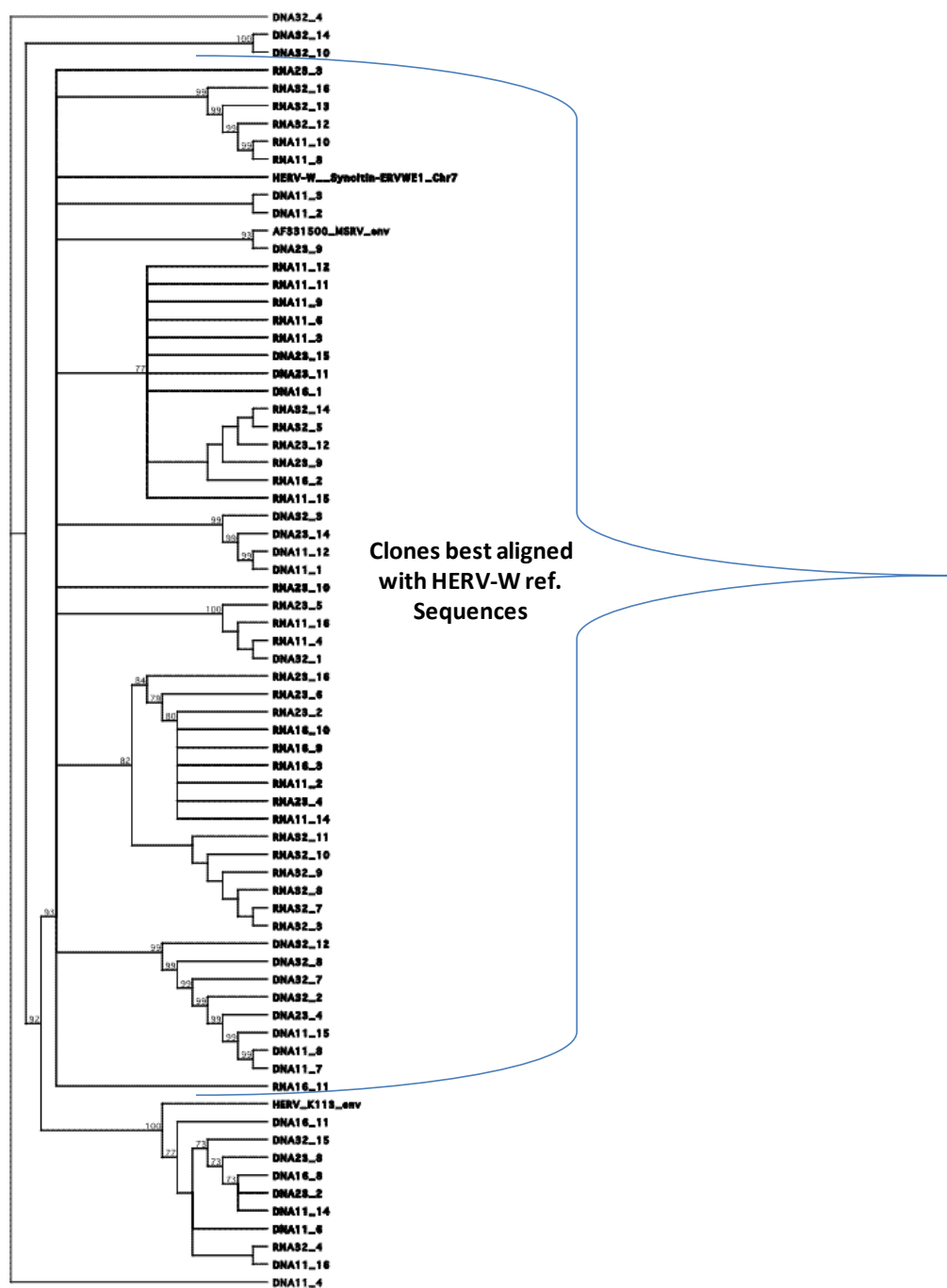


Figure S2C: RNA and DNA clones from HC

Method: Neighbor Joining; Bootstrap (1000 reps); tie breaking = Systematic
Distance: Kimura 2-parameter; Gamma correction = Off
Transition:Transversion Ratio = Estimate (Av. = 3.02); Gaps distributed proportionally

