Supplemental Figure S4A

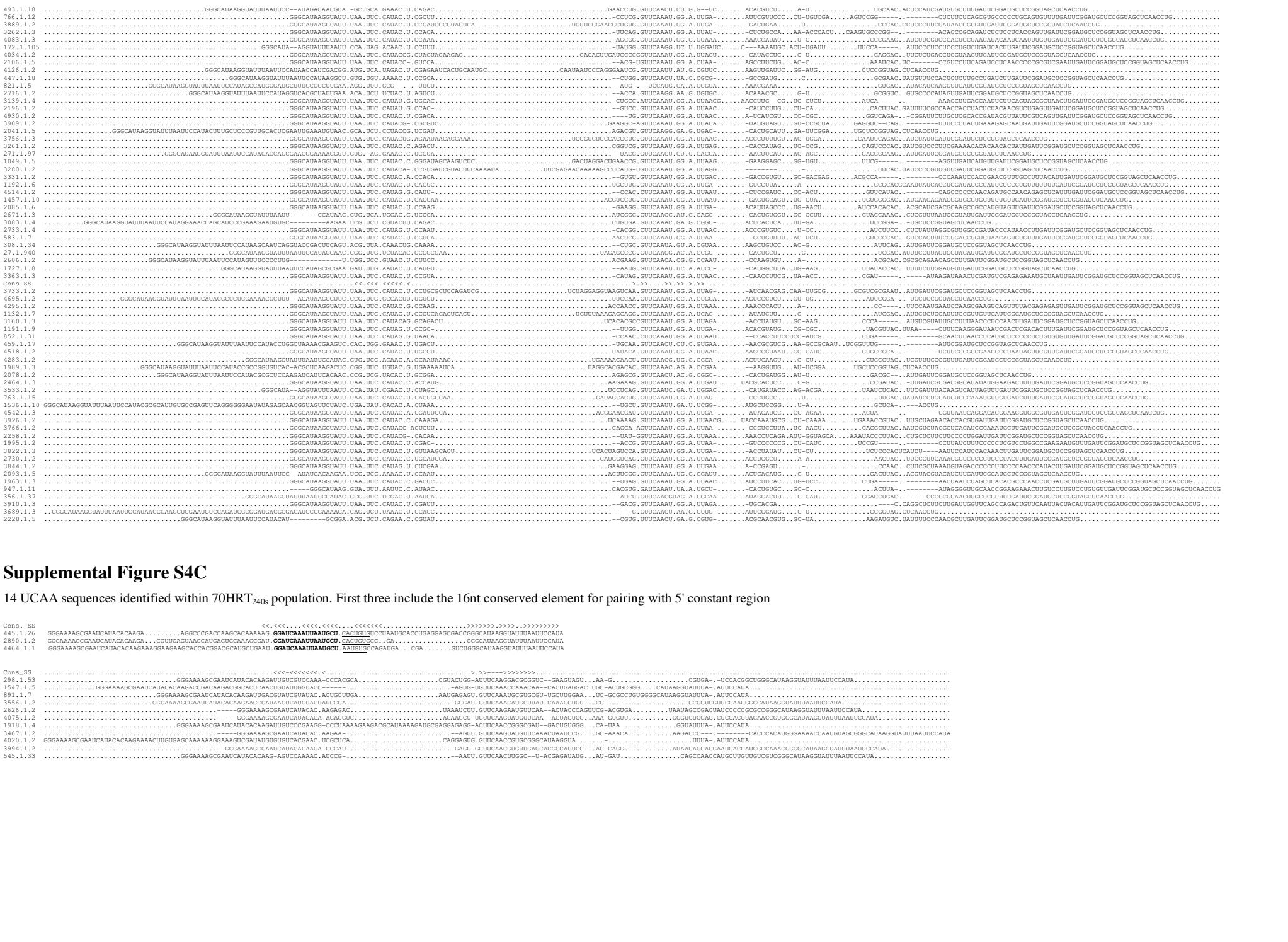
17 UCAA sequences identified within 80HRT$_{14}$ population, with 16nt conserved element for pairing with 5' constant region

```
Cons. SS   <<<<<<<.<<<<..<<<<<<<<<<.....................................................>>>>>....>>>>.>>>>....>>>>.>>>.....................................................
342.1.49   GGGCAUAAGGUAUUUAAUUCCAUAAU.....................................GUGGAUCAAAUUAUUGCU.CACUGUG.CUCAUUUUCUCCCAAUUCUACCCUUUUGGCCCCCCUACUCUCGUGUAUCGCUGUUGAUUCGGAUGCUCCGGUAGCUCAACCUG
3541.1.3   GGGCAUAAGGUAUUUAAUUCCAUACGAAA.....................................GUGAAUUAA.....UGCU.CACUGUG.CCAAACCCUAUACUACCUGUACCGAAUUGUGGGGGAUCGAGCGUACGCUGAAUUGAUUCGGAUGCUCCGGUAGCUCAACCUG
479.1.20   GGGCAUAAGGUAUUUAAUUCCAUAGCAC.....................................GGAUCAAAUUUCUACU.CACUGUG.UCCCCCCAUCCUACUACCCUGAACAAAUCCCUGCACCGUAAGAACCAAUGGUAUUGAUUCGGAUGCUCCGGUAGCUCAACCUG
640.1.28   GGGCAUAAGGUAUUUAAUUCCAUACC.......................................GUGGAUCAAAUUGGUGCU.CACUGUG.CCUAACGAAUGGGGAUCAGAGGGGAAACUGAGUACAGAACGGCAUGUAAACACUUGAUUCGGAUGCUCCGGUAGCUCAACCUG
3176.1.2   GGGCAUAAGGUAUUUAAUUCCAUAGCGC.....................................GGAUCAAAUUAAUGCU.CACUAUG.UUCACCAGUCAUUACAAGUGCCGGAGUUUGCCCUCAACCACAACCAUGGACUUUUGAUUCGGAUGCUCCGGUAGCUCAACCUG
3492.1.2   GGGCAUAAGGUAUUUAAUUCCAUACGGUC....................................GGAUCAAAUUAAUGCU.AAUGUGC.CUGAUCGUCAAAGCACCACAUGUGGAUUGUGUUCGGAUACACCCAUUGCUGUUGAUUCGGAUGCUCCGGUAGCUCAACCUG
3871.1.3   GGGCAUAAGGUAUUUAAUUCCAUACGUUA....................................GGAUCAAAUUAAUGCU.GAAGGCU.CAAACGAAACUGCGCUAGGGGAGGUUGGCGAGUCCGGCUCAGGGACAAUGAUAGUUCGGAUGCUCCGGUAGCUCAACCUG
3994.1.3   GGGCAUAAGGUAUUUAAUUCCAUAUUU......................................UGGGAUCAAAUUAAUGCU.CACUGUG.UCCCUAGACGGAAAGAGGGUAUUCAGACCCACACGAGUCUUAGUCUUCGAGUGUAGUUCGGAUGCUCCGGUAGCUCAACCUG
3523.1.2   GGGCAUAAGGUAUUUAAUUCCAUACUGGC....................................UAUGUCGAAUUUAUGCU.CACUGUG.CCAUAAACGUCGAGAACCCUCACGGUGUGCAGUUUGCAGUACUCUGUGUCAGUACUCGGAUGCUCCGGUAGCUCAACCUG
947.1.11   GGGCAUAAGGUAUUUAAUUCCAUAACCAC....................................GUGGAUCAAAUUAAUGCU.CACUGUG.CGCCACUUAAUAGGGGGUUGCAACCGGAAGAAACUUGUCCUUGUGCCUGUGUUCAUGCCAGAAUUGAUUCGGAUGCUCCGGUAGCUCAACCUG
1424.1.2   GGGCAUAAGGUAUUUAAUUCCAUAACCCAGA..................................GUGGAUCAAAUUAAUGCU.CACGAUG.UCCGACAACCGAUCACCUACCUUGCGUUCACUGUACUCCCUCCUGUUUGAUUCGGAUGCUCCGGUAGCUCAACCUG
3524.1.2   GGGCAUAAGGUAUUUAAUUCCAUACGCUAUGGAC...............................GGAUCAAAUUAAUGCU.CACUAUG.UCUCCCAUCCACCUGCCUCCUCAACCUCACUGUGUUCAUGCCAGAAUUGAUUCGGAUGCUCCGGUAGCUCAACCUG
870.1.5    GGGCAUAAGGUAUUUAAUUCCAUAGUUGACUGAAC..............................UGGAUCAAAUUGAUGCU.CACUGUG.UCCAAAGACCGAAAUGAUUCGUUACCUGGUACUCCCGAGACAUUUUGAUUCGGAUGCUCCGGUAGCUCAACCUG
3059.1.2   GGGCAUAAGGUAUUUAAUUCCAUAGGGCGCAAUCCAAUC..........................GGAUCAAAUUAAUGCU.CACUGUG.CCCGAACUGACUCAAGAGCACGAACGUCAACCACCCGGAACCUUGAUUCGGAUGCUCCGGUAGCUCAACCUG
3788.1.4   GGGCAUAAGGUAUUUAAUUCCAUAGAGCACACCUCACUGGAGAUCGCU.................UGUGGAUCAAAUUGAUGCC.GUUUGCC.UAGAUUGUCCCGUUCAGUGAUCGGUAAACCUUGAUUCGGAUGCUCCGGUAGCUCAACCUG
3311.1.3   GGGCAUAAGGUAUUUAAUUCCAUACCUAGAGACGAAAGCGAUAAUCGGGCCUGGA..........GGAUCAAAUUAAUGCU.GGCGCCA.GGAGCAACGCAUCUAUGCACCUUAGGUGUAUUCGGAUGCUCCGGUAGCUCAACCUG
4946.1.2   GGGCAUAAGGUAUUUAAUUCCAUACACACAAAGGUCAGGCUGAGUUGGAGAACCUCACCCUAAUCGUAAACUGGAUCAAAUUAAUGCU.GAUUACG.CCACCACAUUUGAUUCGGAUGCUCCGGUAGCUCAACCUG
```

Supplemental Figure S4B

151 UCAA sequences identified within the entire 80HRT$_{14}$ population based on a consensus motif (CM) derived only from the 80N random region.

```
Cons. SS   ...........................................<<.<<<.<<<<<.<.....................................>.>>>...>>.>>.>.>>.....................................
4803.1.2   ...........................GGGCAUAAGGUAU.UAA.UUC.CAUACC-UCACAAA.....................UGAUCGA-UGUUCAAAU.GG.A.UUAAC........--CUACCUC...AU-A.................ACGGAU.UU-----.GCGGUAUAGGUCUUGGUUCUCUAAUCGGUGAUCCGAUGCUCCGGUAGCUCAACCUG.........
2966.1.3   ...........................GGGCAUAAGGUAUU.UAA.UUC.CAUAC.U.CCGACCAAAGCACUGUUUUGUGGGGAAUUGUCAACCGACGUGCAGUAGCAAGAGG.GUUCAAAU.GG.A.UUAA-......AUGCAAAGU...U-GA.....................UUCGGA-..-UGCUCCGGUAGCUCAACCUG.........
2650.1.3   ...........................GGGCAUAAGGUAUU.UAA.UUC.CAUAG.U.CACGA.....................................--AACA.CUUCAAAU.GG.A.UUAAC.......AAACCUCU.....U.................UGAAC..CUGCACCCUUGCCAAGGCUAACUCAAUCUUGAGACAUGUUGAUUCGGAUGCUCCGGUAGCUCAACCUG.........
2483.1.2   ..................GGGCAUAAGGUAUUUAAUUCCAUAUCAUC.ACG.UCG.CACACUG.CUUG-.....................................--AAGC.GUUCAAGA.GC.G.CGUAC.......-AAUGAUGU..GG-CAAA..........GGUC-CUAU.CUUGUCUCUCCCUGCUUGAUUCGGAUGCUCCGGUAGCUCAACCUG.........
1791.1.5   ...........................GGGCAUAAGGUAUU.UAA.UUC.CAUAC.U.CGGA-.....................................--GACA.GUUCAAAU.GG.A.UUGG-......AGACUUAUGC..UA-CAAUG........AUAUC-----.--------AGGGUCCCGGACGCUGGUAUGGGAUUGGUCGUUGAUUCGGAUGCUCCGGUAGCUCAACCUG.........
3680.1.2   ...........................GGGCAUAAGGUAUU.UAA.UUC.CAUACAC.CAGAA.....................................--ACGG.GUUCAAAU.GG.A.UUAAA.......--CCGCGUU...C-C...............CACACAC..UUCCACGAUGGGAUCAGAGACGAAAAGAAAGAGAGUUUGAUUCGGAUGCUCCGGUAGCUCAACCUG.........
4326.1.2   ...........................GGGCAUAAGGUAUU.UAA.UUC.CAUAACA.CUGUUAC...................................UCAAACGU.UUUCAAAU.GG.A.UUAGC.......-CAUACCUC...G-.................ACUUUC..-----CUGGUCCUUAUCCCGCUGCUUGCUGCAAAACUUGAUUCGGAUGCUCCGGUAGCUCAACCUG.........
1900.1.6   ...........................GGGCAUAAGGUAUU.UAA.UUC.CAUAC.G.UUAAG.....................................--AGAC.GUUCAAAU.GG.A.UUGAA.......ACGAUGUUGG..GC-AUGAA.......GGAGUG-------.--------CCAAGAAGUGCUGACAAUAGUUGAGCUUUUGAUUCGGAUGCUCCGGUAGCUCAACCUG.........
1753.1.2   ...........................GGGCAUAAGGUAUUUAAUUCCA--UAGGACAUUCUG.UUG.UUU.ACAAC.U.CUACC.....................-GCUGG.GUUCAAUG.UA.A.CGAUA.......AGACUUUGGA..AC-AA.............ACUCCUUACUACUGCACUGUUGAUUCGGAUGCUCCGGUAGCUCAACCUG.........
3107.1.3   ..................GGGCAUAAGGUAUUUAAUUCCAUAGUCCGACCAAAAGUGGUG.CUA.UCU.CAUAC.U.CUGAAAUCCCAG.....................GUACAUUCAACAG.GUUCAAAU.GA.G.UGGUC.......AACCAGUAU..UG-AUUCGG.....AUGCUCCGGUAG.CUCAACCUG.........
2748.1.2   ...........................GGGCAUAAGGUAUU.UAA.UUC.CAUAC.G.CGUAA.....................................GGAUGCU.GUUCAAAU.GG.A.UUGAA.......ACCCGCCUA..GU-CAGAU......CGUUCC-----.--------UCCAAAAGCCCGCACUGCACUAACCUGUUUGAUUCGGAUGCUCCGGUAGCUCAACCUG.........
3623.1.2   ...........................GGGCAUAAGGUAUU.UAA.UUC.CAUACU-.GUUUU.....................................AUCGA-CGUUUAAAU.GG.A.UUAAC.......AAGCCUGUC..UU-CU.............UUG-----.--------UCUUUUAGAUUCGAUUCUCCCGUCGCCUGGAAACUUGAUUCGGAUGCUCCGGUAGCUCAACCUG.........
1679.1.9   ...........................GGGCAUAAGGUAUU.UAA.UUC.CAUACGG.CUAAA.....................................AAGCACUGUUCAAAU.GG.A.UUGAA.......ACCCAUCCC..AA-AGCU.........CCUUUCCUA-.--------CAGUGGCCAACCCUCCUCUCCCCUUGUUGAUUCGGAUGCUCCGGUAGCUCAACCUG.........
2551.1.4   ...........................GGGCAUAAGGUAUUUAAUUCCAUAGGAAA.GUA.UCU.CUAAC.U.UUACA.....................................GUGUUA.GUUCAACA.GA.G.UGCUU.......AGCCUGGAU...GA-CU.............CAUCUUAC.UCAGUCUGGAUGCAAUUGAUUCGGAUGCUCCGGUAGCUCAACCUG.........
2754.1.4   ..................GGGCAUAAGGUAUUUAAUUCCAUAGAACGGACUGGGACUCCAAU.ACG.UCU.GAUAC.U.GGGUU.....................................AGGCCU.GUUCAAAU.CA.G.CGUGC.......--ACUGGCAG.UCC-CUCUUGAG..UGUUGAUUC-----.--------GGAUGCUCCGGUAGCUCAACCUG.........
139.1.107  ...........................GGGCAUAAGGUAU.UAA.UUC.CAUAU.G.CGGCUAGAC.....................UACAUCUGCUC.AUUCAAAU.GG.A.UUGAA.......ACUUUACGU...CA-CU.............CCCUUA-.--------AACUCCUUUCCCAUCGUUACUUUGAUUCGGAUGCUCCGGUAGCUCAACCUG.........
3366.1.2   ...........................GGGCAUAAGGUAU.UAA.UUC.CAUAC.U.UCCCA.....................................-GAGGA.GUUCAAAU.GG.A.UUAG-......GUUUACAG...A-U.................UCCCCAC..UUACUACAAGAUAUGACACAGUGCUGUGUAUGGUGUUGAUUCGGAUGCUCCGGUAGCUCAACCUG.........
941.1.10   ..................GGGCAUAAGGUAUUUAAUUCCAUACCGCUGGCAAACG.GUG.UUC.CUAACUU.CUUCU.....................................UAUCAAAGUUCAACA.GG.A.CGCUA.......A--CUUCCAU..GG-ACU...........CGCCGUCACCACUUGAUUCGGAUGCUCCGGUAGCUCAACCUG.........
2653.1.6   ...........................GGGCAUAAGGUAU.UAA.UUC.CAUAC.U.CUCAC.....................................GAUGAG.GUUCAAAU.GG.C.UUAA-......AUCCCGCCUG..CA-CU.............ACCAAAC..AUCCCUUCAUCCAACGUUCAAAAGUAUUUCCUUGAUUCGGAUGCUCCGGUAGCUCAACCUG.........
842.1.21   ..GGGCAUAAGGUAUUUAAUUCCAUACGCAAGGGGAUACCACAUUAAUGAAGACACAGCUACAUCUCGCAGCCCU.GAA.UUC.AAGAC.U.CAGAG.....................-GACUG.GUUCAACU.UG.A.UUCGG.......AUGCUCCGG...U-A.................GCUCA-..----ACCUG.........
246.1.93   ...........................GGGCAUAAGGUAU.UAA.UUC.CAUAC.U.CCGACCU....................................UCAUGCGAU.GUUCAAAU.GG.A.UUGAUC....C----ACCAAG.AUG-UUC............CUU-----.--GCCUCCUCCCAUCCAACCCUCGAGGAAUUGAUUCGGAUGCUCCGGUAGCUCAACCUG.........
3075.1.2   ...........................GGGCAUAAGGUAU.UAA.UUC.CAUAC.U.CUCCACAAGUCGCAU.....................GCAAACGGCCUGGGAG.GUUCAAAU.GG.A.UUGAA.......-AGUGGAGU...CA-A.................AGGCAA.GUGCACCAAGAUGAUUGAUUCGGAUGCUCCGGUAGCUCAACCUG.........
1752.1.6   ..........GGGCAUAAGGUAUUUAAUUCCAUACCUGGACGCCGCGGCCAUUCGACAUUUCAAAAUU.ACC.UAU.CACAC.G.GUUAA.....................AAUGCU.GUUCAAGU.GA.U.GGUAA.......--AUUAUUG...AU-UCGGA.....UGCUCCGGUAG.CUCAACCUG.....................UCAACCUG.........
1025.1.10  ...........................GGGCAUAAGGUAU.UAA.UUC.CAUACG-.CGAAA.....................................-GCUC-AGUUCAAAU.GG.A.UUAAA.......AGCCUAAC...C-.................-------.--UGUAUUCUUCCUACGCCGCCUGUCUCUCUUCGCTAAACACCAUGGAGCUCCGGUAGCUCAACCUG.........
1036.1.14  ...........................GGGCAUAAGGUAU.UAA.UUC.CAUAC.G.ACAAU.....................................--GAAC.GUUCAAAU.GC.A.UUAAC.......AAGCCUUAU..CC-A.................AA----C.AAAACUGCAGUCUGGUGAGCGUGACCCAACGGUUCUCAUUGAUUCGGAUGCUCCGGUAGCUCAACCUG.........
3464.1.4   ...........................GGGCAUAAGGUAU.UAA.UUC.CAUAC.G.UCACCGUACGCUAAAAGA.................UCACUUGACCAAAAGAGGAC.GUUCAAAU.GG.A.UUAG-......ACCCGCCCC...UA-GC.............UCGCUAC.UCAACUUGAUUCGGAUGCUCCGGUAGCUCAACCUG.........
2537.1.3   ...........................GGGCAUAAGGUAU.UAA.UUC.CAUAGUG.ACACUA.....................................CGAUGUUC.CUUCAAAU.GG.A.UUGAU.......---CGUCUU...A-A.................CCAACAC..CUGUUUCAUCGAUUUUCGACGCGUAACGUUCUUGAUUCGGAUGCUCCGGUAGCUCAACCUG.........
2536.1.3   ...........................GGGCAUAAGGUAU.UAA.UUC.CAUAC.U.UGCGAACAUGACC.....................CGACCAUGAAGCUAA.GUUCAAAU.GG.A.UUAAUCU.ACUACCCAGUCU..UG-CUAU.........GCUUGU---.--------UAUCUCCUUGAUUCGGAUGCUCCGGUAGCUCAACCUG.........
4555.1.2   ...........................GGGCAUAAGGUAUUUAA-UUCC.AUAAC.U.CUGUUGAAG.................................UAUACCACAG.GUUCAAUA.UG.GC-UUA.......-CUAGCACC...CC-AUGUCA.......UGUUUUCUCAC.UUCGUUGGGCACUAUUGAUUCGGAUGCUCCGGUAGCUCAACCUG.........
2386.1.6   ...........................GGGCAUAAGGUAU.UAA.UUC.CAUAC.U.CCGUC.....................................--CACGG.GUUCAAAU.GG.U.UUAC-......ACACCUUU...CC-UC.............ACUCCCAC.GAUACACACUCCCAGCCGUUAUUCCCAGAUGUUUGAUUCGGAUGCUCCGGUAGCUCAACCUG.........
1780.1.4   ...........................GGGCAUAAGGUAU.UAA.UUC.CAUAC.U.CGUCUACCUGAUAUGA.....................GCCGGACACAGGGCGACG.GUUCAAAU.GG.A.UUAG-......GCUCUA--.----------AUUUGCUGUUGAUUCGGAUGCUCCGGUAGCUCAACCUG.........
145.1.147  ..................GGGCAUAAGGUAUUUAAUUCCAUA--CGGUACGUGGAC.GCG.UUG.CAAAC.U.CGAUU.....................................AGGAAA.GUUCAACU.GC.A.CGCU-......AUCCAAUAC...C-U.................ACGGCAC.CAUAUUCGAUUGAUUCGGAUGCUCCGGUAGCUCAACCUG.........
2214.1.3   ...........................GGGCAUAAGGUAUUUAAUUCCAUAGACGAAGACGAUCAG.GUG.UUC.CAAAG.U.ACUCUUUCU.....................UCGCGUGAUA.CUUCAACU.GG.A.CGCUC......CUCAUCUU...C-U.................ACGAAC..UUGAUUCGGAUGCUCCGGUAGCUCAACCUG.........
4077.1.2   ...........................GGGCAUAAGGUAUUUAAUUCCAUACAGCGC.CAG.UUC.GAGAC.G.CUAACCACUUUUUA.....................AGACGACUACGACCGC.GUUCAAUU.CG.A.CUGAA.......ACGAUGCUA...U-GUGUGA......UUGAUU-----.--------CGGAUGCUCCGGUAGCUCAACCUG.........
1473.1.6   ...........................GGGCAUAAGGUAU.UAA.UUC.CAUACG-.CCACUGACUGUGCAACUU.....................CACAAUCCCACAGUAGAU-AGUUCAAAU.GG.A.UUAG-......AGCCUCGAU...AG-CCC...........UGGGUGACGAAUUGAGUUCGGAUGCUCCGGUAGCUCAACCUG.........
1649.1.5   ...........................GGGCAUAAGGUAU.UAA.UUC.CAUACCG.UGACU.....................................AACGCGU.GUUCAAAU.GG.A.UUAA-......-GCCUAUCU...UA-CAG...........UCUGAUUAC..UUGUCUAUGAGACCUUGCGUUCUUGUUGUUGAUUCGGAUGCUCCGGUAGCUCAACCUG.........
4504.1.3   ..........GGGCAUAAGGUAUUUAAUUCCAUAGUAGCGGGUUUCUC.CAG.UCU.AACAC.A.CACAG.....................-CCUGU.GUUCAAGU.UA.G.CUGAU.......AAGAGCCC.....A.................CGAAG..AUCGAUUGGUGUUGAUUCGGAUGCUCCGGUAGCUCAACCUG.........
1011.1.10  ...........................GGGCAUAAGGUAU.UAA.UUC.CAUAC.C.AGUGACAC.....................GGAAGGUAUGAUUGAUCGAUCGCUCGCGCG
```



Supplemental Figure S4C

14 UCAA sequences identified within 70HRT$_{240s}$ population. First three include the 16nt conserved element for pairing with 5' constant region

```
Cons. SS                                                  <<.<<<....<<<<.<<<<....<<<<<<<.....................>>>>>>>.>>>>>.>>>>>>>>>
445.1.26   GGGAAAAGCGAAUCAUACACAAGA.........AGGCCCGACCAAGCACAAAAAG.GGAUCAAAUUAAUGCU.CACUGUGUCCUAAUGCACCUGAGGAGCGACCGGGCAUAAGGUAUUUAAUUCCAUA
2890.1.2   GGGAAAAGCGAAUCAUACACAAGA...CGUUGAGUAACCAUGAGUGCAAAGCGAU.GGAUCAAAUUAAUGCU.CACUGUGCC..GA.................GGGCAUAAGGUAUUUAAUUCCAUA
4464.1.1   GGGAAAAGCGAAUCAUACACAAGAAAGGAAGAAGCACCACGGACGCAUGCUGAAU.GGAUCAAAUUAAUGCU.AAUGUGCCAGAUGA...CGA.......GUCUGGGCAUAAGGUAUUUAAUUCCAUA

Cons_SS    ...............................<<<-<<<<<<<.<.......................................>.>>----->>>>>>>>>
```