**a Summary of ClustalO alignment between zebrafish *ppl*-10 enhancers and PPL-8.3**

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Sequence Two (pairwise), or Sequence Three (3-way)** | **Length (bp)** | **# of identical positions in alignment (\*)** | **# of null characters inserted (-)** | **% identity of human 400 bp** | **% identity, normalized by insertions** | **5-mers** | **6-mers** | **7-mers** | **8-mers** | **9-mers** | **10-mers** | **11-mers** |
| Mouse plus strand (+) | 409 | 231 | 57 | 57.8% | 50.5% | 10 | 0 | 2 | 2 | 2 | 2 | 1 |
| Mouse minus strand (-) | 409 | 159 | 117 | 39.8% | 30.8% | 2 | 2 | 1 | 0 | 1 | 0 | 0 |
| Mouse reverse sequence | 409 | 167 | 85 | 41.8% | 34.4% | 2 | 0 | 0 | 0 | 0 | 0 | 0 |
| Mouse scrambled sequence 1 | 409 | 157 | 71 | 39.3% | 33.3% | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| Mouse scrambled sequence 2 | 409 | 163 | 81 | 40.8% | 33.9% | 3 | 1 | 0 | 0 | 0 | 0 | 0 |
| Mouse scrambled sequence 3 | 409 | 160 | 59 | 40.0% | 34.9% | 1 | 1 | 0 | 0 | 0 | 0 | 0 |
| Zebrafish plus strand (+) | 467 | 181 | 73 | 45.3% | 38.3% | 5 | 0 | 0 | 0 | 0 | 0 | 0 |
| Zebrafish minus strand (-) | 467 | 158 | 107 | 39.5% | 31.2% | 2 | 0 | 0 | 0 | 0 | 0 | 0 |
| Zebrafish reverse sequence | 467 | 168 | 107 | 42.0% | 33.1% | 2 | 0 | 1 | 0 | 0 | 0 | 0 |
| Zebrafish scrambled sequence 1 | 467 | 168 | 95 | 42.0% | 33.9% | 4 | 1 | 0 | 0 | 0 | 0 | 0 |
| Zebrafish scrambled sequence 2 | 467 | 166 | 135 | 41.5% | 31.0% | 2 | 1 | 0 | 0 | 0 | 0 | 0 |
| Zebrafish scrambled sequence 3 | 467 | 174 | 73 | 43.5% | 36.8% | 1 | 2 | 1 | 0 | 0 | 0 | 0 |
| 3-way w/ zf plus strand (+) | 467 | 96 | 158 | 24.0% | 17.2% | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 3-way w/ zf minus strand (-) | 467 | 97 | 227 | 24.3% | 15.5% | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 3-way w/ zf reverse sequence | 467 | 99 | 248 | 24.8% | 15.3% | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 3-way w/ zf scrambled sequence 1 | 467 | 110 | 170 | 27.5% | 19.3% | 1 | 1 | 0 | 0 | 0 | 0 | 0 |
| 3-way w/ zf scrambled sequence 2 | 467 | 86 | 216 | 21.5% | 14.0% | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 3-way w/ zf scrambled sequence 3 | 467 | 90 | 140 | 22.5% | 16.7% | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

**b Details for ClustalO alignment between zebrafish *ppl*-10 enhancers and PPL-8.3**

**Alignment #1.** Shown below is the pair-wise alignment of the core human *periplakin* (*ppl*) enhancer conserved in mammals (400 bp) aligned to the homologous 409 bp block in mouse. These sequences correspond to the plus strand (+) sequences located upstream of *ppl*, which is transcribed to the left in each genome. Alignment #1 serves as a positive control for the described enhancer homology tests.

**9-mer (a)**

Hu\_400+ TTCTGACACAACCTGCTACACAT----CTTGGATCCCACTTGTCAAGCCTGGCCCTA**GGC** 56

Mm\_409+ CTATCCCACAGACTGGTGACCCTGGAGCTCAGACACTCCACTGGAGAGCTATCCCTG**GGC** 60

\* \* \*\*\*\* \*\*\* \* \* \* \*\* \*\* \* \* \* \*\* \*\*\*\* **\*\*\***

**10-mer (b) 10-mer (c)**

Hu\_400+ **CTCTCA**GG------GGTGGGTACATCAAGTG**AGGAAGTCAC**ACTG**TCAGGGCAGA**AAGAG 110

Mm\_409+ **CTCTCA**AATTCACCATGAGAGCTTCTCTGCA**AGGAAGTCAC**CCCA**TCAGGGCAGA**--GTG 118

**\*\*\*\*\*\*** \* \* **\*\*\*\*\*\*\*\*\*\*** \* **\*\*\*\*\*\*\*\*\*\*** \* \*

**8-mer (d) 9-mer (e)** (f) (g) **7-mer (h)**

Hu\_400+ GGGCTG**GGTGGGGC**CGG**ACAGGCTCT**GC-TGGCTCAGG**ATCCC**G**GCAGG**ACAGG**CTGCCC** 169

Mm\_409+ GTTCTA**GGTGGGGC**TAA**ACAGGCTCT**ACCAGGCACAGT**ATCCC**T**GCAGG**GCAGA**CTGCCC** 178

\* \*\* **\*\*\*\*\*\*\*\*** **\*\*\*\*\*\*\*\*\*** \* \*\*\* \*\*\* **\*\*\*\*\*** **\*\*\*\*\*** \*\*\* **\*\*\*\*\*\***

(i) (j)

Hu\_400+ **A**ACCCAGCCCCAAAACTCCCATCTTCTGTCCAACGCCCAAG**CCTGC**TTCCTC**CCTGC**CCC 229

Mm\_409+ **A**GCCTCCTGTTCACG--------------CCCATGCTTTTT**CCTGC**CTGCTG**CCTGC**TCC 224

**\*** \*\* \* \*\* \* \*\* **\*\*\*\*\*** \* \*\* **\*\*\*\*\*** \*\*

(k) **(l) (m)**

Hu\_400+ ---------------ACCTCACCTCACACTGCC**CAGAC**TGGTGGGGCT**GCATT**T**TTGGG**G 274

Mm\_409+ TCCCCTTCTGGGCCGTGCCAGGCTCATGCAGAG**CAGAC**CAGTACAGCC**GCATT**C**TTGGG**C 284

\* \*\*\*\* \* \* **\*\*\*\*\*** \*\* \*\* **\*\*\*\*\*** **\*\*\*\*\***

**7-mer (n)** **8-mer(o) 11-mer (p)**

Hu\_400+ C-CGGTGCCA**GGTGTGA**TGGA-----GGACAGCC**CAGGTCAG**G**AGGTCAGGGCC**CCGTTT 328

Mm\_409+ AAGTGTCTCT**GGTGTGA**ATGACCCTGGGGCTGGT**CAGGTCAG**A**AGGTCAGGGCC**TTGTTC 344

\*\* \* **\*\*\*\*\*\*\*** \*\* \*\* \* \* **\*\*\*\*\*\*\*\*** **\*\*\*\*\*\*\*\*\*\*\*** \*\*\*

(q) (r)

Hu\_400+ **CCTCC**CAAGCCAGGATGACTCAGTGATGGACAGACTAGGCCACAAGGGG-CC**GAACA**CAA 387

Mm\_409+ **CCTCC**AGTGCCCAAGTGATA--------GATGAGTCAGGCTACAAAGGGGCA**GAACA**AGA 396

**\*\*\*\*\*** \*\*\* \*\*\* \*\* \*\*\*\* \*\*\*\* \*\*\* \* **\*\*\*\*\*** \*

(s)

Hu\_400+ AG**CCAAA**TTAGGG 400

Mm\_409+ AA**CCAAA**CCGAGT 409

\* **\*\*\*\*\*** \*

**Alignment #2.** Shown below is the pair-wise alignment of the core human *ppl* enhancer (Hu\_400+) aligned to the reverse complement of the homologous 409 bp block in mouse (Mm\_409-).

Hu\_400+ ------------------**TTCTG**ACACAACCTGCTACACATCTTGGATCCCACTTGTCA- 41

Mm\_409- ACTCGGTTTGGTTTCTTG**TTCTG**CCCCTTTGTAGCCTGACTCATCTATCACTTGGGCACT 60

**\*\*\*\*\*** \* \* \* \*\* \* \*\*\* \* \*

Hu\_400+ ------AGCCT**GGCCCT**AGGCCTCTCAGGGGTGGGTACATCAAGTGAGGAAGTCACACTG 95

Mm\_409- GGAGGGAACAA**GGCCCT**GACCTTCTGACCTG----------ACCAGCCCCAGGGTCATTC 110

\* \* **\*\*\*\*\*\*** \* \*\*\* \* \* \* \* \*\* \*\* \*

**7-mer**

Hu\_400+ TCAGGGCAGAAAGAGGGGCTGGGTGGGGCCGG-----ACAG**GCTCTGC**TGGCTCAGGATC 150

Mm\_409- ACACCAGAGACACTTGCCCAAGAATGCGGCTGTACTGGTCT**GCTCTGC**ATGAGCCTGGCA 170

\*\* \*\*\* \* \* \* \* \* \* \* \* **\*\*\*\*\*\*\*** \* \* \*

Hu\_400+ CCGGCAGGACAGGCTGCC----CAACCCAGCCCCAAAACTC----------------CCA 190

Mm\_409- CGGCCCAGAAGGGGAGGAGCAGGCAGCAGGCAGGAAAAAGCATGGGCGTGAACAGGAGGC 230

\* \* \* \*\* \*\* \* \* \* \*\* \*\*\*\* \*

**9-mer**

Hu\_400+ TCTTCTGTCCAACGCCC---------AA**GCCTG**CT----TCCTCCCT**GCCCCACCT**CACC 237

Mm\_409- TGGGCAGTCTGCCCTGCAGGGATACTGT**GCCTG**GTAGAGCCTGTTTA**GCCCCACCT**AGAA 290

\* \* \*\*\* \* \* **\*\*\*\*\*** \* \* **\*\*\*\*\*\*\*\*\***

Hu\_400+ TCACA**CTGCCC**AGACTGGTGGGGCTGCATTTTTGGGGCCGGTGCCAGGTGTGATGGAGGA 297

Mm\_409- CCACT**CTGCCC**TGATGGGGTG-ACTTCCTTGCAGAGAA--------GCTCTCATGGTGAA 341

\*\*\* **\*\*\*\*\*\*** \*\* \*\* \* \*\* \* \*\* \* \* \* \* \* \*\*\*\* \* \*

Hu\_400+ CAGCCCAGGTCAGGAGGTCAGGGCCCCGTTTCCTCCCAAGCCAGGATGACTCAGTGATGG 357

Mm\_409- TTTGAGAGGCCCA-----------------------------GGGATAGCTCTCCAGTGG 372

\*\*\* \* \*\*\*\* \*\*\* \*\*\*

Hu\_400+ ACAGACTAGGCCACAAGGGGCCGAACACAAAGCCAAATTAGGG 400

Mm\_409- AGTGTCTGAGCTCCAGGGTCACCAGTCTGTGG-GATAG----- 409

\* \* \*\* \*\* \*\* \*\* \* \* \* \* \*

**Alignment #3.** Shown below is the pair-wise alignment of the core human *ppl* enhancer (Hu\_400+) aligned to the reverse sequence of the homologous 409 bp block in mouse (Mm\_409R). This alignment constitutes a negative control as the reverse sequence is a non-biological sequence.

Hu\_400+ TTCTGACACAACCTGCTACACATCTTGGATCCCACTTGTCAAGCCTGGCCCTAGGCCTCT 60

Mm\_409R ---TGAGCCAAACC----------AAAGAACAAGACGGGGAAACATCG------------ 35

\*\*\* \*\*\* \* \*\* \* \* \*\* \* \* \*

Hu\_400+ CAGGGGTGGGTACATCAA---GTGAGGAAGTCACAC-TGTCAGGGCAGAAAGAG-GGGCT 115

Mm\_409R ---GACTGAGTAGATAGTGAACCCGTGACCTCCCTTGTTCCGGGACTGGAAGACTGGACT 92

\* \*\* \*\*\* \*\* \*\* \*\* \* \* \* \*\* \* \* \*\*\*\* \*\* \*\*

Hu\_400+ GGGTGGGGCCGGACAGGCTCTGCTGGCTCAGGA--TCCCGGCAGGACAGGCTGCCCAACC 173

Mm\_409R GGTCGGGGTCCCAGTAAGTGTGGTCTCTGTGAACGGGTTCTTACGCCGACATGACCAGAC 152

\*\* \*\*\*\* \* \* \* \*\* \* \*\* \* \* \* \* \* \*\* \*\*\* \*

Hu\_400+ CAGCCCC-----AAAACTCCCA-----TCTTCTGTCCAACGCCCAAGCCTGCTTCCTCCC 223

Mm\_409R GAGACGTACTCGGACCGTGCCGGGTCTTCCCCTCCTCGTCCGTCGTCCGTCCTTTTTCGT 212

\*\* \* \* \* \*\* \*\* \*\* \* \* \* \* \* \*\*\* \*\*

Hu\_400+ TGCCCCACCTCACCTCACACTGCC**CAGAC**TGGTG---------GGGCTGCATTTTTGGG- 273

Mm\_409R ACCCGCACTTGTCCTCCGACCCGT**CAGAC**GGGACGTCCCTATGACACGGACCATCTCGGA 272

\*\* \*\*\* \* \*\*\*\* \*\* **\*\*\*\*\*** \*\* \* \* \* \* \*\*

Hu\_400+ --------GCCGGTGCCAGGTGTGATGGAGGACAGCCCAGGTCAGGAGGTCAGGGCCCCG 325

Mm\_409R CAAATCGGGGTGGATCTTGGTGAGACGGGACTACCCCACTGAAGGAACGTCTCTTCGAGA 332

\* \*\* \* \*\*\*\* \*\* \*\* \*\* \* \* \* \*\*\* \*

Hu\_400+ TTTCCTCCCAAGC---CAGGATGACTCAGTGAT-------GG**ACAGA**--CTAGGCCACAA 373

Mm\_409R GTACCACTTAAACTCTCCGGGTCCCTATCGAGAGGTCACCTC**ACAGA**CTCGAGGTCCCAG 392

\* \*\* \* \*\* \* \* \*\* \* \*\* **\*\*\*\*\*** \* \*\*\* \* \*\*

Hu\_400+ GGGGCCGAACACAAAGCCAAATTAGGG 400

Mm\_409R TGGTCAGACACCCTAT---------C- 409

\*\* \* \*\* \* \*

**Alignments #’s 4, 5, and 6.** Shown below are three pair-wise alignments of the core human *ppl* enhancer (Hu\_400+) aligned to one of three (S1, S2, and S3) different Fisher-Yates shuffled sequences of the homologous 409 bp plus-strand block in mouse (Mm\_409+S1/S2/S3). These pair-wise alignments serve as negative controls.

Alignment #4

Hu\_400+ TTCTGACACAACCTGCTACACAT**CTTGG**ATCCCACTTGTCAAGCCTGGCCCTAGGCCTCT 60

Mm\_409+S1 --------AGAGCTC------CG**CTTGG**---CCTGTGCTCAAATG------------AAG 31

\* \*\* **\*\*\*\*\*** \*\* \* \*\*\*\*

Hu\_400+ CAGGGGTGGGTACATCAAGTGAGGAAGTCACAC--TGTCAGGGCAGAAAGAGGGGCTGGG 118

Mm\_409+S1 CAGAGACCGGCCAAGCACAAGGGGCGTTTACAACTTGCTGCGGGAAGTAGAGCTTCTGAG 91

\*\*\* \* \*\* \* \*\* \* \*\* \* \*\*\* \*\* \*\* \* \*\*\*\* \*\*\* \*

Hu\_400+ TGGGGCCGGACAGG---CTCTGCTGGCTCAGGATCCCGGCAGGACAGGCTGCCCAACCCA 175

Mm\_409+S1 ACCGACCGGCCGGCACACCCTACTTGGCTTGAACCACCAATTTGTGGTGCACATGATCCT 151

\* \*\*\*\* \* \* \* \*\* \*\* \* \* \* \* \* \* \* \* \*\*

Hu\_400+ GCCCCAAAACTCCCATCTTCTGTCCAACGCCCAAGCCTGCTTCCTCCCTGCCCCACCT-- 233

Mm\_409+S1 TCCGGACCGCACCAACGATTTGACGGAGTCCGCCTGCAGATTGGGGCCGAGCTGTTTTGG 211

\*\* \* \* \*\* \* \* \*\* \* \* \*\* \* \* \*\* \*\* \* \*

Hu\_400+ ----CACCTCACACTGCCCAGACTGG---------TGGGGCTGCATTTTTGGGGCCGGTG 280

Mm\_409+S1 AACCGGAGTATAAGTCCTCTGTGTCTTCGTCTCTCAGTGGTTTCGTTATGT--CCCTCCG 269

\* \* \* \* \* \* \* \* \*\* \* \* \*\* \* \*\* \*

Hu\_400+ CCAGGTGTGATGGAGGACAGCCC-------AGGTCAGGAGG---TCAGGGCCCCGTTTCC 330

Mm\_409+S1 CCTCACGGGATCAATGGCACCGCATCCCCAAGCACGGGTGCGAAGACAGGCAGAGATTCT 329

\*\* \* \*\*\* \* \* \*\* \* \* \*\* \* \*\* \* \*\*\* \* \*\*\*

Hu\_400+ TCCCAAGCCAGGATGACTCAGTGATGGACAGACTAGGCCACAAGGGGCCGAACACAAAGC 390

Mm\_409+S1 GGCCACGTCAATACTCCCCGTAACTCCACAGTACAGCGCTAATAGTGGGTAGTCCGCCCT 389

\*\*\* \* \*\* \* \* \* \* \*\*\*\* \*\* \* \* \* \* \* \*

Hu\_400+ CAAATTAGGG---------- 400

Mm\_409+S1 ATACGGAGAGCCGCCCACCC 409

\* \*\* \*

Alignment #5

Hu\_400+ ---TTCTGACACAACCTGCTACACATCT----------TGGATCCCACTTGTCAAGCCTG 47

Mm\_409+S2 TAAACGAGGAGCTACCTCATACCGACCTAAGGGAGAATCGTCCCGCACCTGTAACCACA- 59

\* \* \*\*\*\* \*\*\* \* \*\* \* \* \*\*\* \*\*\* \* \*

Hu\_400+ GCCCTAGGCCTCTCAGGGGTGGGTACATCAAGTGAGGAAGTCACACTGTCAGGGCAGA-- 105

Mm\_409+S2 ------TTCCTGATCGGTCTAGGGTCATTTCCTTCGTAGTCCTAACCACCACACCCGATT 113

\*\*\* \*\* \* \*\* \*\*\* \* \* \* \* \*\* \*\* \* \*\*

Hu\_400+ ---------------AAGAGGGGCTGGGTGGGGCCGGACAGGCTCT**GCTGG**CTCAGGATC 150

Mm\_409+S2 GAAGACTGGCTCCCAACCGGGAGTTGGGCATGCCACG---GCCCTC**GCTGG**GCCTCCCTC 170

\* \*\* \* \*\*\*\* \* \* \* \* \* **\*\*\*\*\*** \* \*\*

Hu\_400+ CCGGCAGGACAGGCTGCCCAACCCAGCCCCAA-AACTCCCATCTTCTGTCCAACGCCCAA 209

Mm\_409+S2 CTGTGCGCCCGGAATTTGGAGTACGCCCACGGTACCACCCGGACGCGCTAGACAGGTAAG 230

\* \* \* \* \* \* \* \* \*\* \* \* \* \*\*\* \* \* \* \* \*

Hu\_400+ GCCTGCTTCCTCCCTGCC**CCACC**TCACCTCACACTGCCCAGACTGGTGGGGCTGCATTTT 269

Mm\_409+S2 GGATCCATTGAGTCCGGG**CCACC**GTGATGATTACTGGGCAGGAAACTCGGAGCGCAAGGG 290

\* \* \* \* \* \* **\*\*\*\*\*** \*\*\*\* \*\*\* \* \*\* \*\*\*

Hu\_400+ T--GGGGCCGGTGCCAGGTGTGATGGAGGACAGCCCAGGTCAGGAG**GTCAG**GGCCCCGTT 327

Mm\_409+S2 TGCGAAGCAGTTAACTGGTTTCT-----------------------**GTCAG**TAC--C-AT 324

\* \* \*\* \* \* \* \*\*\* \* **\*\*\*\*\*** \* \* \*

Hu\_400+ TCCTC**CCAAGC**-CAGGATGACTCAGTGATGGACAGACTAGGCCACAAGGGGCCGAACACA 386

Mm\_409+S2 TGTTG**CCAAGC**CAACTGTTACGCCTTGTGTGTGAGTCACCAGGGCATGTGCCAACTCAAT 384

\* \* **\*\*\*\*\*\*** \* \* \*\* \* \*\* \* \*\* \* \*\* \* \* \* \*\*

Hu\_400+ AAGCCAAATTAGGG----------- 400

Mm\_409+S2 TAGCCGCAGTCGCGCCTCGAGCTAC 409

\*\*\*\* \* \* \* \*

Alignment #6

Hu\_400+ TTCTGACACAACCTGCTACACATCTTGGATCCC--ACTTGTCAAGCCTGGCCCTAGGCCT 58

Mm\_409+S3 -------TAGTCACGCGTAGCTTATTGGGTAACCTGCCTACACAGTACGAGCGTAGTAAA 53

\* \*\* \* \* \*\*\*\* \* \* \* \* \*\* \* \* \*\*\*

Hu\_400+ CTCAGGGGTGGGTACATCAAGTGAGGAAGTCACACTGTCAGGGCAGAA----AGAG-GGG 113

Mm\_409+S3 AATGCGGGGGGCTGA-ATACGTACCTCATTGCACCTCCGAGGCGCATGCGCGAGCGTCCC 112

\*\*\* \*\* \* \* \*\* \* \* \*\* \*\*\* \*\* \*

Hu\_400+ CTGGGTGGGGCCGGACAGGCTCTGCTGGCTCAGGATCCCGGCAGGACAGGCTGCCC**AACC** 173

Mm\_409+S3 CCGGGGGGTGCCGAACGGCATGCCATGCACCAT------TCACGTGGACACTTCCA**AACC** 166

\* \*\*\* \*\* \*\*\*\* \*\* \* \* \*\* \*\* \* \* \*\* \*\* **\*\*\*\***

Hu\_400+ **C**AGCCCCAAAACTCCCATCTTCTGTCCAACGCCCAAGC----CTGCTTCCTCCCTGCCCC 229

Mm\_409+S3 **C**CG-GACTGGTATCCAATCACCGCTAGATAGCTCGGGGCGGCACGGATTCGATCTTCGCC 225

**\*** \* \* \*\*\* \*\*\* \* \* \* \*\* \* \* \* \* \* \*\* \* \*\*

Hu\_400+ ACCTCACCTCACACTGCCCAGACTGGTGGGGCTGCATTTTTGGGGCCGGTGCCA**GGTGTG** 289

Mm\_409+S3 GTGTCGCAAGGCCG----------AGTCGATGCTCGGGTATCACACCTAAGACT**GGTGTG** 275

\*\* \* \* \*\* \* \* \* \* \*\* \* \* **\*\*\*\*\*\***

Hu\_400+ ATGGAGGACAGCCCAGGTCAG-------------GAGGTCAGGGCCCCGTTTCCTCCC-A 335

Mm\_409+S3 CAGTAATACAACGGTCGTGCGCAGACCCTTTAAACGGTTCGCTGCCACGCTTCGGTTCGG 335

\* \* \*\*\* \* \*\* \* \* \*\* \*\*\* \*\* \*\*\* \*

Hu\_400+ AGCCAGGATG----ACTCAGTGATGGACAGACTAGGCCACAAGGGGC--CGAACACAAAG 389

Mm\_409+S3 GTACAGAATCGAGCTCTCTTCTCTCGCCAGCCGCAAATATCACCCGCGTCACACGTTTTA 395

\*\*\* \*\* \*\*\* \* \* \*\*\* \* \* \* \*\* \* \*\*

Hu\_400+ CCAAATTAGGG--- 400

Mm\_409+S3 CCAGATTGACGCAC 409

\*\*\* \*\*\* \*

**Alignment #7.** Shown below is the pair-wise alignment of the core human *ppl* enhancer (Hu\_400+) aligned to the 467 bp enhancer block from zebrafish (Zf\_467+). The 467 bp zebrafish sequence corresponds to the enhancer fragment with the highest similarity to the core of the human enhancer. These sequences correspond to the plus strand (+) sequences located upstream of *ppl*, which is transcribed to the left in each genome.

Hu\_400+ TTCTGACACAACCTGCTACACATCTTGGAT-------C**CCACT**-TGTCAAGCCTGGCCCT 52

Zf\_467+ ATCTCATTCAAAGAATGTCAAGCACTGTAGTCACCGTG**CCACT**AAATGAACCATGGCACT 60

\*\*\* \* \*\*\* \*\* \*\* \* **\*\*\*\*\*** \* \*\* \* \*\*\*\* \*\*

Hu\_400+ AG-GCCTCTCAGGGGTGGGTACATCAAGTGAGGAAGTCACACTGTCAGGGCAGAAAGAG- 110

Zf\_467+ AAACCCTATGAAGTGATTGTTTTCTTTGTCAGGCAGTATCACTTACTCTAAAACCTGAGT 120

\* \*\*\* \* \* \* \* \*\* \*\* \*\*\* \*\*\* \*\*\*\* \* \* \*\*\*

Hu\_400+ -GGGCTGGGTGGGGC------------CGGACA-GGC**TCTGC**TGGCTCAGGATCCCGGCA 156

Zf\_467+ GAGGCACATTTGCAACATTCTTATTAAATGCCAGTCT**TCTGC**GACCTGTGACACACTTCA 180

\*\*\* \* \* \* \*\* **\*\*\*\*\*** \*\* \* \* \* \*\*

Hu\_400+ GGACAGGCTGCCCAACCC----AGCCCCAAAACTCCCATCTTCTGTCCAACGCCCAAGCC 212

Zf\_467+ ATACTGAGTGTGTAAGATGGGATGGTGTAGGCCTACTAGCTGATGTCTCAC---TAAATC 237

\*\* \* \*\* \*\* \* \* \*\* \* \* \*\* \*\*\*\* \*\* \*\* \*

Hu\_400+ TGCTTCCTCCCTGCCCCACCTCACCTCACACTGCCCAGA-----CTG**GTGGG**GCTGCATT 267

Zf\_467+ TGTCAGATTAGTGCAGAACTGTTCCGTTCCATGCCTGGAAGTTTGTA**GTGGG**CCTGAAGA 297

\*\* \* \*\*\* \*\* \*\* \* \*\*\*\* \*\* \* **\*\*\*\*\*** \*\*\* \*

Hu\_400+ TT--TGGGGCCGGTGC**CAGGT**GT----GATGGAGGACAGCCCAGGTCAGGAGG------- 314

Zf\_467+ CCTTGATTTGCTTTGT**CAGGT**ATGTTTAATTAAGGTTAGCGCTAAACTCTACATGACAAT 357

\* \*\* **\*\*\*\*\*** \* \*\* \*\*\* \*\*\* \* \* \*

Hu\_400+ ---------------TCAGGGCCCCGTTTCCTCCCAAGCCAGGATGACTCAGTGATGGAC 359

Zf\_467+ GGTCCTCCAGGAACAGAAAGTTCACCTTCAATAGACAGCAATGCATGTTTACTTTTCTGC 417

\* \* \* \* \*\* \* \*\*\* \* \* \* \* \* \* \*

Hu\_400+ AGACTAGGC--------CACA**AGGGG**CCGAACACAAAGCCA-AATTAGGG 400

Zf\_467+ AAAGTACCAAACCTCACCGCT**AGGGG**GAGTCGAATAGTTTTGACTGAGGC 467

\* \* \*\* \* \* **\*\*\*\*\*** \* \* \* \* \* \*\*\*

**Alignment #8.** Shown below is the pair-wise alignment of the core human *ppl* enhancer (Hu\_400+) aligned to the reverse complement of the 467 bp block from zebrafish (Zf\_409-) used in Alignment #7.

Hu\_400+ --TTCTGAC----ACAACCTGC------TACACATCTTGGATCCCACTTGTCAAGCCTGG 48

Zf\_467- GCCTCAGTCAAAACTATTCGACTCCCCCTAGCGGTGAGGTTTGGTACTTTGCAGAAAAGT 60

\*\* \* \* \* \* \* \*\* \* \* \* \*\*\*\* \*\* \*

Hu\_400+ CCCTAGGCCT----CTCA--GGGGTGGGTACATC-AAGTGAGGAAGTCACAC**TGTCA**GGG 101

Zf\_467- AAACATGCATTGCTGTCTATTGAAGGTGAACTTTCTGTTCCTGGAGGACCAT**TGTCA**TGT 120

\* \*\* \* \*\* \* \* \* \*\* \* \* \* \*\* \*\* **\*\*\*\*\*** \*

Hu\_400+ CAG------------------AAAGAGGGGCTGGGTGGGGCCGGACAGGCTCTGCTGGCT 143

Zf\_467- AGAGTTTAGCGCTAACCTTAATTAAACATACCTGACAAAGCAAATCAAGGTCTTCAGGCC 180

\* \* \* \* \*\* \*\* \* \*\*\* \* \*\*\*

Hu\_400+ CAGGATCC-CGGCAGGACAGGCTGCCCAACCCA--GCCCCAAAACTCCCATCTTCTGTCC 200

Zf\_467- CACTACAAACTTCCAGGCATGGAACGGAACAGTTCTGCACTAATCTGACAGATTTAGTGA 240

\*\* \* \* \* \* \*\* \* \* \*\*\* \* \* \*\* \*\* \*\* \*\* \*\*

Hu\_400+ AACGCCCAAGCCTGCTTCCTCCCTGCCCCACCTCACCTCACACTGCCCAGACTGGTGGGG 260

Zf\_467- GACATCAGCTAG-----TAGGCCTACACCATCCCATCTTACACACTCAGTATTGAAGTGT 295

\*\* \* \*\*\* \* \*\*\* \* \*\* \*\* \*\*\*\* \* \* \*\* \* \*

Hu\_400+ CTGCATTTT--------TGGGGCCGGTGCCAGGTGTGATGGAGGACAGCCCAGG**TCAGG**A 312

Zf\_467- GTCACAGGTCGCAGAAGACTGGCATTTAATAAGAATGTTGCAAATGTGCCTCAC**TCAGG**T 355

\* \* \*\*\* \* \* \* \*\* \*\* \* \*\*\* **\*\*\*\*\***

Hu\_400+ GGTCAGGGCCCCGTTTCCTCCCAAGCCAGGATGACTCAGTGATGGACAGACTAGGCCACA 372

Zf\_467- TTT--------------AGAGTAAGTGATACTGCCTGACAAAGAAAACAATCACTTCATA 401

\* \*\*\* \* \*\* \*\* \* \* \* \* \* \*\* \*

Hu\_400+ AGGGGCCGAACACAAAGCCAAATTAGGG-------------------------------- 400

Zf\_467- GG-GTTTAGTGCCATGGTTCATTTAGTGGCACGGTGACTACAGTGCTTGACATTCTTTGA 460

\* \* \*\* \* \* \*\*\*\* \*

Hu\_400+ ------- 400

Zf\_467- ATGAGAT 467

**Alignment #9.** Shown below is the pair-wise alignment of the core human *ppl* enhancer (Hu\_400+) aligned to the reverse sequence of the 467 bp enhancer block from zebrafish (Zf\_467R). This alignment constitutes a negative control as the reverse sequence is a non-biological sequence.

Hu\_400+ ---------TTCTGA-----------------------CACAACCTGCTACACATCT--- 25

Zf\_467R CGGAGTCAGTTTTGATAAGCTGAGGGGGATCGCCACTCCAAACCATGAAACGTCTTTTCA 60

\*\* \*\*\* \*\* \* \* \*\* \*\* \* \*

**7-mer**

Hu\_400+ ------------------TGGATC**CCACTTG**TCAAGCCTGGCCCTAGGCCTCTCAGGGGT 67

Zf\_467R TTTGTACGTAACGACAGATAACTT**CCACTTG**AAAGACAAGGACCTCCTGGTAACAGTACA 120

\* \* **\*\*\*\*\*\*\*** \* \* \*\* \*\*\* \* \*\*\*

Hu\_400+ GGGTACATCAAGTGAGGAAGTC---------------ACACTGTCAGGG**CAGAA**AGAGGG 112

Zf\_467R TCTCAAATCGCGATTGGAATTAATTTGTATGGACTGTTTCGTTTAGTTC**CAGAA**GTCCGG 180

\* \*\*\* \* \*\*\*\* \* \* \* **\*\*\*\*\*** \*\*

Hu\_400+ GCTGGGTGGGGCCGGACAGGCTCTGCTGGCTCAGGATCCCGGCAGGACAGGCTGCCCAAC 172

Zf\_467R GTGATGTTTGAAGGTCCGTACCTTGCCTTGTCAAGAC-----GTGATTAGACTGTCTAAA 235

\* \*\* \* \* \* \* \*\*\* \*\*\* \*\* \* \*\* \*\*\* \* \*\*

Hu\_400+ CCAGCCCCAAAACTCCCATCTTCTGTCCAACGCCCAAGCCTGCTTCCTCCCTGCC--CCA 230

Zf\_467R TCACTCTGT----------AGTCGATCATCCGGATGTGGTAGGGTAGAATGTGTGAGTCA 285

\*\* \* \*\* \*\* \*\* \* \* \* \*\* \*\*

Hu\_400+ CCTCACCTCACACTGCCCAGACTG--GTGGGGCTGCATTTTT---GGGGCCGGTGCCAGG 285

Zf\_467R TAACTTCACACAGTGTCCAGCGTCTTCTGACCGTAAATTATTCTTACAACGTTTACACGG 345

\* \* \*\*\*\* \*\* \*\*\*\* \* \*\* \* \*\*\* \*\* \* \* \* \*\*

Hu\_400+ TGTGATGGAGGACAGCCCAGGTCAGGAGGTCAGGGCCCCGTTTCC-TCCCAAGCCAGGAT 344

Zf\_467R AGTGAGTCCAAAA--TCTCATTCACTA--TGACGGACTGTTTCTTTTGTTAGTGAAGTAT 401

\*\*\*\* \* \* \*\*\* \* \* \* \*\* \* \*\* \* \* \*\* \*\*

Hu\_400+ GACTCAGTGATGGACAGACTAGGCCACAAGGG---------GC**CGAAC**ACAAAGCCAAAT 395

Zf\_467R CCCAAATCACGGTACCAAGTAAATCACCGTGCCACTGATGTCA**CGAAC**TGTAAG-AAACT 460

\* \* \* \*\* \* \*\* \*\*\* \* **\*\*\*\*\*** \*\*\* \*\* \*

Hu\_400+ TAGGG-- 400

Zf\_467R TACTCTA 467

\*\*

**Alignments #’s 10, 11, and 12.** Shown below are three pair-wise alignments of the core human *ppl* enhancer (Hu\_400+) aligned to one of three (S1, S2, and S3) different Fisher-Yates shuffled sequences of the 467 bp plus-strand block from zebrafish (Zf\_467+S1/S2/S3). These pair-wise alignments serve as negative controls.

Alignment #10

Hu\_400+ ---------------------------------TTCTGACACAACCTGCTACACATCTTG 27

Zf\_467+S1 AACCGTGTGGCATTCTTCGGTGAAACCGGTGATTTGTACCTCACTGAATCAAGCATTATA 60

\*\* \* \* \*\* \* \*\*\* \*

Hu\_400+ GATCCCACTTGTCAAGCCTGGCC------CTAGGCCTCTCAGGGGTGGGTACAT------ 75

Zf\_467+S1 TAGGCAAACCCCTACGGCTAGCCCAATCAATGCGTATATCTTGAGTCTGTATTGTAATTA 120

\* \* \* \* \* \*\* \*\*\* \* \* \* \*\* \* \*\* \*\*\*

Hu\_400+ -CAAGTGA**GGAAGT**CACA--CT**GTCAG**GGCAGAAAGAGGGGCTGGGTGGGGCCGGACAGG 132

Zf\_467+S1 ATCCTTGG**GGAAGT**AATCCCCG**GTCAG**CTCACAAAGC--TACGGGGTCTGTAATAAGTCA 178

\*\* **\*\*\*\*\*\*** \* \* **\*\*\*\*\*** \*\* \*\*\*\* \* \*\*\*\* \* \*

Hu\_400+ CTCTGCTGGCT-----------CAGGATCC----CGGCAGGACAGGCTGCCCAACCCAGC 177

Zf\_467+S1 CTACGTTGCTTAGAAGCAGCTTTAGCATAGATGTAGTCTCTACAGTGTTAAAGCTCCACT 238

\*\* \* \*\* \* \*\* \*\* \* \* \*\*\*\* \* \*\*\*

Hu\_400+ C------------CCAAAACTCCCATCTTCTGTCCAACGCCCAAGCCTGCTTCCTCCCT- 224

Zf\_467+S1 CACTAGAATGATCTCAGATTATAATTCTTGTGTGTAACGTTAGCCCATCGTGTTGACCAC 298

\* \*\* \* \*\*\*\* \*\*\* \*\*\*\* \* \* \* \*\*

Hu\_400+ --GCCCCACCTCACCTCACACTGCCCAGACTGGTGGGGCTGCATTTTTGGGGCCGGTG-- 280

Zf\_467+S1 GCTGCACTATCCAGTCCAGACGTTTGAAATTGCTGTGCATAAGTTATATCACTCCGATAG 358

\* \* \*\* \*\* \*\* \* \* \*\* \*\* \* \* \*\* \* \* \*

Hu\_400+ CC**AGGTG**TGA-TGGAGGACAGCCCAGGTCAG**GAGGT**CAGGGCCCCGT**TTCCT**CCCAAGCC 339

Zf\_467+S1 GG**AGGTG**GGTCTGTCTAACACTGAAGTTCTT**GAGGT**TAAA------C**TTCCT**G---AATC 409

**\*\*\*\*\*** \* \*\* \*\*\* \*\* \*\* **\*\*\*\*\*** \* **\*\*\*\*\*** \* \*

Hu\_400+ AGGATGACTCAGTGATGGACAGACTAGGCCACAAGGGGCCGAACACAAAGCCAAATTAGG 399

Zf\_467+S1 AAATGGAATAAATACGTACACTTTTAGTACTTCGAAGTGC---TGCAACGCAGTGTTGCA 466

\* \*\* \* \* \* \*\*\* \* \* \* \*\*\* \*\* \*\*

Hu\_400+ G 400

Zf\_467+S1 A 467

Alignment #11

Hu\_400+ -TTCTGACAC**AACCT**--GCTACAC---------------ATC**TTGGAT**CCCACTTGTCAA 42

Zf\_467+S2 CAAAGGAGAG**AACCT**TAGGAACACTTATAGCACGGGAATTTT**TTGGAT**TCCGTTAATGGA 60

\*\* \* **\*\*\*\*\*** \* \*\*\*\* \* **\*\*\*\*\*\*** \*\* \* \* \*

Hu\_400+ G-CCTGGCCCTAGGCCTCTCAGGGGTGGGTAC----ATCAAGT----------GAGGAAG 87

Zf\_467+S2 ACTGTGCCTATACTAATATCAAACTTGATGTGATATTTAACCTTTAAAATACAGTGAAAG 120

\*\* \* \*\* \* \*\*\* \*\* \* \* \* \* \* \*\*\*

Hu\_400+ TCACACTGTCAGGGCAGAAAGAG----GGGCTGGGTGGGGCCGGACAGGCTCTGCTGGCT 143

Zf\_467+S2 ATGTACTTATTATTTATATAGATTGTATGTCTCATTAACGCAAACCGTTGTCTACTTCCC 180

\*\*\* \* \* \*\*\* \* \*\* \* \*\* \* \*\*\* \*\* \*

Hu\_400+ CAGGATCCCGGCAGGACAGGCTGCCCAACCCAGCCCCAAAACTCCCATCTTCTGTCCAAC 203

Zf\_467+S2 -----TATTGGTTGACTAAGCTACACGTCTTTGCCCGT-----ACACTGTTAGGTATACA 230

\* \*\* \* \* \*\*\* \* \* \* \*\*\*\* \* \* \*\* \*\* \*

Hu\_400+ GCCCAAGCCTGCTTCCTCCCTGCCCCACCTCACCTCACACTGCCCAGACTGGTGGGGCTG 263

Zf\_467+S2 AACCA---------------------ATTAGGTCTCCCGCTCCAGAGTAAGTGGGGGTTG 269

\*\*\* \* \*\*\* \* \*\* \* \*\* \* \*\*\*\* \*\*

Hu\_400+ CATTTTTGGGGCCGGTGCCAGGTGTGATGGAGGACAGCCCAGGTCAGGAGGTCAGGGCCC 323

Zf\_467+S2 AAATCATCGGAGCGACGCGTCATATAGTTTCTTAC---GGAGATAGGGCGCAAAGTGCAA 326

\* \* \* \*\* \*\* \*\* \* \* \* \*\* \*\* \* \*\* \* \*\* \*\*

Hu\_400+ CGTT---TCCT-----CCCAAGCCAG-------GATGACTCAGTGATGGACAGACTAGGC 368

Zf\_467+S2 CTTCGATTAATATGCCGCCCATAGAACATTCAACATTACTTCGAAGCTGCCCCACCCCAC 386

\* \* \* \* \*\* \* \* \*\* \*\*\* \* \* \* \*\* \*

Hu\_400+ CACAA---------GGGGCCGA---ACACAAAGCCAAA**TTAGG**G---------------- 400

Zf\_467+S2 GTGCAGGGTCTTTTGGCGGCGAGAAGGTCAACTACGTT**TTAGG**TAAGATTTTCTGTGACT 446

\* \*\* \* \*\*\* \*\*\* \* **\*\*\*\*\***

Hu\_400+ --------------------- 400

Zf\_467+S2 GTTGGTCACGCCCCGAGTCCT 467

Alignment #12

Hu\_400+ ---TTCTGACACAACCTGCTACACATCTTGGATCCCACTTGT----------CAAGCCTG 47

Zf\_467+S3 AGGAGTAGGCAACTAAAGATGCGTATTTTAGGTTCCTCTTCAGCCCAAACTACACACCCT 60

\* \*\* \* \* \* \*\* \*\* \* \* \*\* \*\*\* \*\* \*\*

Hu\_400+ GCCCTAGGCCTC**TCAGGG**GTGGGTACATCAAGTGAGGAAGTCACACTGTCAGGGCAGAAA 107

Zf\_467+S3 AACGTGGGCT--**TCAGGG**ATGTCTTTTGCATCTTACCTAATTTACACGGAGCCGCAGTAA 118

\* \* \*\*\* **\*\*\*\*\*\*** \*\* \* \*\* \* \* \* \* \* \*\*\*\* \*\*

Hu\_400+ GAGGGGCTGGGTGGGGCCGGACAGGCTCTGCTGGCTCAGGAT-CCCGGCAG-GACAGGCT 165

Zf\_467+S3 TTAAGTATACTTTTGCAGAAGTAGTCTGCCCATAAATTGAAAGCTGGTCGCAGCTTGTTA 178

\* \* \* \* \*\* \*\* \* \* \* \* \* \* \* \*

**7-mer**

Hu\_400+ **GCCCAAC**CCAGCCCCAAAACTCC**CATCTT**CTGTCCAA--CGCCCAAGCCTGCTTCCTCCC 223

Zf\_467+S3 **GCCCAAC**TCGTATCCAGTCATTG**CATCTT**GTGACTTTGCAGGCTAAGCTCCCCTCATAAG 238

**\*\*\*\*\*\*\*** \* \*\*\* \* **\*\*\*\*\*\*** \*\* \* \* \* \*\*\*\* \* \*\* \*

Hu\_400+ TG----CCCCACCTCACCTCACACTGCCCAGACTGGTG**GGGCT**GCATTTTT-GGG-GCCG 277

Zf\_467+S3 GGGTTTACTCGCTCATCCTATGCGTAATACTCATACAT**GGGCT**TCAAGTTTAGGTAGCCC 298

\* \* \* \* \*\*\* \* \* **\*\*\*\*\*** \*\* \*\*\* \*\* \*\*\*

Hu\_400+ GTGCCAGGTGTG-------ATGGAGGACAGCCCAGGTCAGGAGGTCAGGGCCCCGTTTCC 330

Zf\_467+S3 ATTGACGGTAGAATTACCAATTGAATATTGAGGATTAAATATGGCACGGGGACCTAGACG 358

\* \*\*\* \*\* \*\* \* \* \* \* \*\* \*\*\* \*\* \*

Hu\_400+ TCCCAA-GCCAGGATGACTCAGTGATGGACAGACTAGGCCACAAGGGGCCGAACACAAAG 389

Zf\_467+S3 TCACAAAGTCTTCGTTAATCT-AGGTGTACAATCTTTGTACTCATGTGGCGTCCGAAAGG 417

\*\* \*\*\* \* \* \* \* \*\* \* \*\* \*\*\* \*\* \* \* \* \* \*\* \* \*\* \*

Hu\_400+ CCAAATTAGGG--------------------------------------- 400

Zf\_467+S3 ATAAAATGAGGAAATGTTGGTCTTCAACAAACACTTCGTTCATAAGGTTT 467

\*\*\* \* \*\*

**Alignments # 13.** For reference, shown below is a pair-wise alignment of the core human *ppl* enhancer (Hu\_400+) aligned to the full-length 812 bp enhancer from the zebrafish *ppl* locus (Zf\_812+).

Hu\_400+ ------------------------------------------------------------ 0

Zf\_812+ CCCACCTACATTCTGGAACGGGGAGGCTCGGAGAAAAACCAGCCAATCCTGCCTGGCCCC 60

Hu\_400+ ------------TTCTGACACAACCTGCTACACATCTTGGATC----------------C 32

Zf\_812+ AGACATTTATTATCATGAAAAAGAGTGTTAAACATGCTTTTAAAGAAGTCATTGTGTTGT 120

\* \*\*\* \* \* \*\* \*\* \*\*\*\* \*

Hu\_400+ CACTTGT--------------------------------------CAAGCCTGGCCCTAG 54

Zf\_812+ GACTAATAAGATGTGTTGTTAAAAGTGTCTCTTTAGGGAATCTGCCATCAAACGCTGTAA 180

\*\*\* \* \*\* \*\* \*\*

Hu\_400+ GCCTCTCAGGGGTGGGTACATCAAGTGAGGAAGTCACACTGTCAGGGCAGAAAGAGGGGC 114

Zf\_812+ TTCTCCTCGGCTTG-----CTTAAGACAGAAAGGAACATTGCCTTACAGATAAG-GAGGA 234

\*\*\* \*\* \*\* \* \*\*\* \*\* \*\*\* \*\*\* \*\* \* \*\*\* \* \*\*

Hu\_400+ TGGGTGGGGCCGGACAGGCTCTGCTGGCTCA----GGATCCCG-GCAGGACAGGCTGCCC 169

Zf\_812+ ATGATGACAGAGCAACAGTAATGCACACTGATCTACTATACTATCTGAAACATGCAGCCA 294

\* \*\* \* \* \* \*\*\* \*\* \* \*\* \* \*\*\* \*\* \*\*\*

Hu\_400+ AACCCAGCCCCA-----AAACTCCCATCTTCTGTCCAACGCCCAAGC------------- 211

Zf\_812+ CACCCATTCAGTCACTCTTTCTGTCATTTTCCACCTCACACCGTGATCTCATTCAAAGAA 354

\*\*\*\*\* \* \*\* \*\*\* \*\*\* \* \*\* \*\*

Hu\_400+ ---------CTGCTTCCTCCCTGCCCCACC---TCACCTCACACTGCCCAGACTGGTGGG 259

Zf\_812+ TGTCAAGCACTGTAGTCACCGTGCCACTAAATGAACCATGGCACTAAACCCTATGAAGTG 414

\*\*\* \* \*\* \*\*\*\* \* \* \* \*\*\*\* \* \*\* \* \*

Hu\_400+ GCTGCATTTTTGGG--GCCGGTGCCAGGTGTGATGGAGGACAGCCCAGGTCAGGAGGTCA 317

Zf\_812+ ATTGTTTTCTTTGTCAGGCAGTATCACTTA-----CTCTAAAACCTGAGTGAGGCACATT 469

\*\* \*\* \*\* \* \* \* \*\* \*\* \* \* \* \*\* \*\* \*\*\*

Hu\_400+ GGGCCCCGTTTCCTCCCAAGCCAGGATGACTCAGTGATGGACAGACTAG----------- 366

Zf\_812+ TGCAACATTCTTATTAAATGCCAGTCTTCTGCGACCTGTGACACACTTCAATACTGAGTG 529

\* \* \* \* \* \* \*\*\*\*\* \* \* \*\*\*\* \*\*\*

Hu\_400+ -G---------------------------------------------------------- 367

Zf\_812+ TGTAAGATGGGATGGTGTAGGCCTACTAGCTGATGTCTCACTAAATCTGTCAGATTAGTG 589

\*

Hu\_400+ ------------------------------------------------------------ 367

Zf\_812+ CAGAACTGTTCCGTTCCATGCCTGGAAGTTTGTAGTGGGCCTGAAGACCTTGATTTGCTT 649

Hu\_400+ ----------------------------------------CCACAAGGGG---------- 377

Zf\_812+ TGTCAGGTATGTTTAATTAAGGTTAGCGCTAAACTCTACATGACAATGGTCCTCCAGGAA 709

\*\*\*\* \*\*

Hu\_400+ CCGAACACAAAGCCAAATTAGGG------------------------------------- 400

Zf\_812+ CAGAAAGTTCACCTTCAATAGACAGCAATGCATGTTTACTTTTCTGCAAAGTACCAAACC 769

\* \*\*\* \* \* \* \*\*\*

Hu\_400+ ------------------------------------------- 400

Zf\_812+ TCACCGCTAGGGGGAGTCGAATAGTTTTGACTGAGGCTTGGAA 812

**Alignments # 14.** For reference, shown below is a pair-wise alignment of the full-length human *ppl* enhancer (Hu\_489+) aligned to the full-length 812 bp enhancer from the zebrafish *ppl* locus (Zf\_812+). Relative to the 400 bp core enhancer used in the majority of pair-wise alignments, the full-length enhancer sequences overlaps a non-conserved Alu element (AluJr4 sub-family) on the *ppl*-proximal side and a MIR-element on the *ppl*-distal side.

Hu\_489+ ------------------------------------------------------------ 0

Zf\_812+ CCCACCTACATTCTGGAACGGGGAGGCTCGGAGAAAAACCAGCCAATCCTGCCTGGCCCC 60

Hu\_489+ ------------TTCTGACACAACCTGCTACACATCTTGGATC----------------C 32

Zf\_812+ AGACATTTATTATCATGAAAAAGAGTGTTAAACATGCTTTTAAAGAAGTCATTGTGTTGT 120

\* \*\*\* \* \* \*\* \*\* \*\*\*\* \*

Hu\_489+ CACTTGT--------------------------------------CAAGCCTGGCCCTAG 54

Zf\_812+ GACTAATAAGATGTGTTGTTAAAAGTGTCTCTTTAGGGAATCTGCCATCAAACGCTGTAA 180

\*\*\* \* \*\* \*\* \*\*

Hu\_489+ GCCTCTCAGGGGTGGGTACATCAAGTGAGGAAGTCACACTGTCAGGGCAGAAAGAGGGGC 114

Zf\_812+ TTCTCCTCGGCTTG-----CTTAAGACAGAAAGGAACATTGCCTTACAGATAAG-GAGGA 234

\*\*\* \*\* \*\* \* \*\*\* \*\* \*\*\* \*\*\* \*\* \* \*\*\* \* \*\*

Hu\_489+ TGGGTGGGGCCGGACAGGCTCTGCTGGCTCA----GGATCCCG-GCAGGACAGGCTGCCC 169

Zf\_812+ ATGATGACAGAGCAACAGTAATGCACACTGATCTACTATACTATCTGAAACATGCAGCCA 294

\* \*\* \* \* \* \*\*\* \*\* \* \*\* \* \*\*\* \*\* \*\*\*

Hu\_489+ AACCCAGCCCCA-----AAACTCCCATCTTCTGTCCAACGCCCAAGC------------- 211

Zf\_812+ CACCCATTCAGTCACTCTTTCTGTCATTTTCCACCTCACACCGTGATCTCATTCAAAGAA 354

\*\*\*\*\* \* \*\* \*\*\* \*\*\* \* \*\* \*\*

Hu\_489+ ---------CTGCTTCCTCCCTGCCCCACC---TCACCTCACACTGCCCAGACTGGTGGG 259

Zf\_812+ TGTCAAGCACTGTAGTCACCGTGCCACTAAATGAACCATGGCACTAAACCCTATGAAGTG 414

\*\*\* \* \*\* \*\*\*\* \* \* \* \*\*\*\* \* \*\* \* \*

Hu\_489+ GCTGCATTTTTGGG--GCCGGTGCCAGGTGTGATGGAGGACAGCCCAGGTCAGGAGGTCA 317

Zf\_812+ ATTGTTTTCTTTGTCAGGCAGTATCACTTA-----CTCTAAAACCTGAGTGAGGCACATT 469

\*\* \*\* \*\* \* \* \* \*\* \*\* \* \* \* \*\* \*\* \*\*\*

Hu\_489+ GGGCCCCGTTTCCTCCCAAGCCAGGATGACTCAGTGATGGACAGACTAG----------- 366

Zf\_812+ TGCAACATTCTTATTAAATGCCAGTCTTCTGCGACCTGTGACACACTTCAATACTGAGTG 529

\* \* \* \* \* \* \*\*\*\*\* \* \* \*\*\*\* \*\*\*

Hu\_489+ -G---------------------------------------------------------- 367

Zf\_812+ TGTAAGATGGGATGGTGTAGGCCTACTAGCTGATGTCTCACTAAATCTGTCAGATTAGTG 589

\*

Hu\_489+ ------------------------------------------------------------ 367

Zf\_812+ CAGAACTGTTCCGTTCCATGCCTGGAAGTTTGTAGTGGGCCTGAAGACCTTGATTTGCTT 649

Hu\_489+ ----------------------------------------CCACAAGGGG---------- 377

Zf\_812+ TGTCAGGTATGTTTAATTAAGGTTAGCGCTAAACTCTACATGACAATGGTCCTCCAGGAA 709

\*\*\*\* \*\*

Hu\_489+ CCGAACACAAAGCCAAATTAGGG------------------------------------- 400

Zf\_812+ CAGAAAGTTCACCTTCAATAGACAGCAATGCATGTTTACTTTTCTGCAAAGTACCAAACC 769

\* \*\*\* \* \* \* \*\*\*

Hu\_489+ ------------------------------------------- 400

Zf\_812+ TCACCGCTAGGGGGAGTCGAATAGTTTTGACTGAGGCTTGGAA 812

**Alignments # 15.** For reference, shown below is a three-way multiple sequence alignment of the core human *ppl* enhancer (Hu\_400+), the homologous 409 bp block from mouse *ppl* locus (Mm\_409+), and the 467 bp block from the zebrafish *ppl* locus (Zf\_467+), which is located in a similar position as the mammalian enhancer. Highlighted are two of the 18 conserved mammalian blocks with some similarity to zebrafish sequences.

Hu\_400+ --TTCTGACACAACCTGCTACACAT------CTTGGATCCCACTTGTCAAGCCTGGCCCT 52

Mm\_409+ --CTATCCCACAGACTGGTGACCCT-GGAG-CTCAGACACTCCACTGGAGAGCTATCCCT 56

Zf\_467+ ATCTCATTCAAAGAATGTCAAGCACTGTAGTCACCGTGCCACTAAATGAACCATGGCACT 60

\* \*\* \* \*\* \* \* \* \* \* \* \* \*\*

**b. 10-mer**

Hu\_400+ AGGCCTCTCAGG------GGTGGGTACATCAAGTG**AGGAAGTCAC**ACTGTC----AGGGC 102

Mm\_409+ GGGCCTCTCAAATTCACCATGAGAGCTTCTCTGCA**AGGAAGTCAC**CCCATC----AGGGC 112

Zf\_467+ AAACCCTATGAAG-----TGATTGTTTTCTTTGTC**AGG**C**AGT**AT**C**ACTTACTCTAAAACC 115

\*\* \* **\*\*\* \*\*\* \*** \* \* \* \*

**e. 9-mer f.**>>

Hu\_400+ AGAAAGAGGGGCT------GGGTG----GGGCCGG**ACAGGCTCT**GC-TGGCTCAGG**ATCC** 151

Mm\_409+ AGA--GTGGTTCT------AGGTG----GGGCTAA**ACAGGCTCT**ACCAGGCACAGT**ATCC** 160

Zf\_467+ TGAGTGAGGCACATTTGCAACATTCTTATTAAATGC**CAG**T**CTT**CTGCGACCTGTGACA**C**A 175

\*\* \* \*\* \* \* **\*\*\*** **\*\*** \* \* **\***

> **g.**>>> **h. 7-mer**

Hu\_400+ **C**G**GCAGG**A**CAG**G**CTGCCCA**ACCCA----GCCCCAAAACTCCCATCTTCTGTCCAACGCCC 207

Mm\_409+ **C**T**GCAGG**G**CAG**A**CTGCCCA**GCCTC----CTGTTCACG--------------CCCATGCTT 202

Zf\_467+ **C**TT**CA**ATA**C**T**G**AG**TG**TGT**A**AGATGGGATGGTGTAGGCCTACTAGCTGATGTCTCACTAAA 235

**\*** **\*\*** **\*** **\*** **\*\*** **\*** \* \*

Hu\_400+ -AAGCCTGCTTCCTCCCTGCCCC---------------ACCTCACCTCACACTGCCCAGA 251

Mm\_409+ -TTTCCTGCCTGCTGCCTGCTCCTCCCCTTCTGGGCCGTGCCAGGCTCATGCAGAGCAGA 261

Zf\_467+ TCTGTCAGATTAGTGCAGAACTGTTCCGTTCCATGCCTGGAAGTTTGTAGTGGGCCTGAA 295

\* \* \* \* \* \* \* \*

**l.**>>> **m.**>>>

Hu\_400+ CTGGTGGGGCT**GCATT**T**TTGGG**GC---------------CGGTGCCAGGTGTGATGGA-- 294

Mm\_409+ CCAGTACAGCC**GCATT**C**TTGGG**CAA--------------GTGTCTCTGGTGTGAATGACC 307

Zf\_467+ GACCTTGATTT**GC**T**TT**G**T**CA**GG**TATGTTTAATTAAGGTTAGCGCTAAACTCTACATGACA 355

\* **\*\*** **\*\*** **\*** **\*\*** \* \* \*\*

Hu\_400+ ---GGACAGCCCAGGTCAGGAGGTCAGGGCCCCGTTTCCTCCCAAGCCAGGATGACTCAG 351

Mm\_409+ CTGGGGCTGGTCAGGTCAGAAGGTCAGGGCCTTGTTCCCTCCAGTGCCCAAGTGATA--- 364

Zf\_467+ ATGGTCC------TCCAGGAACAGAAAGTTCACCTTCAATAGACAGCAATGCATGTTTAC 409

\* \* \* \* \* \* \* \*\* \* \*\*

Hu\_400+ TGATGGACAGACTAGGCCA-------CAAGGGG-CCGAACACAAAGCCAAATTAGGG- 400

Mm\_409+ -----GATGAGTCAGGCTA-------CAAAGGGGCAGAACAAGAAACCAAACCGAGT- 409

Zf\_467+ TTTTCTGCAAAGTACCAAACCTCACCGCTAGGGGGAGTCGAATAGTTTTGACTGAGGC 467

\* \* \*\*\* \* \* \* \* \*

\* 96 count (3-way identical characters)

- 158 count (null characters)

**Alignments # 16.** For reference, shown below is a three-way multiple sequence alignment of the core human *ppl* enhancer (Hu\_400+), the homologous 409 bp block from mouse *ppl* locus (Mm\_409+), and the reverse complement of the 467 bp block from the zebrafish *ppl* locus (Zf\_467-). This alignment serves as a control alignment for Alignment #15, which features far fewer insertions of null characters (158 dashes versus 227 dashes). However, the number of alignment columns with 3-way identity is similar in both (96 and 97 \* columns).

Hu\_400+ ------TTCTGACACAACCTGCTACACAT----CTTGGATC--CCACTTGTCAAGCCTGG 48

Mm\_409+ ------CTATCCCACAGACTGGTGACCCTGGAGCTCAGACA--CTCCACTGGAGAGCTAT 52

Zf\_467- GCCTCAGTCAAAACTATTCGACTCCCCCTAGCGGTGAGGTTTGGTACTTTGCAGAAAAGT 60

\* \* \* \* \* \* \* \* \* \*

**a. 9-mer** **c. 10-mer**

Hu\_400+ CCCTA**GGCCTCTCA**GG------GGTGGGTACATCAAGTG-AGGAAGTCACACTG**TCAGGG** 101

Mm\_409+ CCCTG**GGCCTCTCA**AATTCACCATGAGAGCTTCTCTGCA-AGGAAGTCACCCCA**TCAGGG** 111

Zf\_467- AAACAT**GC**A**T**TG**C**TGTCTATTGAAGGTGAACTTTCTGTTCCTGGAGGACCATTG**TCA**T-**G** 119

**\*\*** **\*** **\*** \* \* \*\* \* **\*\*\*** **\***

**e. 9-mer**

Hu\_400+ **CAGA**AAGAGGGGCT-------------------GGGTGGGGCCGG**ACAGGCTCT**G**C**-TGG 141

Mm\_409+ **CAGA**--GTGGTTCT-------------------AGGTGGGGCTAA**ACAGGCTCT**A**C**CAGG 150

Zf\_467- T**AGA**GTTTAGCGCTAACCTTAATTAAACATACCTGACAAAGCAAAT**CA**A**G**G**TCT**T**C**AGGC 179

**\*\*\*** \* \*\* \* \*\* **\*\*** **\*** **\*\*\*** **\*** \*

Hu\_400+ CTCAGGATCCCGGCAGGACAGGCTGCCCAACC--CAGCCCCAAAACTCCCA--TCTTCTG 197

Mm\_409+ CACAGTATCCCTGCAGGGCAGACTGCCCAGCC--TCCTGTTCACG--------------- 193

Zf\_467- CCACTACAAACTTCCAGGCATGGAACGGAACAGTTCTGCACTAATCTGACAGATTTAGTG 239

\* \* \* \* \*\* \* \* \* \*

Hu\_400+ TCCAACGCCCAAGCCTGCTTCCTCCCTGCCCC---------------ACCTCACCTCACA 242

Mm\_409+ -CCCATGCTTTTTCCTGCCTGCTGCCTGCTCCTCCCCTTCTGGGCCGTGCCAGGCTCATG 252

Zf\_467- AGACATCAGCTAGTAGGCC-------TACACCATCCCATCTTACACACTCAGTATTGAAG 292

\* \*\* \* \* \*\* \* \* \*

**n. 7-mer**

Hu\_400+ C---TGCCCAGACTGGTGGGGCTGCATTTTTGGGGC-CGGTGC**CAGGTGTGA**TG**GA**----- 294

Mm\_409+ C---AGAGCAGACCAGTACAGCCGCATTCTTGGGCAAGTGTCT**C**T**GGTGTGA**A**TGA**----- 305

Zf\_467- TGTGTCACAGGTCGCAGAAGACTGGCATTTAATAAGAATGTTG**CA**AA**TGTG**CC**T**C**A**CTCAG 353

\* \* \* \* \* \* \*\* **\*** **\*\*\*\*** **\***

**p. 11-mer**

Hu\_400+ ---------------GGACAGCCCAGGTCAGG-----------------**AGGTCAGGGCC** 322

Mm\_409+ ----------CCCTGGGGCTGGTCAGGTCAGA-----------------**AGGTCAGGGCC** 338

Zf\_467- GTTTTAGAGTAAGTGATACTGCCTGACAAAGAAAACAATCACTTCATAGG**G**T**T**T**AG**T**GCC** 413

\* \* \*\* **\*** **\*** **\*\*** **\*\*\***

Hu\_400+ CCGTTTCCTCCCAAGCCAGGATG-ACTCAGTGATGGACAGACTAGGCCACAAGGGG-CCG 379

Mm\_409+ TTGTTCCCTCCAGTGCCCAAGTG-ATA--------GATGAGTCAGGCTACAAAGGGGCAG 388

Zf\_467- ATGGTTCATTTAGTGGCACGGTGACTACAGTGCTTGACATTCTTTGAATGA--------- 464

\* \* \* \* \* \* \*\* \*\* \* \*

Hu\_400+ AACACAAAGCCAAATTAGGG 400

Mm\_409+ AACAAGAAACCAAACCGAGT 409

Zf\_467- ----------------GAT- 467

\* 97 count (3-way identical characters)

- 227 count (null characters)

**Alignments # 17.** For reference, shown below is a three-way multiple sequence alignment of the core human *ppl* enhancer (Hu\_400+), the homologous 409 bp block from mouse *ppl* locus (Mm\_409+), and the (non-biological) reverse sequence of the 467 bp block from the zebrafish *ppl* locus (Zf\_467R). This alignment serves as a control alignment for Alignment’s #15 and #16, which features far fewer insertions of null characters (158 dashes versus 227 dashes). While the number of alignment columns with 3-way identity is similar (99 \* columns versus 96 and 97 \* columns in Alignments #15 and #16, respectively), Alignment #16 features many more insertions of null characters (248 dashes inserted versus 158 and 227 dashes in Alignments #15 and #16, respectively).

Hu\_400+ -------TTCTGACACAACCTGCTACACAT------------CTTGGATCCCACTTGTCA 41

Mm\_409+ -------CTATCCCACAGACTGGTGACCCTGG--------AGCTCAGACACTCCACTGGA 45

Zf\_467R CGGAGTCAGTTTTGATAAGCTGAGGGGGATCGCCACTCCAAACCATGAAACGTCTTTTCA 60

\* \* \* \*\*\* \* \* \*\* \* \* \*

Hu\_400+ AGCCTGGCCCTAGGCCTCT-----CAGG------GGTGGGTACATCAAGTGAGGAAGTCA 90

Mm\_409+ GAGCTATCCCTGGGCCTCT-----CAAATTCACCATGAGAGCTTCTCTGCAAGGAAGTCA 100

Zf\_467R TTTGTACGTAACGACAGATAACTTCCACTTGAAAGACAAGGACCTCCTGGTAACAGTACA 120

\* \* \* \* \* \* \* \* \*\*

Hu\_400+ CACTGTCAGGGCAGAAAGAGGGGCTGGGTGGGGCCGGACAGGCTCTGC-TGGCTCAGGAT 149

Mm\_409+ CCCCATCAGGGCAGA--GTGGTTCTAGGTGGGGCTAAACAGGCTCTACCAGGCACAGTAT 158

Zf\_467R T-CTCAAATCGCG----ATTGGAATTAATTTGTATGGACTGTTTCGTTTAGTTCCAGAAG 175

\* \* \*\* \* \* \* \* \*\* \* \*\* \* \*\*\* \*

Hu\_400+ CCCGGCA------GGACAGGCTGCCCAACCCAGCCCCAAAACTCCCATCTTCTGTCCAAC 203

Mm\_409+ CCCTGCA------GGGCAGACTGCCCAGCCTCCTGTTCACG--------------CCCAT 198

Zf\_467R TCCGGGTGATGTTTGAAGGTCCGTACCTTGCCTTGTCAAGACGTGATTAGACTGTCTAAA 235

\*\* \* \* \* \* \* \* \* \* \*

Hu\_400+ GCCCAAGCCTGCTTCCTCCCTGCCCC-----------------------------ACCTC 234

Mm\_409+ GCTTTTTCCTGCCTGCTGCCTGCTCCTCCCCTTCTGGGCCG--------------TGCCA 244

Zf\_467R TCACT-----CTGTAGT---CGATCATCCGGATGTGGTAGGGTAGAATGTGTGAGTCATA 287

\* \* \* \* \*

Hu\_400+ ACCTCACA--CTGCCCAGACTG--GTGGGGCTGCATTTTTGGGGC-CGGTGCCAGGTGTG 289

Mm\_409+ GGCTCATG--CAGAGCAGACCA--GTACAGCCGCATTCTTGGGCAAGTGTCTCTGGTGTG 300

Zf\_467R ACTTCACACAGTGTCCAGCGTCTTCTGACCGTAAATTATTCTTACAACGTTTA------- 340

\*\*\* \* \*\*\* \* \*\*\* \*\* \*\*

Hu\_400+ ATGGA-----GGACAGCCCAGGTCAGGAGGTCAGGGCCCCGTTTCCTCCCAAGCCAGGAT 344

Mm\_409+ AATGACCCTGGGGCTGGTCAGGTCAGAAGGTCAGGGCCTTGTTCCCTCCAGTGCCCAAGT 360

Zf\_467R ------------------CACGGAGTGAGTCCAAAATCTCATTCACTATGACGGA---CT 379

\*\* \* \*\* \*\* \* \*\* \*\* \* \*

Hu\_400+ GACTCAGTGATGGACAGACTAGGCCACAAGG----------------------------- 375

Mm\_409+ GATA--------GATGAGTCAGGCTACAAAG----------------------------- 383

Zf\_467R GTTTCTTTTGTTAGTGAAGTATCCCAAATCACGGTACCAAGTAAATCACCGTGCCACTGA 439

\* \* \* \* \*

Hu\_400+ -GG-CCGAACACAAAGCCAAATTAGGG- 400

Mm\_409+ -GGGCAGAACAAGAAACCAAACCGAGT- 409

Zf\_467R TGTCACGAACTGTAAGAAACTTACTCTA 467

\* \*\*\*\* \*\* \*

\* 99 count (3-way identical characters)

- 248 count (null characters)

**Alignments #’s 18, 19, and 20.** Shown below are three 3-way alignments of the core mammalian *ppl* enhancers (Hu\_400+ and Mm\_409+) aligned to one of three (S1, S2, and S3) different Fisher-Yates shuffled sequences of the 467 bp plus-strand block from zebrafish (Zf\_467+S1/S2/S3). These multiple-sequence alignments serve as negative controls.

Alignment #18

Hu\_400+ ----TTCTGACACAACCTGCTACACAT----CTTGGATCCC-------------ACTTGT 39

Mm\_409+ ----CTATCCCACAGACTGGTGACCCTGGAGCTCAGACACT-------------CCACTG 43

Zf\_467+S1 AACCGTGTGGCATTCTTCGGTGAAACCGGTGATTTGTACCTCACTGAATCAAGCATTATA 60

\* \* \*\* \* \* \* \* \*

Hu\_400+ CAAGCCTGGCCCTAGGCCTCTCAGG-------------------------GGTGGGTACA 74

Mm\_409+ GAGAGCTATCCCTGGGCCTCTCAAATTCAC-------------------CATGAGAGCTT 84

Zf\_467+S1 TAGGCAAACCCCTACGGCTAGCCCAATCAATGCGTATATCTTGAGTCTGTATTGTAATTA 120

\* \*\*\*\* \* \*\* \*

Hu\_400+ TCAAGTGA**GGAAGT**CACACTGTCAGGGCAGAAAGAGGGGCTGGGTGGGGCCGGACAGGCT 134

Mm\_409+ CTCTGCAA**GGAAGT**CACCCCATCAGGGCAGA--GTGGTTCTAGGTGGGGCTAAACAGGCT 142

Zf\_467+S1 ATCCTTGG**GGAAGT**AATCCCCGGTCAGCTCACAAAGCTACGGGGTCTGT--AATAAGTCA 178

**\*\*\*\*\*\*** \* \* \*\* \* \* \* \*\*\* \* \*\* \*

Hu\_400+ CTGC-TGGCTCAGGATCCCGGCAGGACAGGCTG--CCCAACCCAGCCCCAAAACTCCCAT 191

Mm\_409+ CTACCAGGCACAGTATCCCTGCAGGGCAGACTG--CCCAGCCTCCTGTTCACG------- 193

Zf\_467+S1 CTACGTTGCTTAGAAGCAGCTTTAGCATAGATGTAGTCTCTACAGTGTTAAAGCTCCACT 238

\*\* \* \*\* \*\* \* \* \* \*\* \* \*

Hu\_400+ C-------TTCTGTCCAACGCCCAAGCCTGCTTCCTCCCTGCCCC--------------- 229

Mm\_409+ --------------CCCATGCTTTTTCCTGCCTGCTGCCTGCTCCTCCCCTTCTGGGCCG 239

Zf\_467+S1 CACTAGAATGATCTCAGATTATAATTCTTGTGTGTAACGTTAGCCCATCGTG-TTGACCA 297

\* \* \* \*\* \* \* \* \*\*

Hu\_400+ ACCTCACCTCACACTGCC**CAGAC**TGGTGGGGCTGCATTTTTGGGGC-CGGT---GCCAGG 285

Mm\_409+ TGCCAGGCTCATGCAGAG**CAGAC**CAGTACAGCCGCATTCTTGGGCAAGTGT---CTCTGG 296

Zf\_467+S1 CG-CTGCACTATCCAGTC**CAGAC**GTTTGAA-----ATTGCTGTGCATAAGTTATATCACT 351

\* \* \* **\*\*\*\*\*** \* \*\*\* \*\* \* \*\* \*

Hu\_400+ TGTGATGGA-----GGACAGCCCAGGTCAGGAGGTCAGGGCCCCGTTTCCTCCCAAGCCA 340

Mm\_409+ TGTGAATGACCCTGGGGCTGGTCAGGTCAGAAGGTCAGGGCCTTGTTCCCTCCAGTGCCC 356

Zf\_467+S1 CCGATAGGGAGGTGGGTCTGTCTAACACTGAAGTTCTTGAGGTTAAA-CTTCCTGAATCA 410

\* \*\* \* \* \* \* \* \*\* \*\* \* \* \*\*\* \*

Hu\_400+ GGATGACTCA-GTGATGGACAGACTAGGCCACAAGGGG-CCGAACACAAAGCCAAATTAG 398

Mm\_409+ AAGTGATA---------GATGAGTCAGGCTACAAAGGGGCAGAACAAGAAACCAAACCGA 407

Zf\_467+S1 AATGGAATAAATACGTACACTTTTAGTACTTCGAAGTGCTGCAACGCAGTGTTGCAA--- 467

\*\* \* \* \* \* \* \* \*\*\* \*

Hu\_400+ GG 400

Mm\_409+ GT 409

Zf\_467+S1 -- 467

\* 110 count (3-way identical characters)

- 170 count (null characters)

Alignment #19

Hu\_400+ ----------TTCTGACACAACCTGCTACACAT----CTT---GGAT-CCCACTTGTCAA 42

Mm\_409+ ----------CTATCCCACAGACTGGTGACCCTGGAGCTC---AGAC-ACTCCACTGGAG 46

Zf\_467+S2 AAAGGAGAGAACCTTAGGAACACTTATAGCACGGGAATTTTTTGGATTCCGTTAATGGAA 60

\* \* \*\* \* \* \*\* \* \*

Hu\_400+ GCCTGGCCCTAGGCCTCTCAGG------------------GGTGGGTACATCAAGTGAGG 84

Mm\_409+ AGCTATCCCTGGGCCTCTCAAATT------------CACCATGAGAGCTTCTCTGCAAGG 94

Zf\_467+S2 CTGTGCCTATACTAATATCAAACTTGATGTGATATTTAACCTTTAAAATACAGTGAAAGA 120

\* \* \* \* \*\*\* \* \*\*

Hu\_400+ AAGTCACACTGTCAGGGCAGAAAGAGGGGCTGGGTGGGGCCGGACAGGCTCTGC-TGGCT 143

Mm\_409+ AAGTCACCCCATCAGGGCAGA--GTGGTTCTAGGTGGGGCTAAACAGGCTCTACCAGGCA 152

Zf\_467+S2 TGTACTTATTATTTATATAGATTGTATGTCTCATTAACGCAAACCGTTGTCTACTTCCCT 180

\* \* \*\*\* \* \*\* \* \*\* \* \*\*\* \* \*

Hu\_400+ CAGGATCCCGGCAGGACAGGCTGCCCAACCCAGCCCCAAAACTCCCATCTTCTGTCCAAC 203

Mm\_409+ CAGTATCCCTGCAGGGCAGACTGCCCAGCCTCCTGTTCACG--------------CCCAT 198

Zf\_467+S2 A-----------TTGGTTGACTAAGCTACACGTCTTTGCCCGTACACTGTTAGGTATACA 229

\* \* \*\* \* \*

Hu\_400+ GCCCAAGCCTGCTTCCTCCCTGCCCC---------------ACCTCACCTCACACTGCCC 248

Mm\_409+ GCTTTTTCCTGCCTGCTGCCTGCTCCTCCCCTTCTGGGCCGTGCCAGGCTCATGCAGAGC 258

Zf\_467+S2 A-------------ACCAATTAGGTCTCCCGCTCCAGAGTAAGTGGGGGTTGAAATCATC 276

\* \* \* \* \*

Hu\_400+ AGACTG----GTGGGGCTGCATTTTTGG--GGC-CGGTGCCAGGTGTGATGGA-----GG 296

Mm\_409+ AGACCA----GTACAGCCGCATTCTTGG--GCAAGTGTCTCTGGTGTGAATGACCCTGGG 312

Zf\_467+S2 GGAGCGACGCGTCATATAGTTTCTTACGGAGATAGGGCGCAAAGTGCAACTTCGATT-AA 335

\*\* \*\* \* \* \* \* \* \* \*\*\* \*

Hu\_400+ ACAGCCCAGGTCAGGAGGTCAGGGCCCCGTTTCCTCCCAAGCCAGGATG-ACTCAGTGAT 355

Mm\_409+ GCTGGTCAGGTCAGAAGGTCAGGGCCTTGTTCCCTCCAGTGCCCAAGTG-ATA------- 364

Zf\_467+S2 TATGCCGCCCATAGAACATTCA----ACATT-ACTTCGAAGCTGCCCCACCCCACGTGCA 390

\* \*\* \* \* \*\* \*\* \* \*\*

Hu\_400+ GGACAGACTAGGCCACAAGGGG-CCGAACACAAA---GCCA-AAT--TAGGG-------- 400

Mm\_409+ -GATGAGTCAGGCTACAAAGGGGCAGAACAAGAA---ACCA-AAC--CGAGT-------- 409

Zf\_467+S2 GGGTC-TTTTGGCGGCGAGAAGGTCAACTACGTTTTAGGTAAGATTTTCTGTGACTGTTG 449

\* \*\*\* \* \* \* \* \* \* \* \*

Hu\_400+ ----------------- 400

Mm\_409+ ----------------- 409

Zf\_467+S2 GTCACGCCCCGAGTCCT 466

\* 86 count (3-way identical characters)

- 216 count (null characters)

Alignment #20

Hu\_400+ TTCTGACACAACCTGCTACACAT----CTTGGATCCCACTTGTCAAGCCTGGCCCTAG-- 54

Mm\_409+ CTATCCCACAGACTGGTGACCCTGGAGCTCAGACACTCCACTGGAGAGCTATCCCTGG-- 58

Zf\_467+S3 ---AGGAGTAGGCAACTAAAGATGCGTATTTTAGGTTCCTCTTCAGCCCAAACTACACAC 57

\* \* \* \* \* \* \* \* \* \*

Hu\_400+ --GCCTCTCAGG------GGTGGGTACATCAAGTGAGGAAGTCACACTGTCAGGGCAGAA 106

Mm\_409+ --GCCTCTCAAATTCACCATGAGAGCTTCTCTGCAAGGAAGTCACCCCATCAGGGCAGA- 115

Zf\_467+S3 CCTAACGTGGGCTTCAGGGATGTCTTTTGCATCTTACCTAATTTACACGGAGCCGCAGTA 117

\* \* \* \* \*\*\*\*

Hu\_400+ AGAGGGGCTGGGTGGGGCCGGACAGGCTCTGC-TGGCTCAGGATCCCGGCAGGACAGGCT 165

Mm\_409+ -GTGGTTCTAGGTGGGGCTAAACAGGCTCTACCAGGCACAGTATCCCTGCAGGGCAGACT 174

Zf\_467+S3 ATTAAGTATACTTTTGCAGAAGTAGTCTGCCCATAAATTGAAAGCTGGTCGCAGCTTGTT 177

\* \* \* \*\* \*\* \* \* \* \* \* \*

Hu\_400+ GCCCAACCCAGC-CCCAAAACTCCCATCTTCTGTCCAA--CGCCCAAGCCTGCTTCCTCC 222

Mm\_409+ GCCCAGCCTCCT-GTTCACG--------------CCCA--TGCTTTTTCCTGCCTGCTGC 217

Zf\_467+S3 AGCCCAACTCGTATCCAGTCATTGCATCTTGTGACTTTGCAGGCTAAGCTCCCCTCATAA 237

\*\* \* \* \* \* \* \* \*

Hu\_400+ CTGCCC-C---------------ACCTCACCTCACACTGCCCAGACTGGTGGGGCTG--- 263

Mm\_409+ CTGCTC-CTCCCCTTCTGGGCCGTGCCAGGCTCATGCAGAGCAGACCAGTACAGCCG--- 273

Zf\_467+S3 GGGGTTTACTCGCTCATCCTATGCGTAATACTCATACATGGGCTTCAAGTTTAGGTAGCC 297

\* \*\*\*\* \* \* \*\* \*

Hu\_400+ CATTTTTGGGGC-------------CGGTGCCAGGTGTGATGGA-----GGACAGCCCAG 305

Mm\_409+ CATTCTTGGGCA------------AGTGTCTCTGGTGTGAATGACCCTGGGGCTGGTCAG 321

Zf\_467+S3 CATTGACGGTAGAATTACCAATTGAATATTGAGGATTAAATATGGCACGGGGACCTAGAC 357

\*\*\*\* \*\* \* \* \* \* \*\* \*

Hu\_400+ GTCAGGAGGTCAGGGCCCCGTTTCCTCCCAAGCCAGGATGACTCAGTGATGGACAGACTA 365

Mm\_409+ GTCAGAAGGTCAGGGCCTTGTTCCCTCCAGTGCCCAAGTGATA--------GATGAGTCA 373

Zf\_467+S3 GTCACAAAGTCTTCGTTAATCTAGGTGTACAATCTTTGTACTCATGTG--GCGTCCGAAA 415

\*\*\*\* \* \*\*\* \* \* \* \* \* \*

Hu\_400+ GGCCACAAGGGG-CCG-----AACACAAAGCCAAATTAGGG----------- 400

Mm\_409+ GGCTACAAAGGGGCAG-----AACAAGAAACCAAACCGAGT----------- 409

Zf\_467+S3 GGATAAAATGAGGAAATGTTGGTCTTCAACAAACACTTCGTTCATAAGGTTT 467

\*\* \* \*\* \* \* \* \*\* \* \* \*

\* 90 count (3-way identical characters)

- 140 count (null characters)