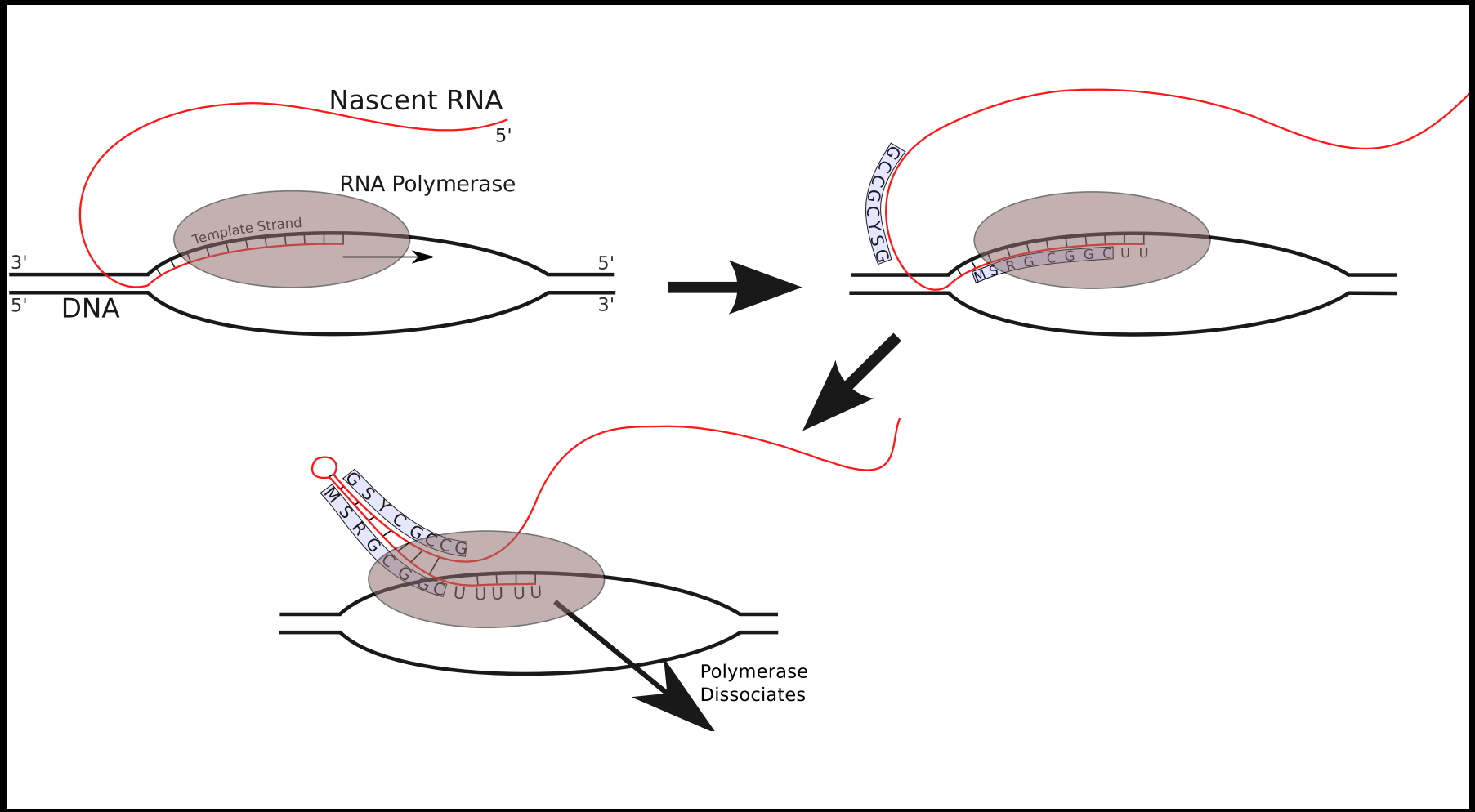
Discovering bacterial transcription termination associated motifs through whole genome clustering

Lars Barquist

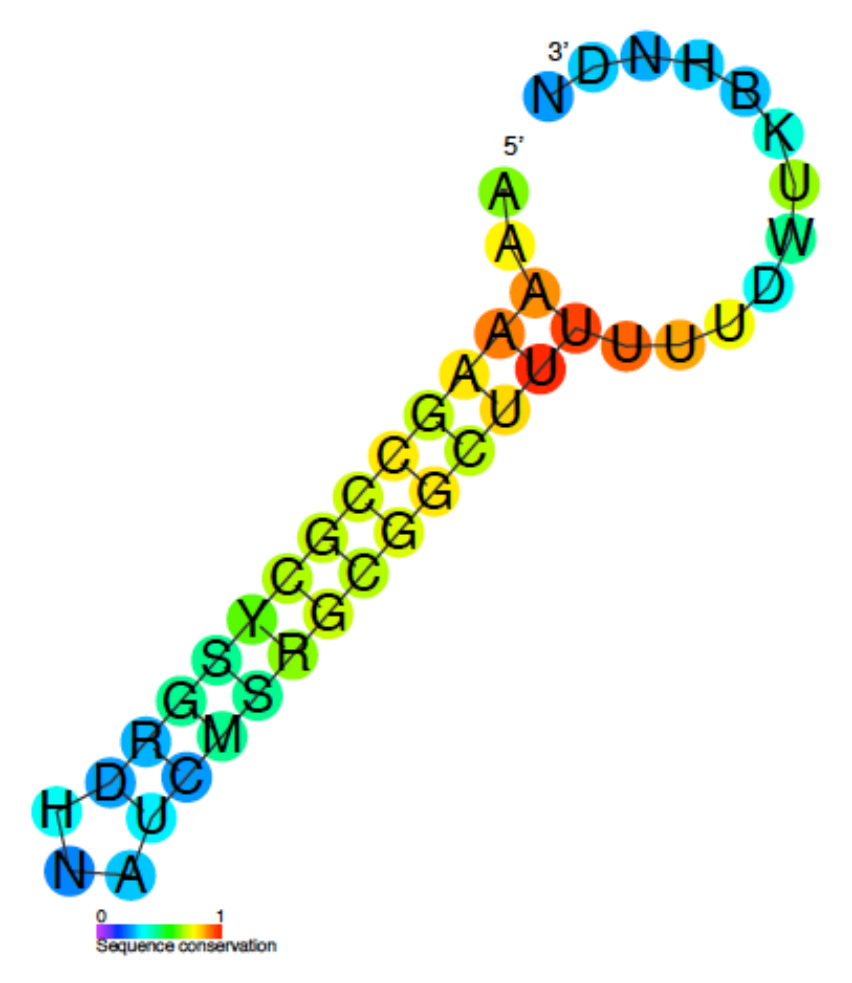
Rho-independent termination



Why care?

- Genomic “landmarks”
- Cis-regulatory components
- Fundamental biological process

A CM for Rho-independent terminators



Constructed from an alignment of 171 E. coli and 891 B. subtilis experimentally validated terminator sequences.

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RNIE: genome-wide prediction of bacterial intrinsic terminators

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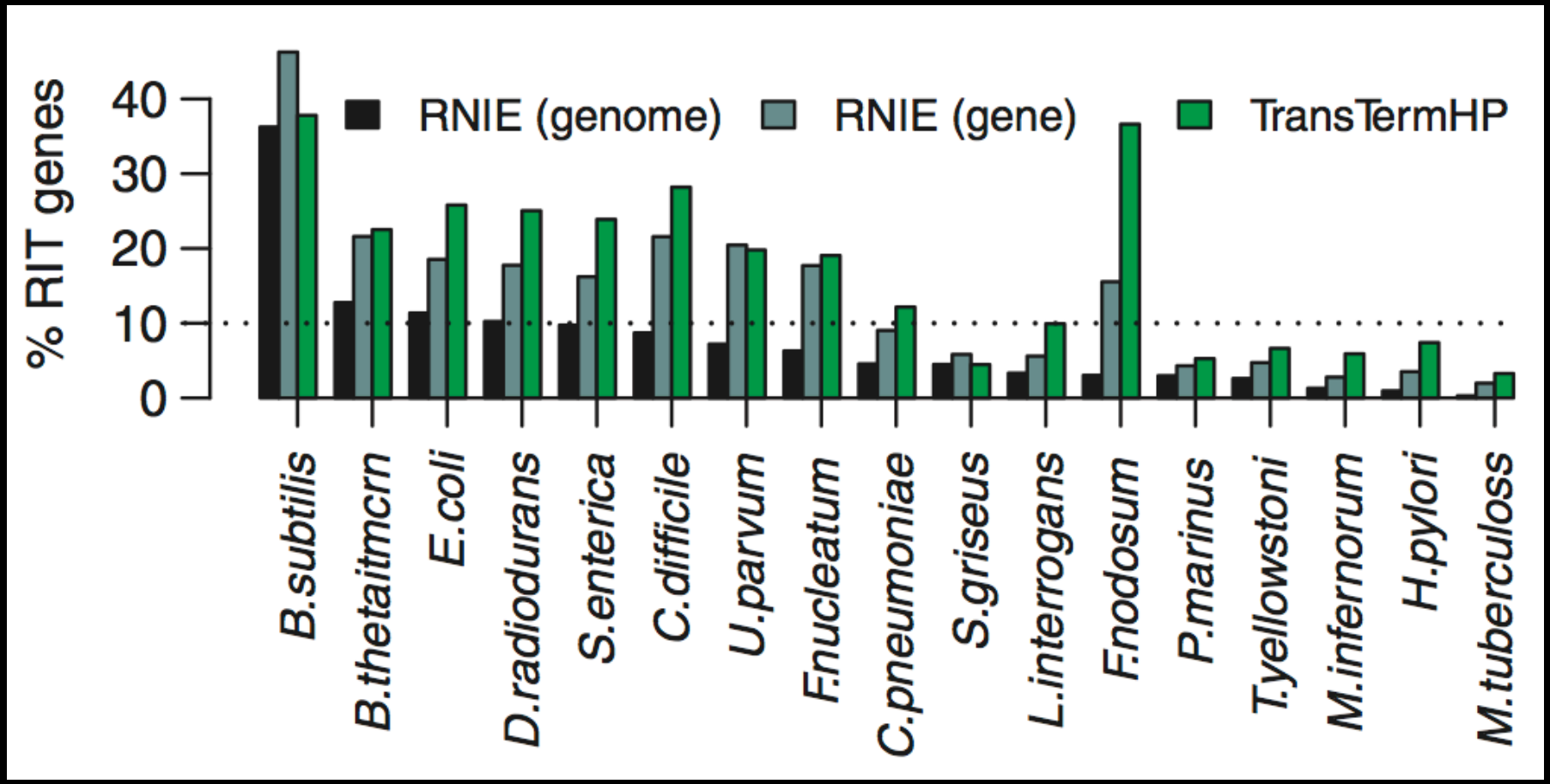
Missing terminators?



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>MT2818|100-bp terminator sequence|3054490,3054589|strand:1
GGAUGCUGCUGGUGCUGUAGCCCGGCGAGCAGACGCAAAAUCGCCUCAUUUCGGCACGAAAUGGGCGAUUUUGCGUCUGCUCGGCGGGCUACUCGCCGCC
>MT0690|100-bp terminator sequence|757228,757327|strand:-1
GCCUGCUCGGCGACCGCUGACGGCCCCGGGCGAGCAGUCGCAUAAGCCCCCGACACGCCGAGCGUGCGGGGGCUUAUGCGUCUGCUCGCCGGCCGACAAU
>MT0884|100-bp terminator sequence|958341,958440|strand:-1
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>MT2121|100-bp terminator sequence|2319422,2319521|strand:-1
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>MT1437|100-bp terminator sequence|1567875,1567974|strand:1
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>MT1127|100-bp terminator sequence|1223826,1223925|strand:1
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>MT2865|100-bp terminator sequence|3099695,3099794|strand:-1
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>MT2819|100-bp terminator sequence|3054498,3054597|strand:-1
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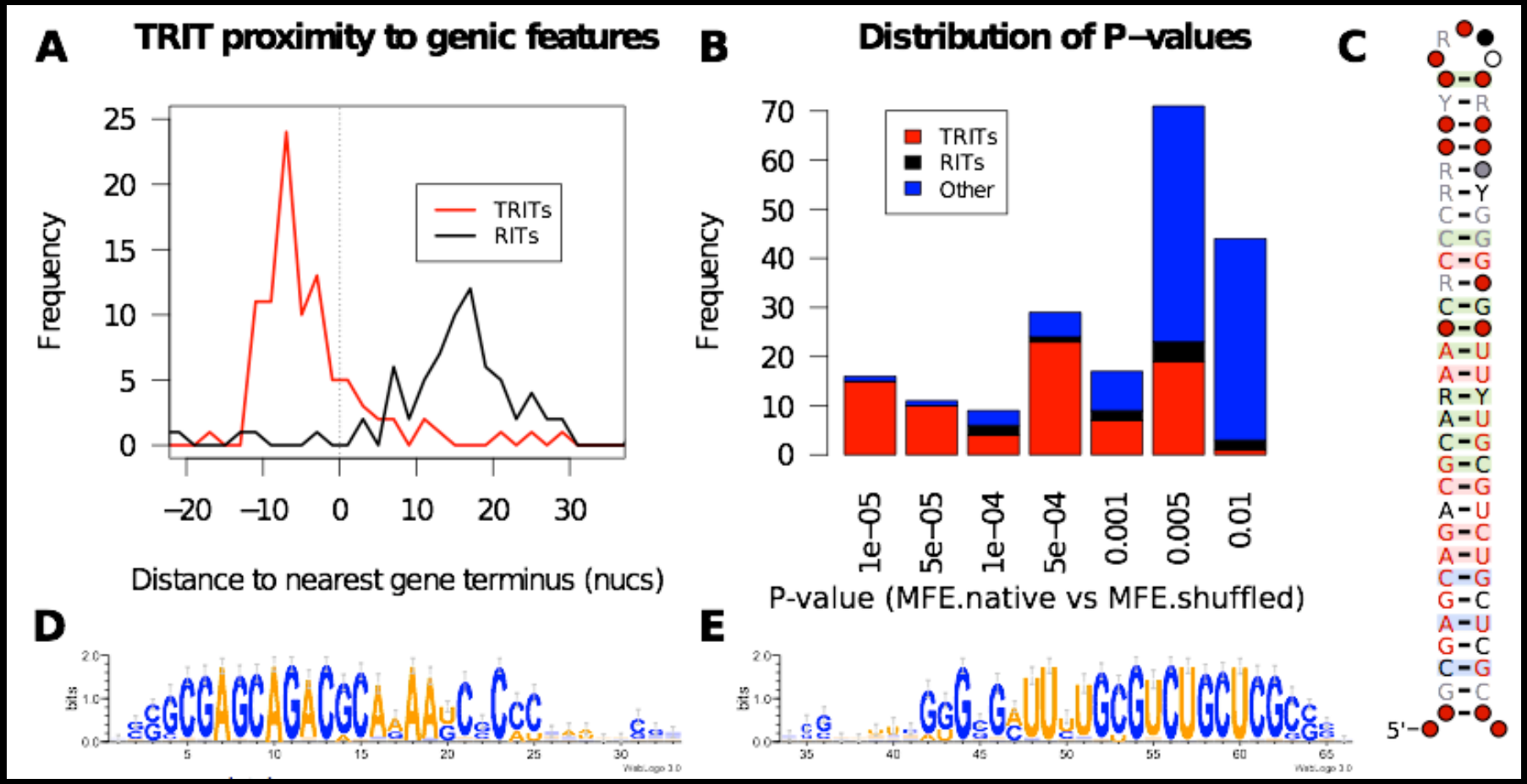
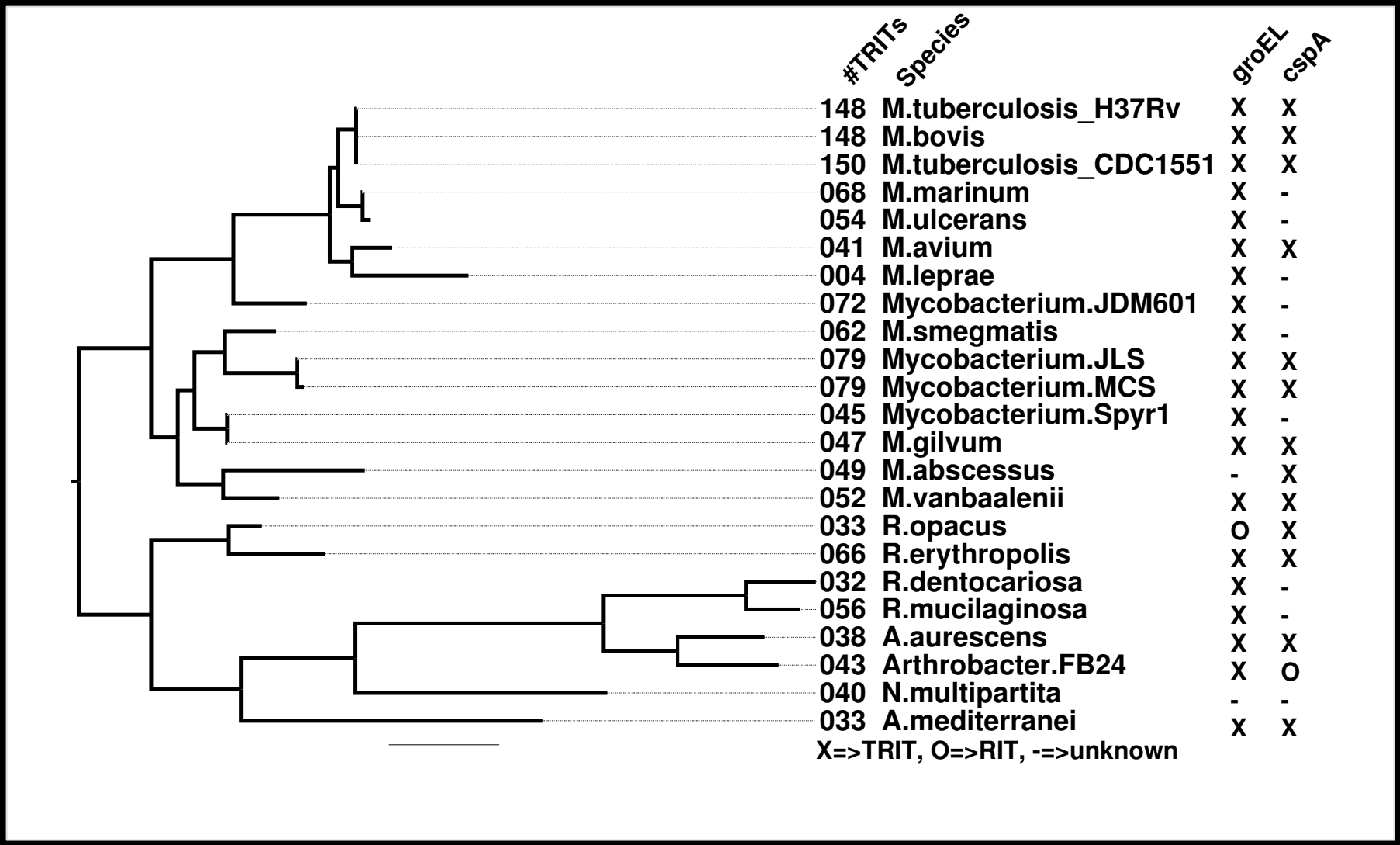
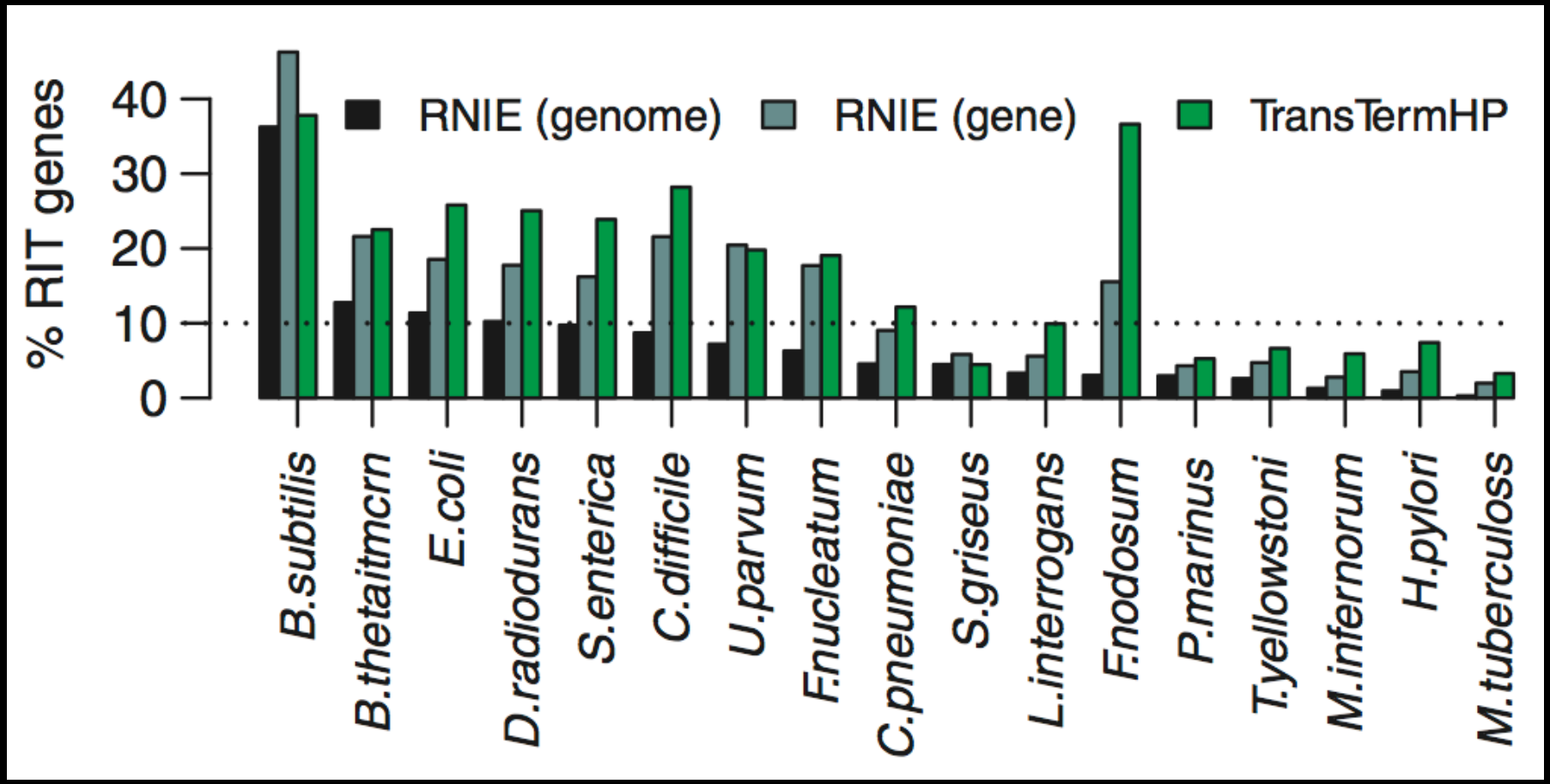
Mycobacterium tuberculosis



Missing terminators?



Missing terminators?



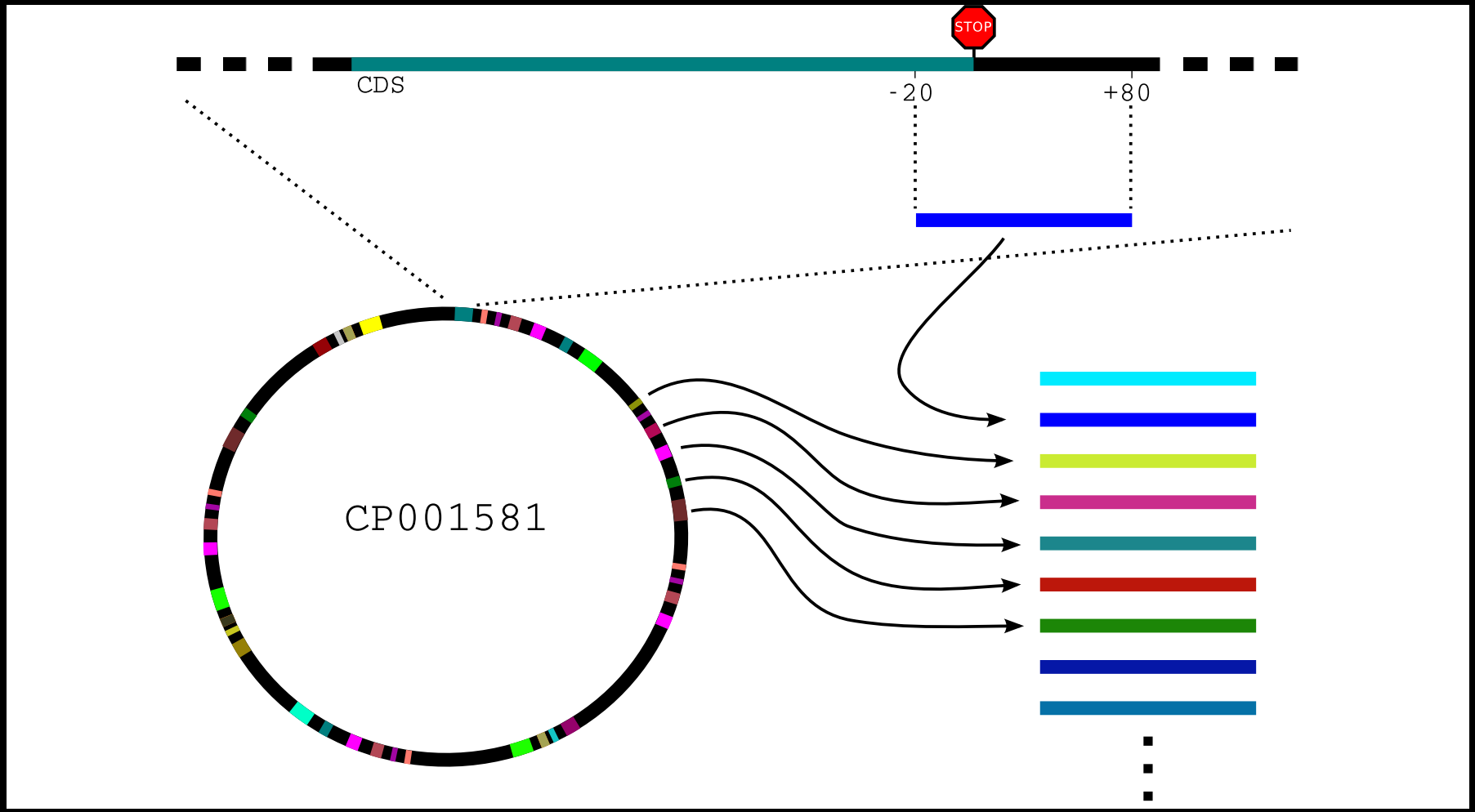
Questions

Are there terminator “families”?

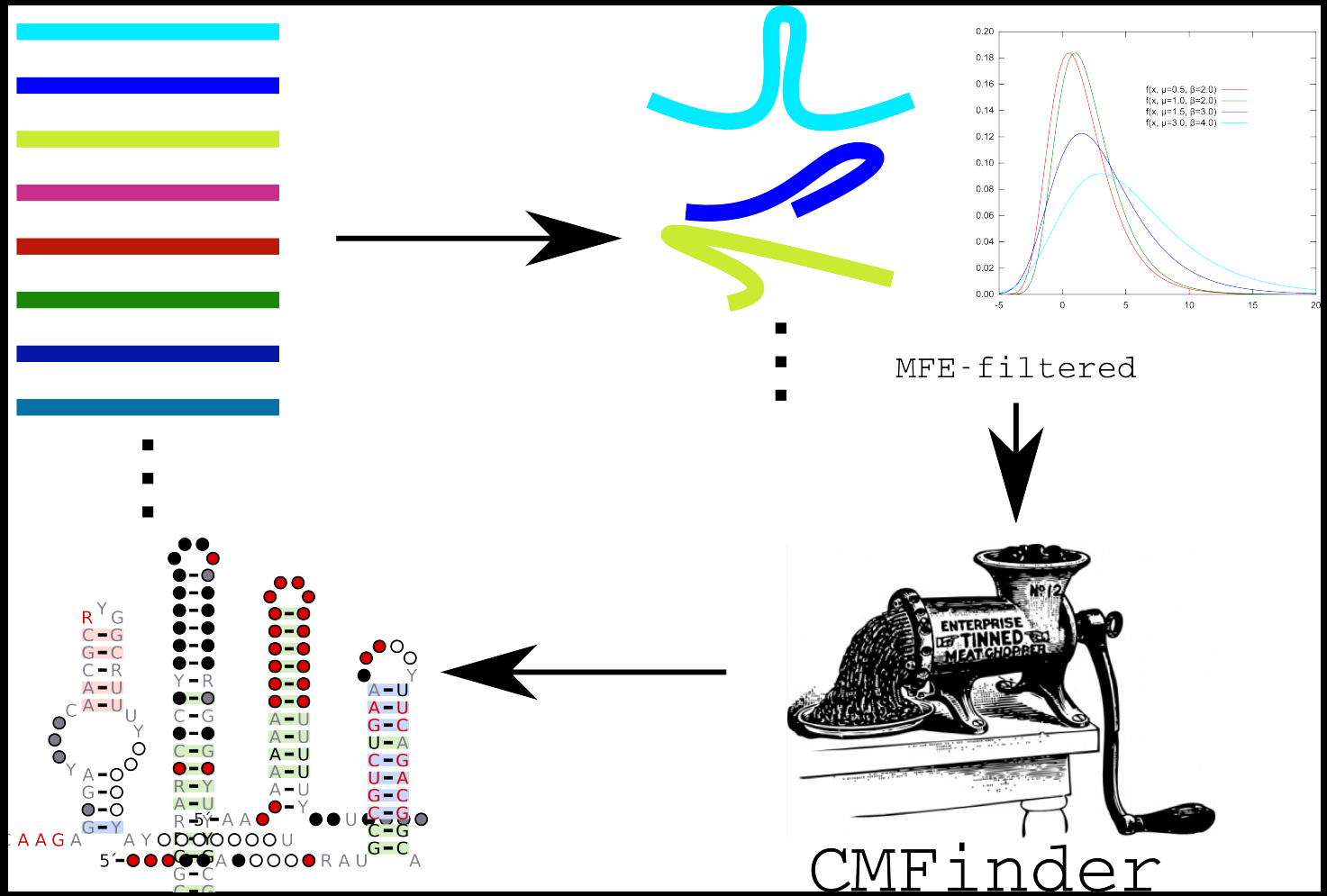
How many are there?

Do these families have a shared origin?

Mining EMBL

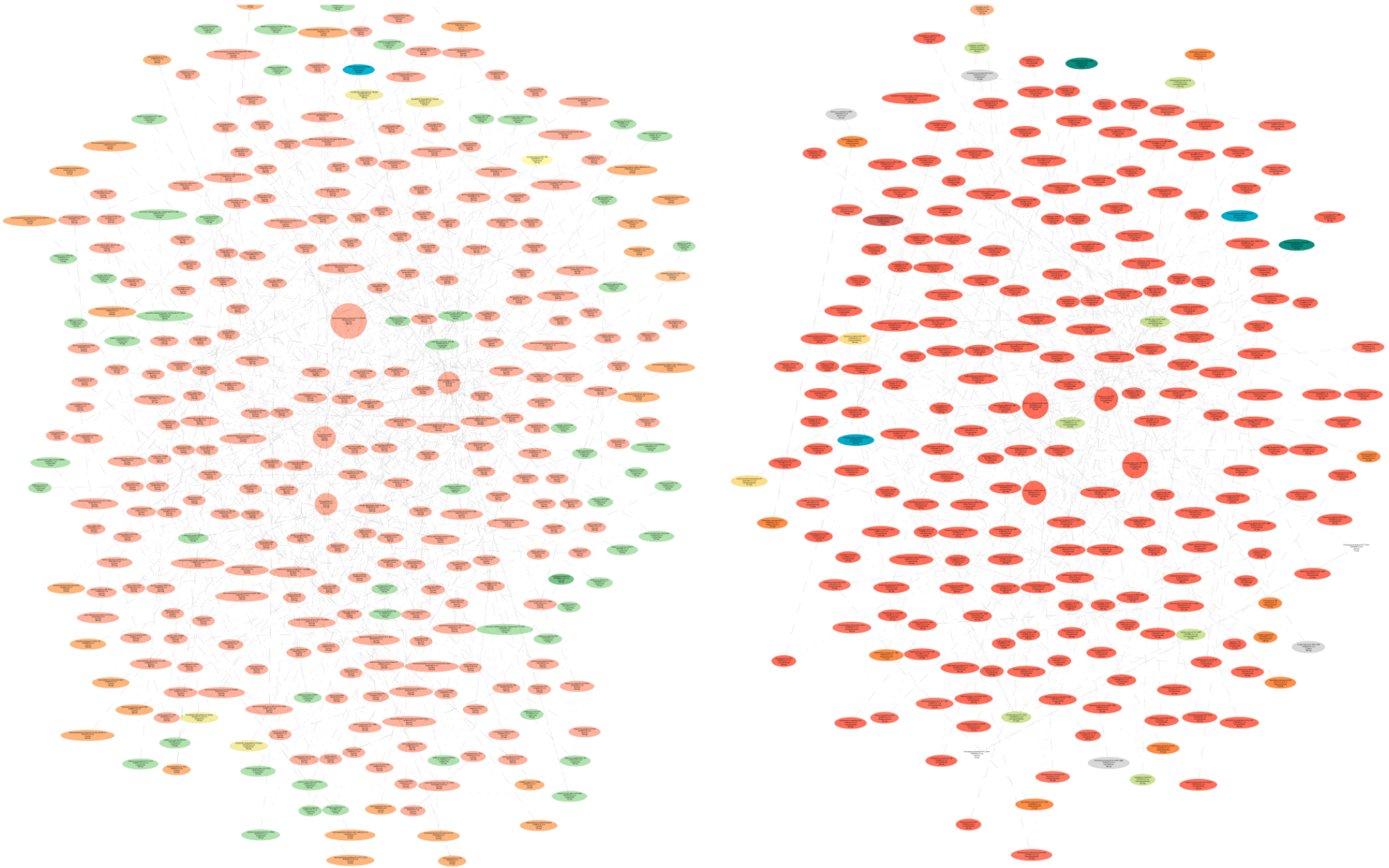


Mining EMBL



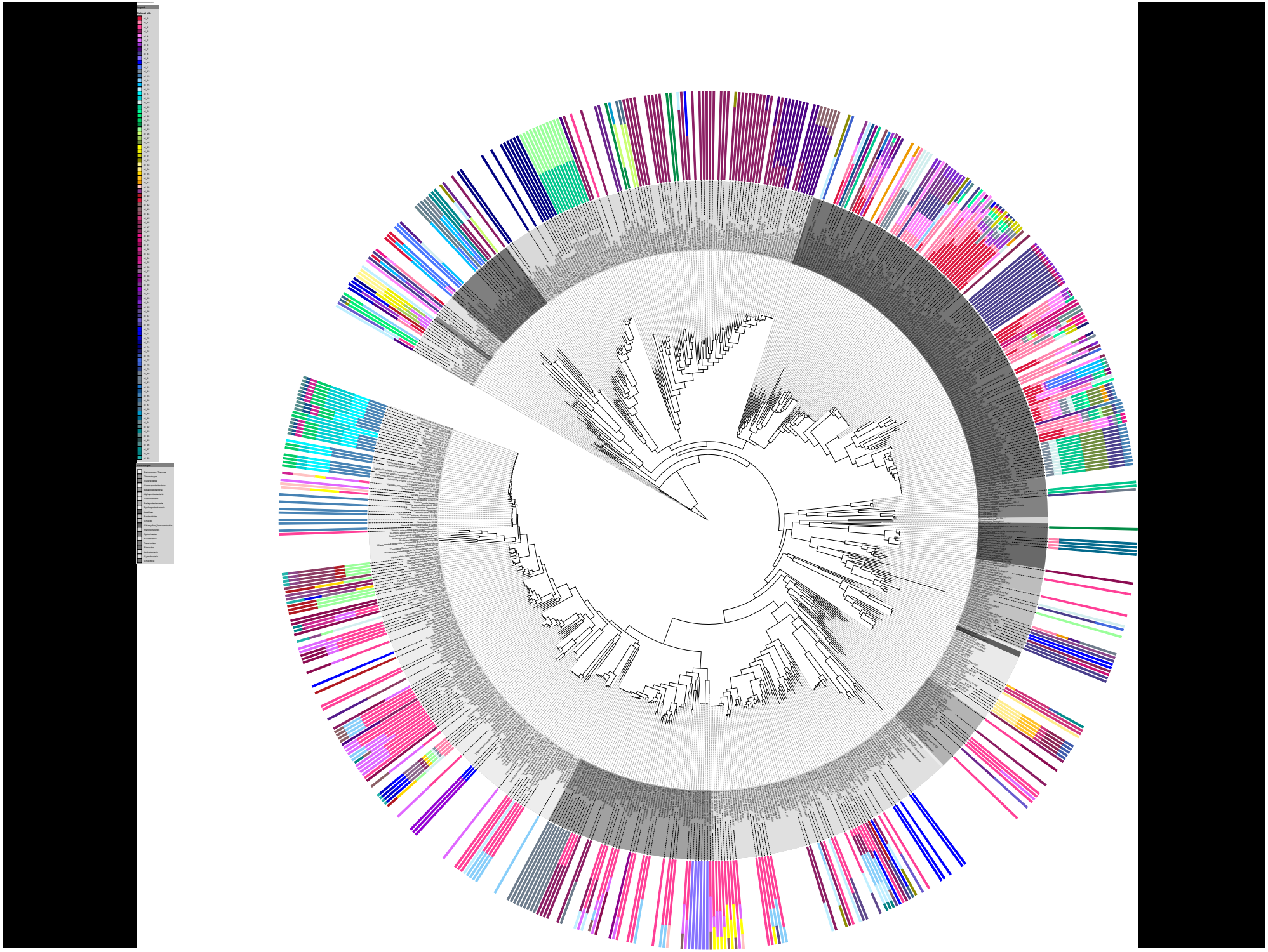
Clustering CMs

- Emit 1000 sequences from one model, score with the other & vice versa
- Average -lg(E-values) & shift positive
- Feed in to MCL (see Enright et al. TRIBE-MCL)
- Results in ~100 (non-trivial) clusters

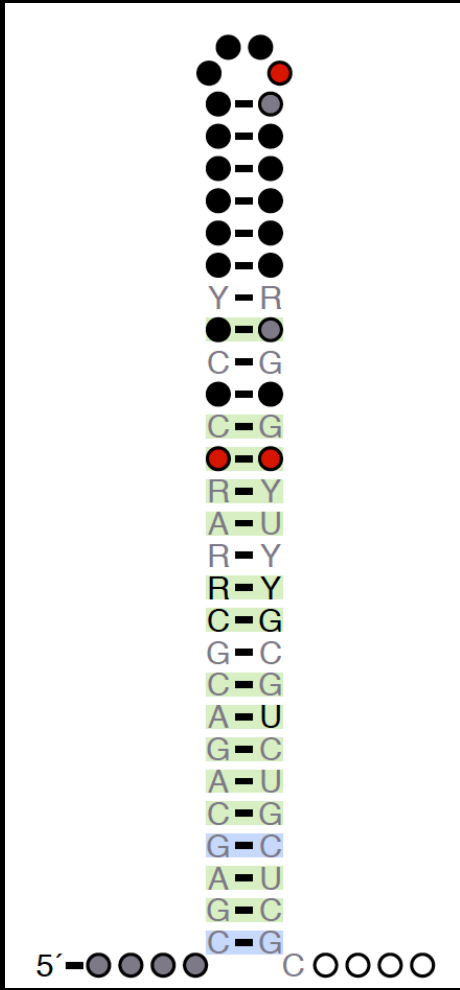


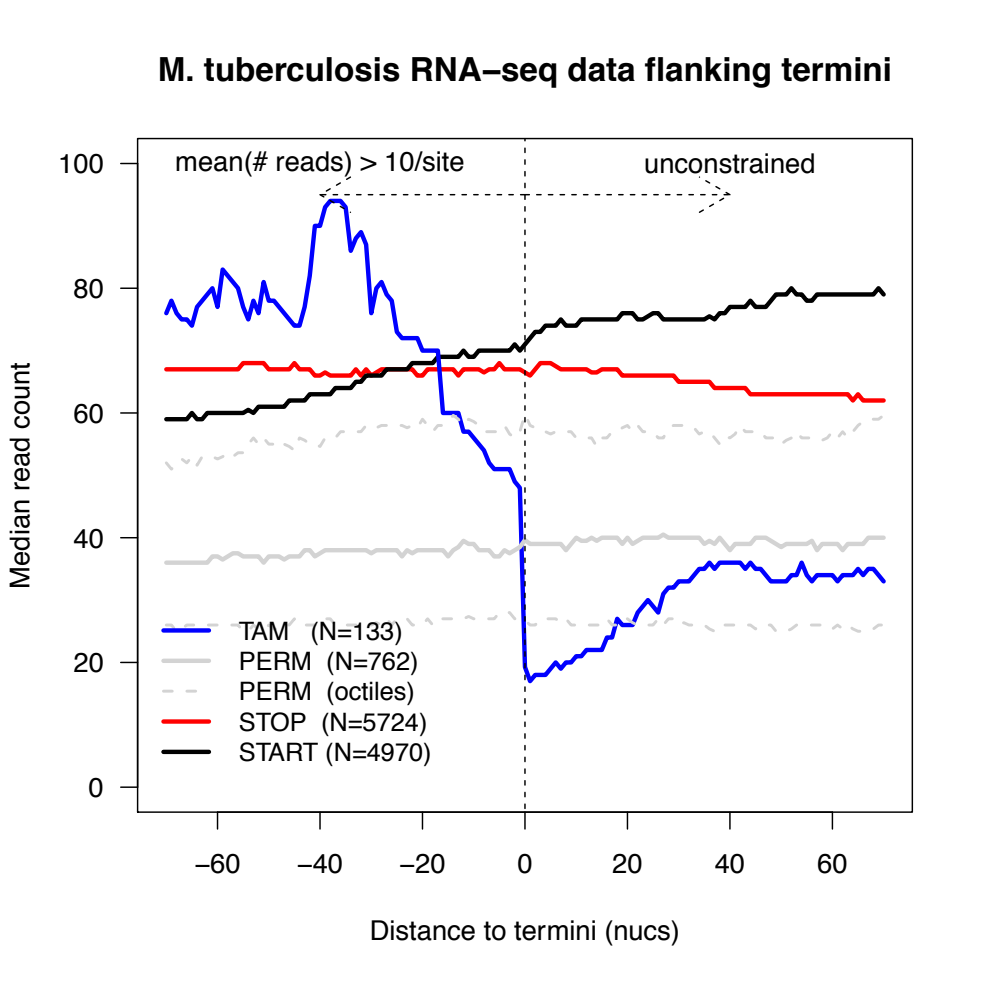
Cluster 0
73% Bacillales

Cluster 3
81% Actinobacteria



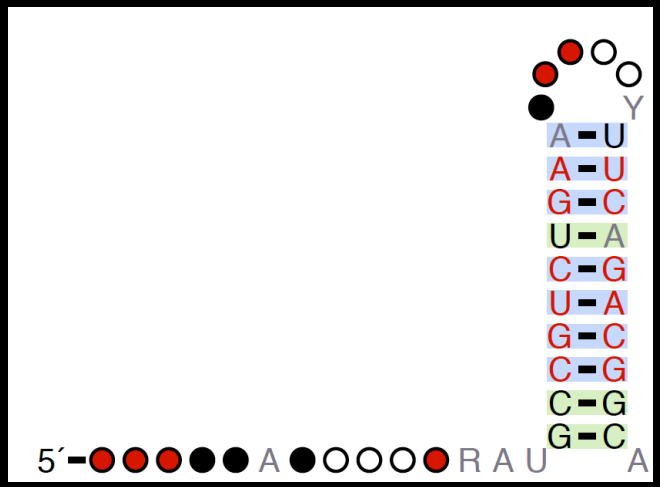
Actinobacterial Terminator



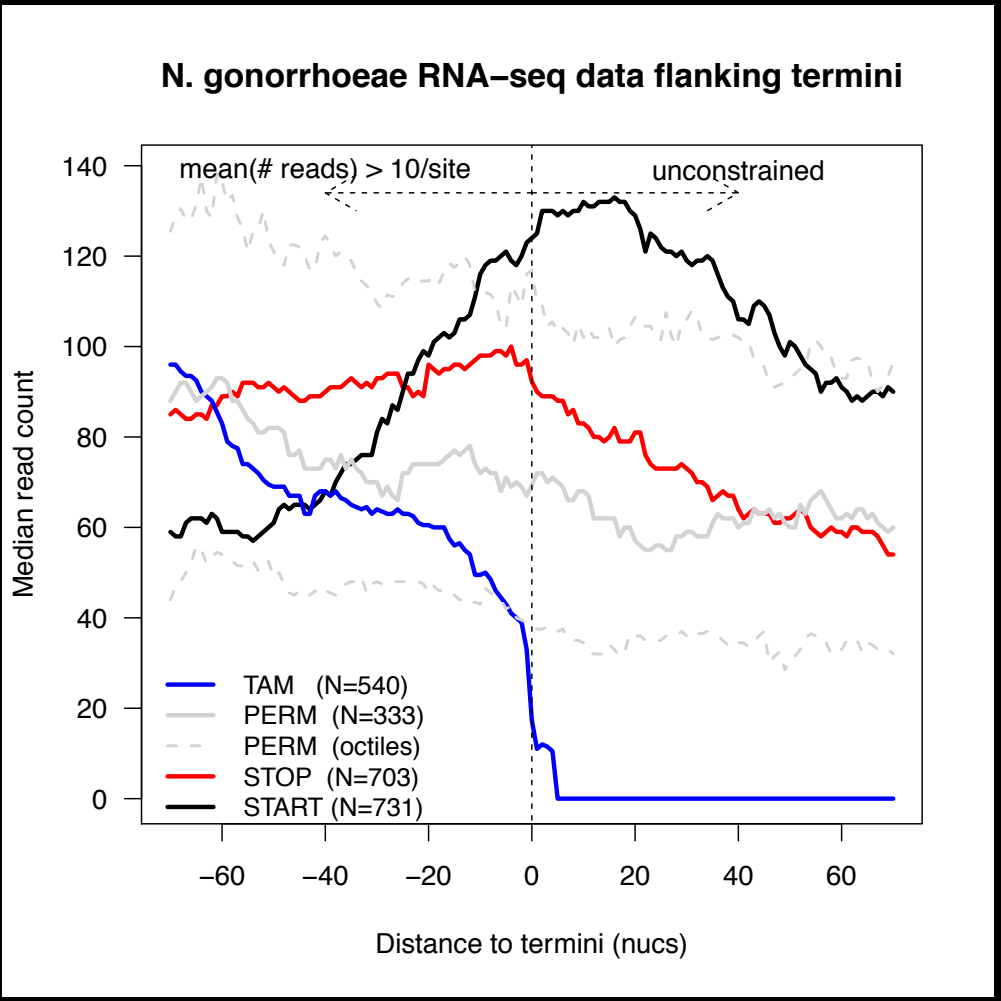


Data courtesy of KB Arnvig, NIMH

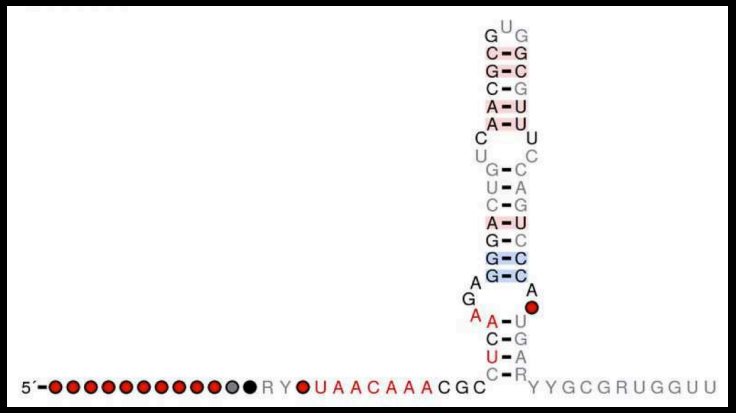
Neisseria DNA Uptake Terminator



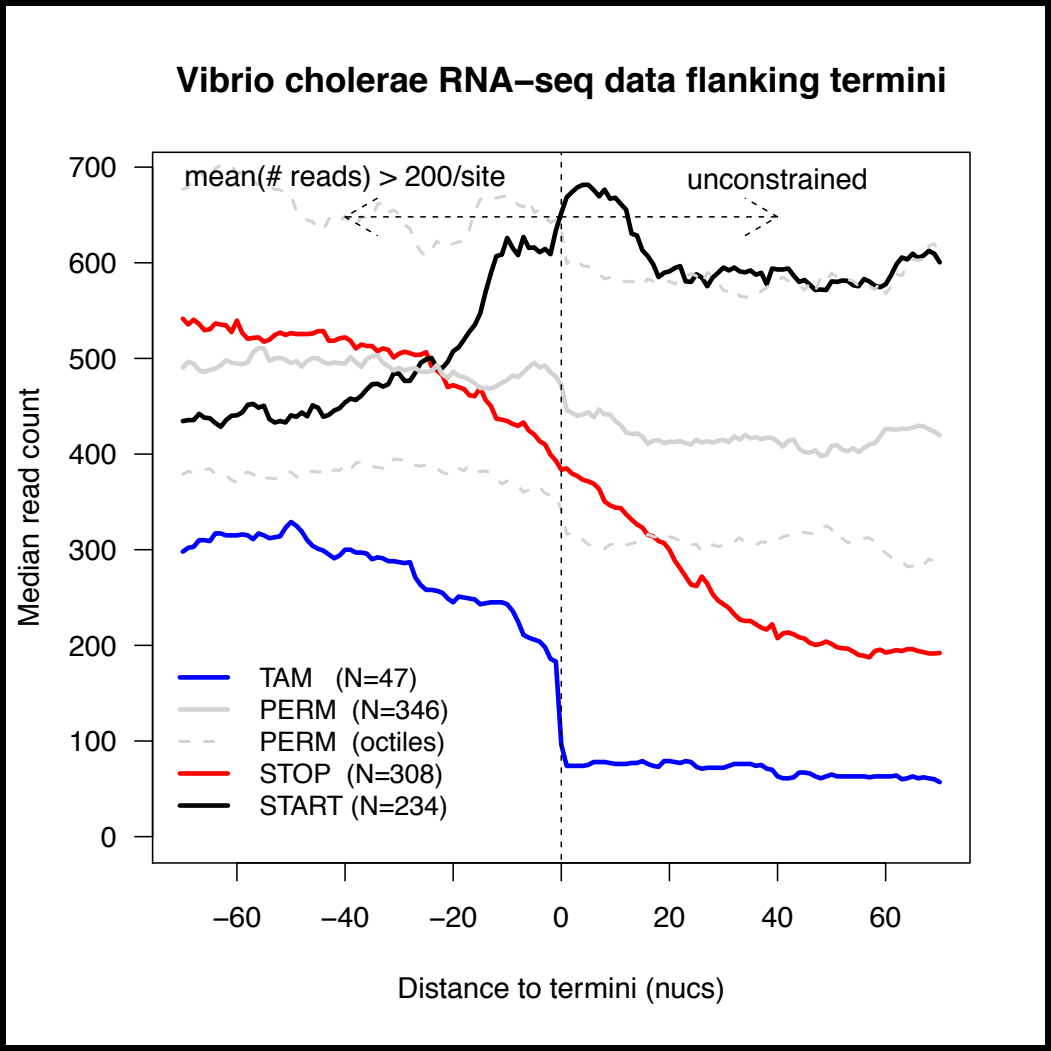
~600/genome, high percent id
Patchy poly-U tail
Exapted DNA Uptake sequence?



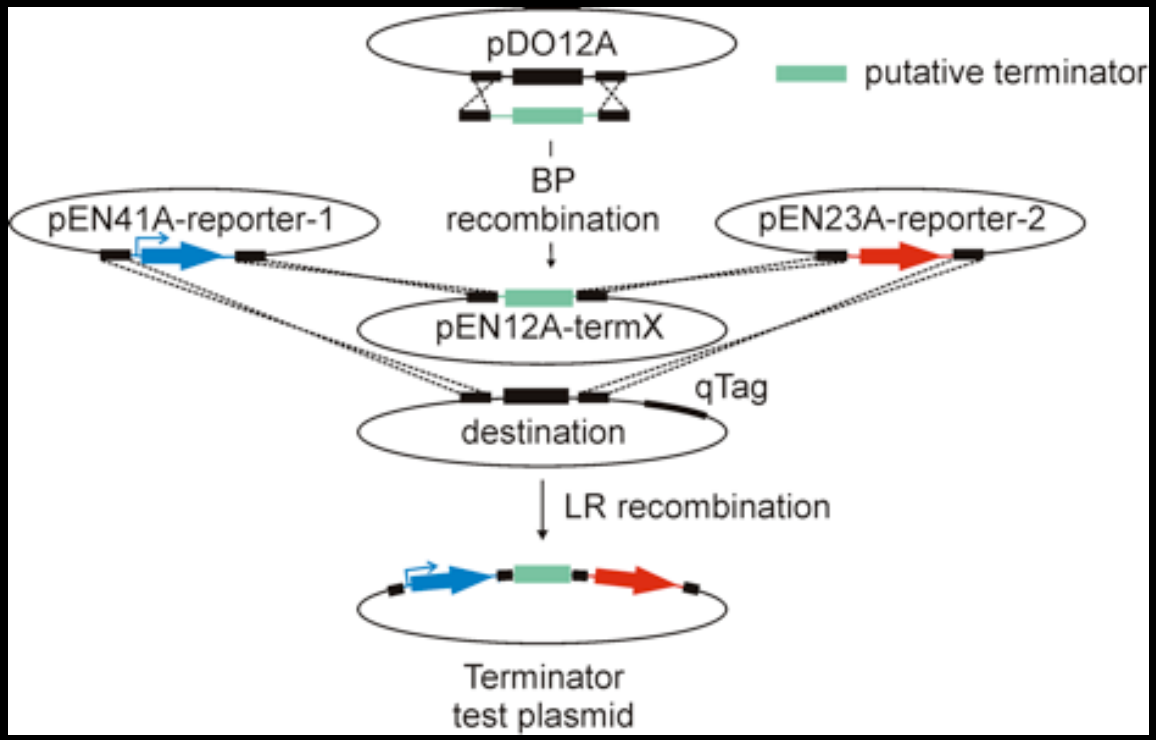
Vibrio Superintegron Terminus-Associated Motif

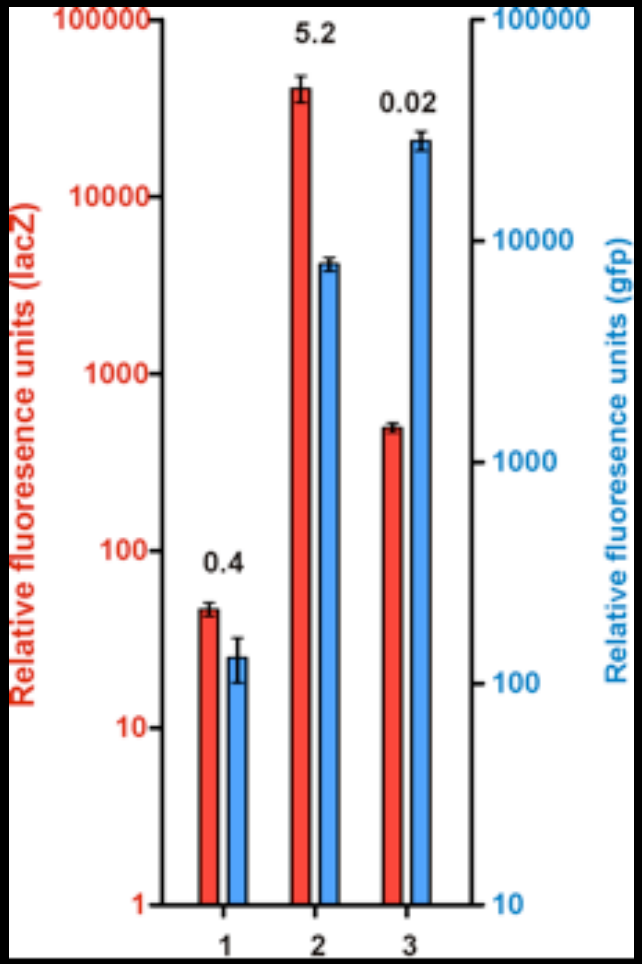


attC SI recombination site



Experimental Validation





Courtesy of D Schnappinger,
Weill Cornell Medical College

Conclusions so far...

- Rho-independent termination has arisen independently multiple times
- G/C-rich hairpin + poly-U tail appears to be the dominant (but not the only!) model for RI termination
- Connections to horizontal transfer?

Acknowledgements

Paul Gardner — University of Canterbury
James Hadfield — New Zealand

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Dirk Schnappinger — Weill Cornell Medical College, USA