

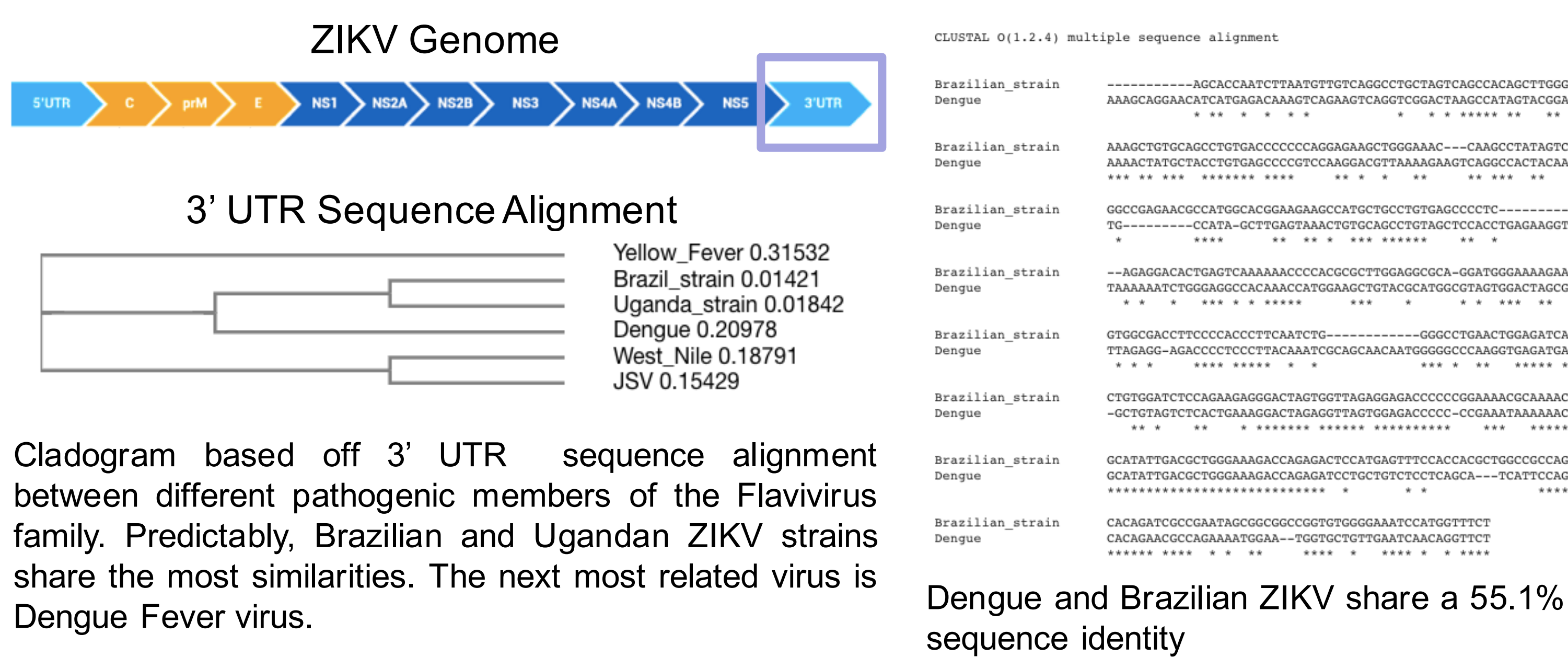
Interactions of the Zika virus 3' UTR with Host Proteins

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Abstract

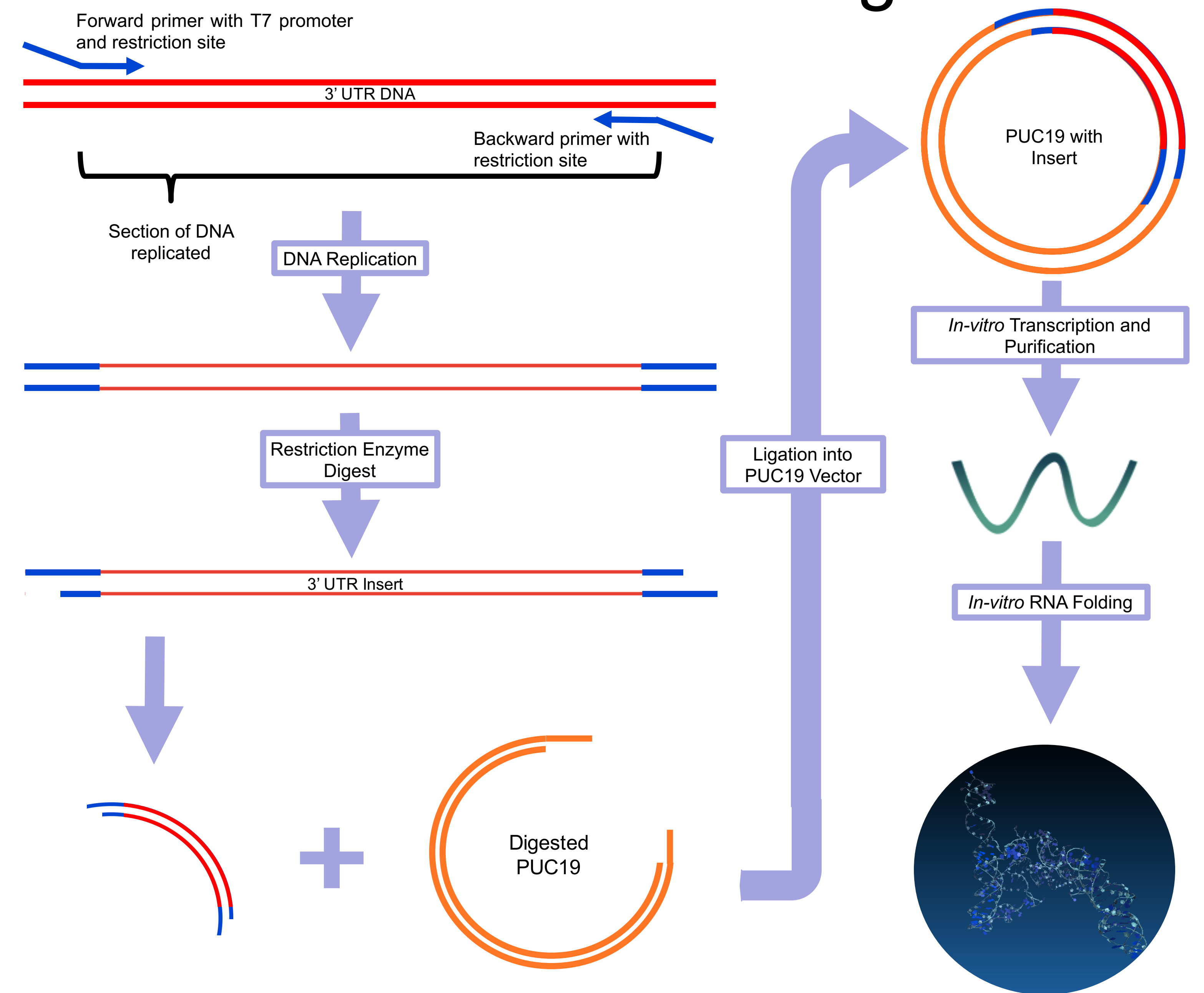
- Zika Virus (ZIKV) is a mosquito born virus
- ZIKV infection in pregnant women causes microcephaly in the developing fetus
- The genome of ZIKV is single stranded plus sense RNA
- ZIKV has untranslated regions (UTRs) that play important regulatory roles in productive infections
- The mechanisms by which these UTRs act in the cell are poorly understood
- In-vitro expression of UTRs can be used to “fish” for host proteins relevant in ZIKV infection and uncover potential druggable targets

UTR Comparisons

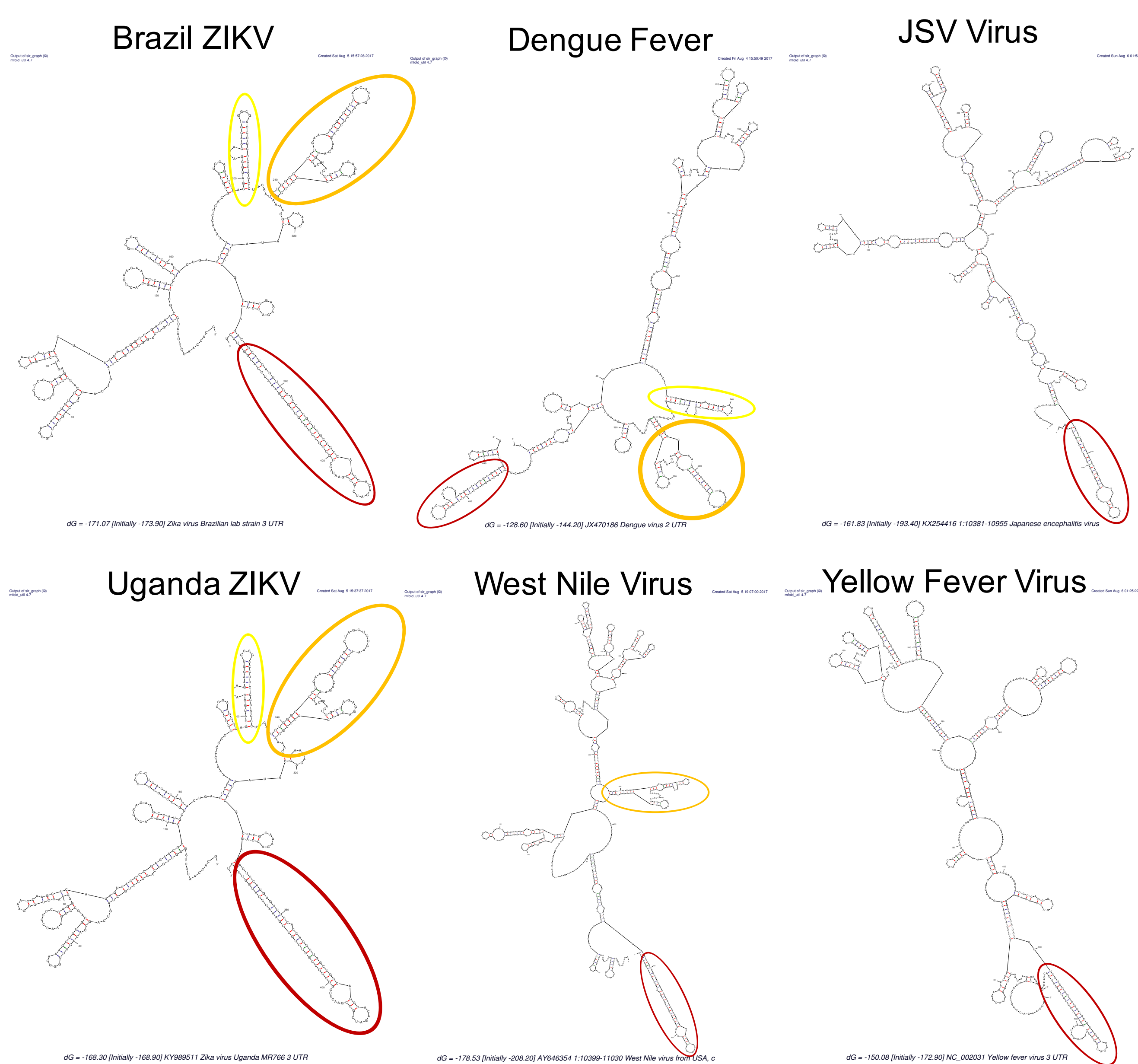


Cladogram based off 3' UTR sequence alignment between different pathogenic members of the Flavivirus family. Predictably, Brazilian and Ugandan ZIKV strains share the most similarities. The next most related virus is Dengue Fever virus.

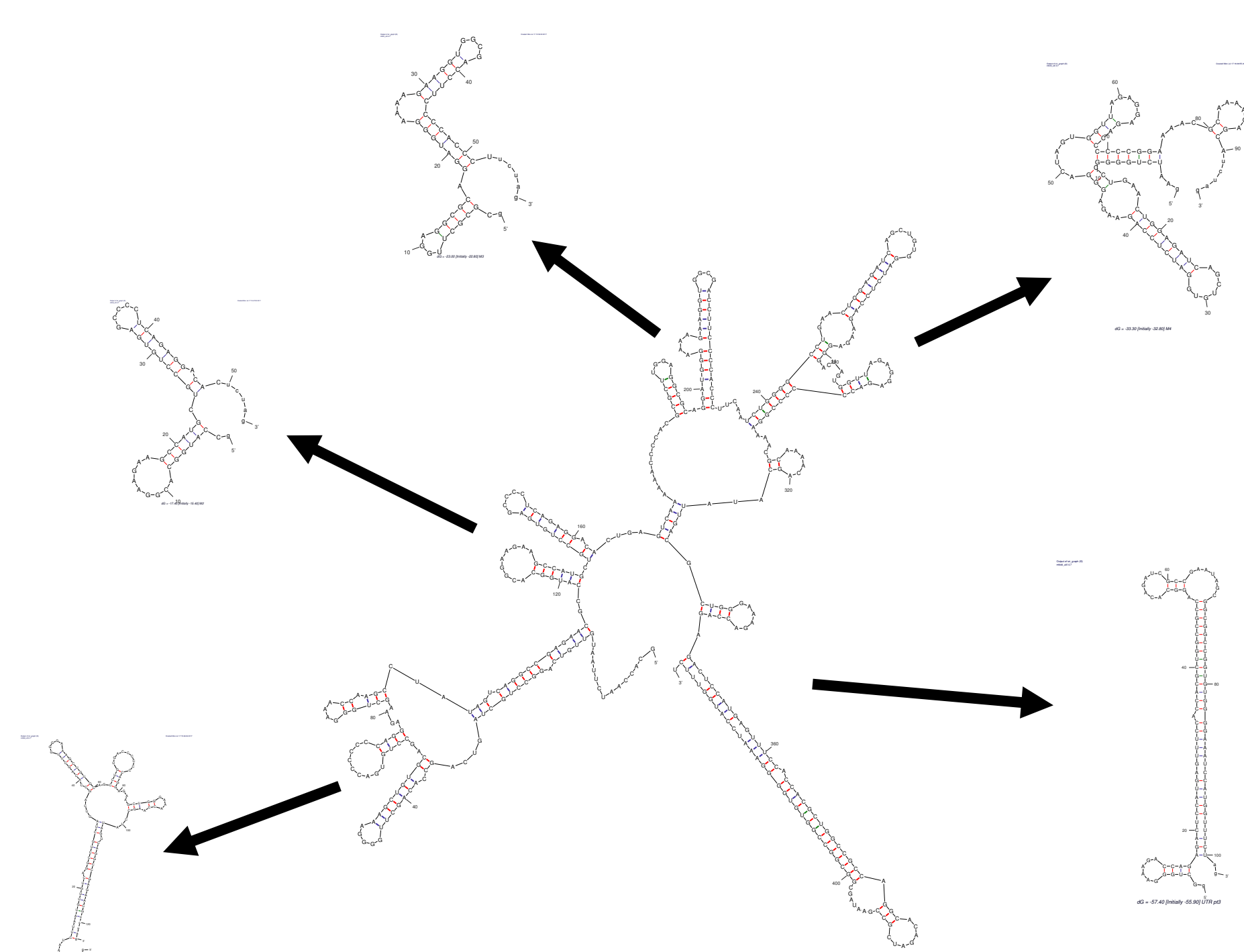
Molecular Cloning



Folded 3' UTRs

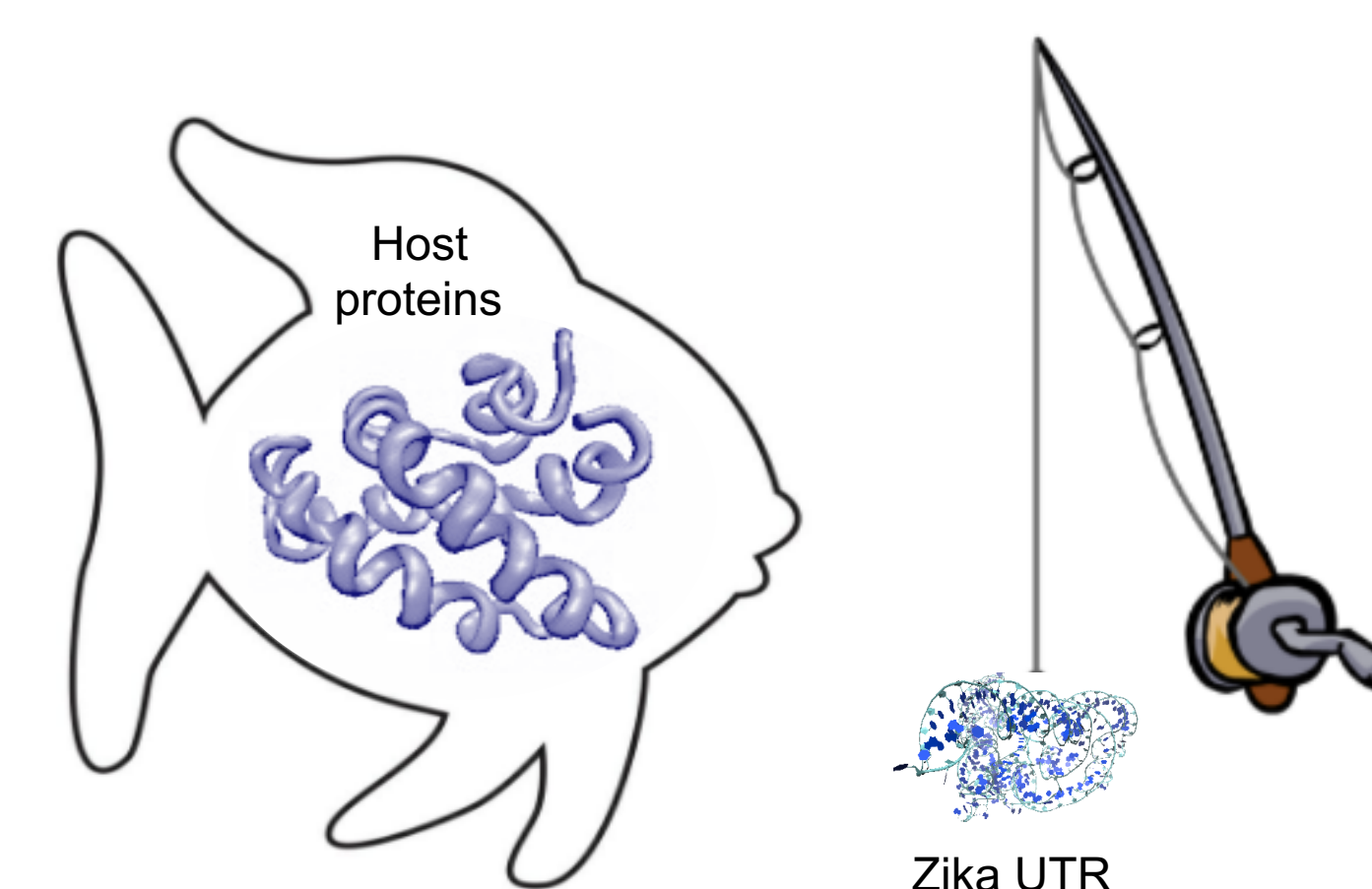


The figure above illustrates the structural similarities between 3' UTRs of 5 different Flaviviridae species. The structure enclosed by the red circle is found in nearly every Flavivirus, suggesting evolutionary conservation and physiological relevance. Structures circled in orange are found in ZIKV, Dengue, and West Nile. Structures circled in yellow are found in ZIKV and Dengue, which are most similar to each other by both genome sequence and 3' UTR structure.



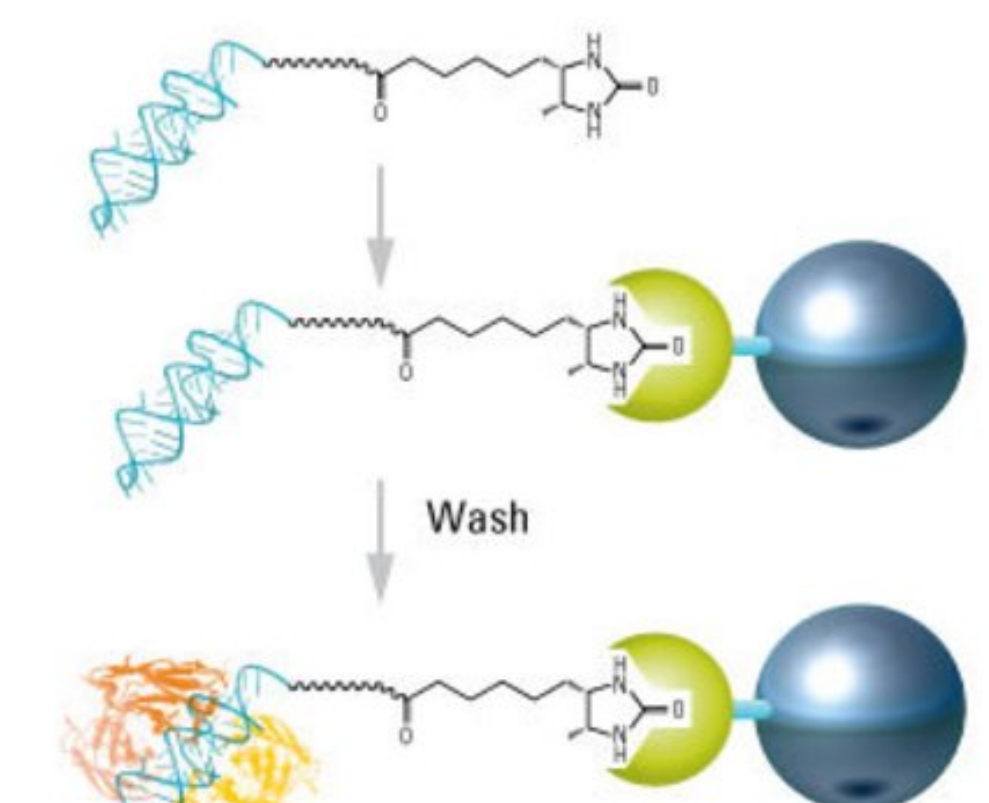
The figure on the left shows that each individual structure is stable on its own even with unavoidable modifications from molecular cloning.

Pulling Down Host-Proteins



The 3' UTR is used as a “bait” to “fish” for relevant host proteins. Any protein that interacts with the 3' UTR will bind to it.

1. RNA is attached to a biotin molecule
2. Biotin-RNA complexes are attached to metal beads
3. RNA complexes bind host proteins in cell lysate
4. Proteins are eluted and characterized by mass spectrometry and/or Western blotting



References

1. Zhu Z, Chan JF, Tee KM, Choi GK, Lau SK, Woo PC, Tse H, Yuen KY. March 16 2016. Comparative genomic analysis of pre-epidemic and epidemic Zika virus strains for virological factors potentially associated with the rapidly expanding epidemic. *Emerging Microbes & Infections* 5, e22; doi:10.1038/emi.2016.48

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