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Structural analysis of monomeric RNA-dependent polymerases

R. Jácome¹, A. Becerra², S. Ponce de León¹, A. Lazcano^{2,3,*}

¹ Facultad de Medicina, Universidad Nacional Autónoma de México, México, ² Facultad de Ciencias, Universidad Nacional Autónoma de México, México, ³ Miembro de El Colegio Nacional, México. *alar@ciencias.unam.mx

Introduction: Due to their role in replication, transcription, and reverse transcription, RNA-dependent RNA polymerases (RdRp) and reverse transcriptases (RT) are key enzymes in the viral biological cycle. Over 20 distinct viral RNA polymerases crystals from the four main RNA viral groups have been obtained. They are characterized by a right hand architecture with three functional subdomains, i.e. fingers, palm and thumb [1]; and a two metal ion mechanism of action. We present here a phylogenetic tree built based on comparisons of RdRps and RTs' tertiary structures.

Material and Methods: Pairwise structural comparisons between the different RdRps and RTs were performed with the Secondary Structure Matching program. A geometric distance measure was then estimated for each of the comparisons using the Structural Alignment Score, which is calculated according to the following formula: $(\text{RMSD} \times 100) / \text{number of aligned residues}$. The program FITCH, was used to transform the geometric distance into an evolutionary distance

Results: The unrooted phylogeny we have constructed using structural comparisons is shown in Fig.1. Single-stranded positive and double-stranded RNA viruses do not form well-defined clades, they are interspersed in different branches, each of them clustering one or two viral families. In the tree shown in Fig. 1, one branch groups ss(-)RNA viruses, i.e., the LaCrosse virus and the Orthomyxoviridae family polymerases. The longest and most distant branch groups together the RTs with the eukaryotic telomerase stemming close to the root of this clade.

Conclusion: In this work we have constructed a tertiary structure-based phylogeny that includes viral RdRps and RTs, as well as an eukaryotic telomerase. All known viral RNA polymerases are homologous monomeric enzymes. It is interesting to note that the tree presented here [1] is not consistent with the Baltimore classification of RNA viruses, suggesting the polyphyly of changes in template organization. The conserved structural similarity of the RdRps palm subdomain with the viral and cellular DNA polymerases is consistent with the hypothesis that it is one of oldest identifiable structural domains present in extant viruses and cells [2].

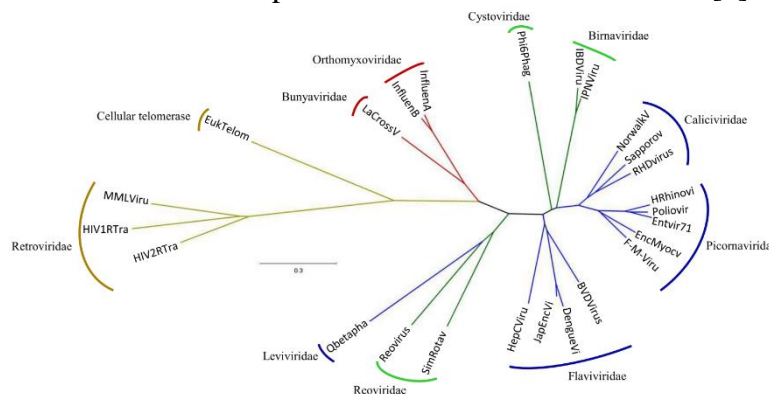


Figure 1. Unrooted dendrogram based on the comparisons of RdRps and RTs tertiary structures

References: [1] Jácome R, Becerra A, Ponce de León S, Lazcano A. PlosOne. 2015. 10.1371/journal.pone.0139001. [2] Delaye L, Vázquez H, Lazcano A. In: J. Chela-Flores, T. Owen, and F. Raulin, editors. First steps in the origin of life in the Universe: Proceedings of the Sixth Trieste Conference on Chemical Evolution. Kluwer Academic Publisher, Dordrecht. 2001: 223-230.