Reverse Transcriptase-Related Genes at the Intersection of Environmental Stress Response Pathways

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Abstract

In eukaryotes, domestication of reverse transcriptases (RT) is exceptionally rare. Throughout the course of evolution, it occurred during the major evolutionary transition converting circular into linear chromosomes in a primordial eukaryote, when telomerase RT (TERT) was recruited for maintenance of chromosome ends. This is in stark contrast to other retrotransposon ORFs (*gag*, *env*), which have been repeatedly co-opted for eukaryotic host functions. In another landmark evolutionary event, the RT domain was co-opted during the emergence of Prp8, the core component of the eukaryotic spliceosome, although it lost its polymerizing activity due to replacement of catalytic residues. The only known case of RT domain recruitment for catalytic function other than TERT is observed in *rvt* genes, a distinct type of RT which is widespread in free-living, mostly soil-dwelling, organisms, and is often subject to horizontal transfers. Most *rvt* genes are single-copy; harbor intact catalytic residues; and are exceptional in not being restricted to eukaryotes, raising the possibility that *rvt* domestication predated the emergence of TERT and Prp8. Here, we define the overlap in sets of host genes co-responding to different stresses accompanied by massive *rvt* induction in diverse hosts, revealing association with the corresponding host pathways; elucidate the molecular basis for conversion from templated to non-templated synthesis; uncover the capacity for self-organizing multimer formation upon horizontal transfers into heterologous hosts; and establish the nature of nucleic acids and extension products associated with rvt in its native host, enabling us to determine the prerequisites for efficient utilization of exogenous nucleic acids. Collectively, the data accumulated from phylogenetic, biochemical, genomic, transcriptomic, structural, and functional analyses of *rvt* genes in bacteria, fungi, and metazoans support their involvement in the host response to a diverse range of environmental stresses *via* template-independent polymerization, and outline the prerequisites for successful RT domestication.

Keywords: Reverse transcriptase, Domestication, Stress response, Adaptation

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