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Analysis of the *Tomato spotted wilt virus* RNA-dependent RNA polymerase adaptative evolution and constrained domains using homology protein structure modeling

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Tomato spotted wilt virus (TSWV; genus *Orthotospovirus*, family *Tospoviridae*) has a huge impact on a large range of plants worldwide. In this study, we determined the sequence of the large (L) segment which encodes the RNA-dependent RNA polymerase gene from a TSWV isolate (LYE51), collected from the south of France.. The analysis of the phylogenetic relationships of TSWV-LYE51 with other TSWV isolates shows that it is closely related to other European isolates. A 3D model of the RdRp was built based on the RdRp structure of the *La Crosse virus* (genus *Orthobunyavirus*, family *Peribunyaviridae*) using the LYE51 RdRp sequence. Finally, an analysis of positive and negative selection was carried out on 31 TSWV full-length RNA L sequences and confronted with the phylogeny and the protein structure data. We show that the 19 codons that are under positive selection correlate with the isolate geographical origin and are distributed all along the gene. On the contrary, the codons associated with negative selection concentrate especially in two highly constrained domains, the thumb domain and the endonuclease in charge of the cap-snatching mechanism. Those two domains could constitute good targets to develop genetic resistance by loss-of-susceptibility.

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