

Supplementary Material

An Insight into Emerging Begomoviruses and Their Satellite Complex causing Papaya Leaf Curl Disease

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Table S1. Known genes regulating the amount and efficacy of Begomovirus transmission in *B. tabaci*.

Gene	Acronym	Action site	Consequence	Reference
Defensin	<i>BtDef</i>	Expressed in ➤ Salivary gland ➤ Midgut ➤ Fat bodies ➤ Ovaries	➤ DsRna-silencing lowers the large quantity expression of begomovirus in midgut.	[1]
Cyclophilin B	<i>CypB</i>	Expressed in ➤ Salivary gland ➤ Midgut	➤ Oral feeding with CypB antibodies reduces the begomovirus transmission	[2]
Knottin-1	<i>Knot-1</i>	Expressed in ➤ Abdomen	➤ Controls the amount of virus. ➤ DsRna-silencing accelerates the ingested quantity of virus and transmitted to host(plant) by various order of magnitude.	[3]
Peptidoglycan recognition protein	<i>BtPGRP</i>	Co-localized with begomovirus in midgut	➤ Up-regulated upon ingestion of begomovirus.	[4, 5]
HSP70	<i>HSP70</i>	Expressed in ➤ Midgut epithelial cells ➤ Co-localized with begomovirus in midgut	➤ Controls or inhibit virus transmission. ➤ Oral feeding with <i>HSP70</i> antibodies enhances the begomovirus transmission	[6]
Midgut protein	<i>MGP</i>	Expressed in ➤ Midgut	➤ Interacts with Coat protein of virus to ease transmission.	[7]
Components of clathrin-mediated endocytosis	<i>CME</i>	Expressed in ➤ Midgut barrier	➤ Transport of viruses transversely the gut barrier into the haemolymph	[8]

Table S2. Mechanistic action of various Begomoviruses-encoded RNA silencing suppressor protein (VSRs) to counter RNAi-mediated host defense.

Begomovirus(es)	VSRs	Regulate Host Biology	Reference
<i>African cassava mosaic virus</i>	AC2	Interacts with transcriptional gene silencing	[9]
<i>Tomato golden mosaic virus</i>	AC2	Prevents transcriptional gene silencing and inactivates adenosine kinase	[10, 11]
<i>Tomato yellow leaf curl virus</i>	AC2	Interacts with transcriptional gene silencing	[9]
	V2	Unites with Suppressor of gene silencing3(SGS3) and inhibits secondary siRNA production	[12]
	C4	Inhibits intercellular circulation of siRNA	[13]
<i>Tomato yellow leaf curl China virus</i>	βC1	Suppresses S-adenosyl-homocysteine-hydrolase and transcriptional gene silencing; Degrades SGS3 and stimulates Rgs-CaM (regulator of gene silencing calmodulin-like protein), thus inhibit secondary siRNA production	[14, 15]
<i>Tomato leaf curl New Delhi virus</i>	AC4	Cleaves Argonautes4 and affects transcriptional gene silencing	[16]
<i>Mungbean yellow mosaic virus</i>	AC4	Sequesters and suppresses systemic movement of siRNA	[17]
<i>Mungbean yellow mosaic India virus</i>	AC5	Represses the expression of CHH cytosine transferase, thus obstruct RNA-directed DNA methylation	[18]
	AC2	Interferes with RNA dependent RNA polymerase6 and Argonautes1	[19]
<i>Cotton leaf curl Multan virus</i>	C4	Interferes with S-adenosyl methionine synthetase and inhibits transcriptional gene silencing	[20]

References

- [1] Wang, Z.Z.; Bing, X.L.; Liu, S.S.; Chen, X.X. RNA interference of an antimicrobial peptide, Btdef, reduces tomato yellow leaf curl China virus accumulation in the whitefly *Bemisia tabaci*. *Pest Manag. Sci.* **2017**, *73*, 1421–1427. doi: 10.1002/ps.4472.
- [2] Kanakala, S.; Ghanim, M. Implication of the whitefly *Bemisia tabaci* Cyclophilin B protein in the transmission of tomato yellow leaf curl virus. *Front. Plant Sci.* **2016**, *7*, 1702. doi: 10.3389/fpls.2016.01702.
- [3] Hariton-Shalev, A.; Sobol, I.; Ghanim, M.; Liu, S.S.; Czosnek, H. The Whitefly *Bemisia tabaci* knottin-1 gene is implicated in regulating the quantity of tomato yellow leaf curl virus ingested and transmitted by the insect. *Viruses* **2016**, *8*, 205. doi: 10.3390/v8070205.
- [4] Wang, Z.Z.; Shi, M.; Huang, Y.C.; Wang, X.W.; Stanley, D.; Chen, X.X. A peptidoglycan recognition protein acts in whitefly (*Bemisia tabaci*) immunity and involves in Begomovirus acquisition. *Sci. Rep.* **2016a**, *6*, 37806. doi: 10.1038/srep37806.
- [5] Wang, L.L.; Wang, X.R.; Wei, X.M.; Huang, H.; Wu, J.X.; Chen, X.X.; Liu, S.S.; Wang, X.W. The autophagy pathway participates in resistance to tomato yellow leaf curl virus infection in whiteflies. *Autophagy* **2016b**, *12*, 1–15 doi: 10.1080/15548627.2016.1192749.
- [6] Götz, M.; Popovski, S.; Kollenberg, M.; Gorovits, R.; Brown, J.K.; Cicero, J.; Czosnek, H.; Winter, S.; Ghanim, M. Implication of *Bemisia tabaci* heat shock protein in begomovirus whitefly interactions. *J. Virol.* **2012**, *84*, 13241–13252 doi: 10.1128/JVI.00880-12.
- [7] Rana, V.P.; Popli, S.; Saurav, G.K.; Raina, H.S.; Chaubey, R.; Ramamurthy, V.V.; Rajagopal, R. A *Bemisia tabaci* midgut protein interacts with begomoviruses and plays a role in virus transmission. *Cell. Microbiol.* **2016**, *18*, 663–678. doi: 10.1111/cmi.12538.
- [8] Pan, L.L.; Chen, Q.F.; Zhao, J.J.; Guo, T.; Wang, X.; Hariton-Shalev, A.; et al. Clathrin-mediated endocytosis is involved in tomato yellow leaf curl virus transport across the midgut barrier of its whitefly vector. *Virology* **2017**, *502*, 152–159. doi: 10.1016/j.virol.2016.12.029.
- [9] Trinks, D.; Rajeswaran, R.; Shivaprasad, P.V.; Akbergenov, R.; Oakeley, E.J.; Veluthambi, K.; et al. Suppression of RNA silencing by a geminivirus nuclear protein, AC2, correlates with transactivation of host genes. *J. Virol.* **2005**, *79*(4), 2517–27. doi: 10.1128/JVI.79.4.2517-2527.2005.
- [10] Wang, H.; Buckley, K.J.; Yang, X.; Buchmann, R.C.; Bisaro, D.M. Adenosine kinase inhibition and suppression of RNA silencing by geminivirus AL2 and L2 proteins. *J. Virol.* **2005**, *79*(12), 7410–8. doi: 10.1128/JVI.79.12.7410-7418.2005.
- [11] Buchmann, R.C.; Asad, S.; Wolf, J.N.; Mohannath, G.; Bisaro, D.M. Geminivirus AL2 and L2 proteins suppress transcriptional gene silencing and cause genome-wide reductions in cytosine methylation. *J. Virol.* **2009**, *83*(10), 5005–13. doi: 10.1128/JVI.01771-08.
- [12] Glick, E.; Zrachya, A.; Levy, Y.; Metz, A.; Gidoni, D.; Belausov, E.; Citovsky, V.; Gafni, Y. Interaction with host SGS3 is required for suppression of RNA silencing by tomato yellow leaf curl virus V2 protein. *Proc. Natl. Acad. Sci. U. S. A.* **2008**, *105*(1), 157–61. doi: 10.1073/pnas.0709036105.
- [13] Rosas-Díaz, T.; Zhang, D.; Fan, P.; Wang, L.; Ding, X.; Jiang, Y.; et al. A virus-targeted plant receptor-like kinase promotes cell-to-cell spread of RNAi. *Proc. Natl. Acad. Sci. U. S. A.* **2018**, *115*(6), 1388–1393. doi: 10.1073/pnas.1715556115.
- [14] Yang, X.; Xie, Y.; Raja, P.; Li, S.; Wolf, J.N.; Shen, Q.; et al. Suppression of Methylation-Mediated Transcriptional Gene Silencing by βC1-SAHH Protein Interaction during Geminivirus-Betasatellite Infection. *PLoS Pathog.* **2011**, *7*(10), e1002329. doi: 10.1371/journal.ppat.1002329.
- [15] Li, F.; Zhao, N.; Li, Z.; Xu, X.; Wang, Y.; Yang, X.; et al. A calmodulin-like protein suppresses RNA silencing and promotes geminivirus infection by degrading SGS3 via the autophagy pathway in *Nicotiana benthamiana*. *PLoS Pathog.* **2017**, *13*(2), e1006213. doi: 10.1371/journal.ppat.1006213.
- [16] Vinutha, T.; Gaurav, K.; Varsha, G.; Tomas, C.; Peter, P.; Ramesh, S.V.; Shelly, P. Tomato geminivirus encoded RNAi suppressor protein, AC4 interacts with host AGO4 and precludes viral DNA methylation. *Gene* **2018**, *678*, 184–195. doi: 10.1016/j.gene.2018.08.009.
- [17] Carluccio AV, Prigiallo MI, Rosas-Díaz T, Lozano-Duran R, Stavolone L. S-acylation mediates Mungbean yellow mosaic virus AC4 localization to the plasma membrane and in turns gene silencing suppression. *PLoS Pathog.* **2018**, *14*(8), e1007207. doi: 10.1371/journal.ppat.1007207.

- [18] Li, F.; Xu, X.; Huang, C.; Gu, Z.; Cao, L.; Hu, T.; Ding, M.; Li, Z.; Zhou, X. The AC5 protein encoded by Mungbean yellow mosaic India virus is a pathogenicity determinant that suppresses RNA silencing-based antiviral defenses. *New Phytol.*, **2015**, 208(2), 555–69. doi:10.1111/nph.13473.
- [19] Kumar, R.V.; Singh, A.K.; Singh, A.K.; Yadav, T.; Basu, S.; Kushwaha, N.; Chattopadhyay, B.; Chakraborty, S. Complexity of begomovirus and betasatellite populations associated with chilli leaf curl disease in India. *J. Gen. Virol.*, **2015**, 96, 3157–3172. doi:10.1099/jgv.0.000254.
- [20] Ismayil, A.; Haxim, Y.; Wang, Y.; Li, H.; Qian, L.; Han, T.; et al. *Cotton Leaf Curl Multan virus* C4 protein suppresses both transcriptional and post-transcriptional gene silencing by interacting with SAM synthetase. *PLoS Pathog.*, **2018**, 14(8), e1007282. doi: 10.1371/journal.ppat.1007282.