In Silico PepYLCV

by Jamsari Jamsari

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In silico analysis of PepYLCV-βC1 protein interaction with pepper-SnRK1 for pathogenicity prediction

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B Nova[1] and J Jamsari[1*]

[1] Doctoral Program of Agriculture Science, Departement of Agriculture, Andalas University, Padang, West Sumatra, 25163, Indonesia
[2]Department of Agrotechnology, Agriculture Faculty, Universitas Andalas, Padang, West Sumatera, 25136, Indonesia

E-mail: ajamsari@yahoo.com

Abstract. Pepper yellow leaf curl virus [PepYLCV] is a monopartite begomovirus that is usually associated with a beta satellite which encodes a pathogenicity protein [βC1] responsible for symptom appearance. A recent study revealed that plants overexpressing SnRK1 were delayed for symptom appearance and lower levels of satellite DNA. The current study provided the interaction of PepYLCV BC1 and Pepper SnRK1 protein by using computational approaches including homology modeling and protein-protein docking. The reliability of the 3D model was validated by using the Procheck server. Findings suggest that ubiquitin-associated [UBA] and auto-inhibitory sequence [AIS] domains of Pepper-SnRK1 are involved in the PepYLCV-βC1 interaction. Findings provide computational data support for domain-level interactions to predict the pathogenicity of new monopartite begomoviruses that lack known experimental data.

1. Introduction

Geminiviruses pose a serious threat to food security and sustainability worldwide by causing massive losses to food and agricultural products such as pepper, cassava, tomatoes, maize, and cotton. The genomes of geminivirus consist of one [monopartite] or two [bipartite] circular single-stranded DNA [ssDNA] molecules packaged in twinned icosahedral particles [1]. Monopartite begomoviruses are associated with ssDNA elements referred to as alpha or beta satellites. Alpha-satellites are self-replicating ssDNA and encode replication initiator proteins and share replication origin characteristics. Beta-satellites are pathogenic determinants that depend entirely on their helper virus for replication, encapsulation, and vector transmission functions.

Previous studies have isolated Pepper yellow leaf curl virus [PepYLCV] from West Sumatera and associated with Pepper yellow leaf curl disease [PepYLCD] [2]. PepYLCV is a monopartite begomovirus and encodes a single protein called BC1 which is a pathogenic determinant and is crucial for the development of symptoms and the reinforcement of host-virus accumulation. Previous studies have shown that BC1 interacts with many host proteins to control plant immune responses [3][4][5][6][7] and facilitates infection and transmission of begomovirus [8][9][10][11][12], one of these is the protein SnRK1 [13][14]. Here, we describe the computational protein-protein interaction that regulates PepYLCV-BC1 with Pepper-SnRK1 protein.

2. Materials and Method

2.1. Protein Sequence

The PepYLCV-BC1 information was obtained from the PepYLCV genome NCBI database [2]. The Pepper SnRK1 information was obtained from Capsicum annum NCBI database [15].

2.2. In silico three-dimensional protein modeling

The three-dimensional structure of PepYCLV-BC1 was predicted using Phyre2 [16]. Quality assessment was performed with ProFunc [17].

2.3. Domain and binding site prediction

CASTp binding site was used to determine possible and potential binding sites [18].

2.4. Protein-protein interaction

Protein-protein interaction was confirmed with PatchDock and FireDock [19][20].

3. Results and Discussion

3.1. In silico three-dimensional protein modeling

Phyre 2 analysis showed PepYLCV-BC1 encodes a 118 aa protein and Pepper-SnRK1 encodes a 512 aa protein. Among all models predicted with Phyre2, the most accurate model was selected based on the Ramachandran plot for PepYLCV-BC1 [Figure 1A] and Pepper-SnRK1 [Figure 1B].

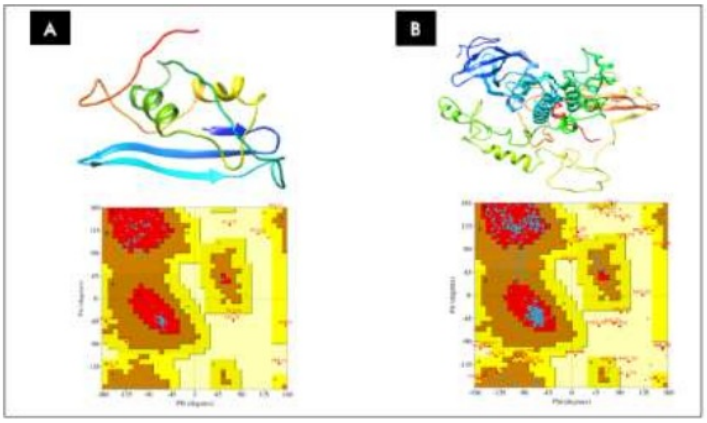

Figure 1. Ramachandran Plot of PepYLCV-BC1 and Pepper-SnRK1.

Three-dimension modeling protein and Ramachandran plot of [A] PepYLCV-BC1 [B] Pepper-SnRK1. Most favored regions are shown as [a, b, L]. Ramachandran Plot analysis of PepYLCV-BC1 showed that 85.3% of residues located in the favoured region, 6.9% in the allowed region, and 7.8% in the outlier region. Further, analysis of Pepper-SnRK1 showed 82.2% residues located in the favoured region, 11.6% in the allowed region, and 6.3% in the outlier region. This result signifying the accuracy of models.

3.2. Domain and binding site prediction

PROCHECK analysis showed PepYLCV-BC1 consisting of only one domain, Beta-satellite pathogenicity beta C1 [115 aa] [Figure 2A]. Further, Pepper-SnRK1 consisting of three domains,

Protein kinase domain [250 aa], Ubiquitin-associated domain [40 aa], and Kinase-associated domain [41 aa] [Figure 2B].

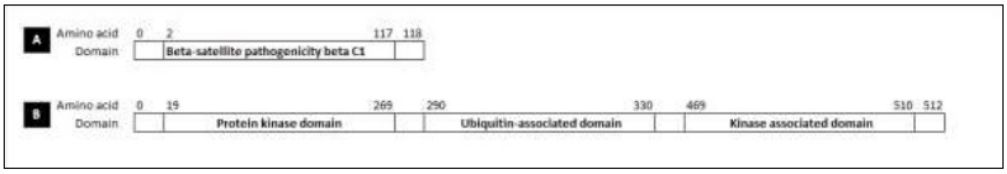

Figure 2. Domain analysis of PepYLCV-BC1 and Pepper-SnRK1.

Sequence motifs of [A] PepYLCV-BC1 [B] Pepper-SnRK1. The name of the motif is written within the box. Amino acid/residue position shown in the number above the box. SnRK1 are essentially protein kinases associated with different physiological mechanisms that regulate energy metabolism in plants that provide nutrients against biotic and abiotic stress [21]. The plant protein SnRK acts as an antiviral agent, generating pathogen resistance by phosphorylation of pathogen or host protein [13]. The experimental assay showed positive interaction between Cotton leaf curl mutant beta-satellite [CLCuMB]-BC1and Cotton-SnRK1 within the Ubiquitin-associated domain and kinase-associated domain [near C –terminal domain] [22]. Our research was also showed a similar finding between PepYLCV-BC1 [Figure 3A] and Pepper-SnRK1 [Figure 3B].

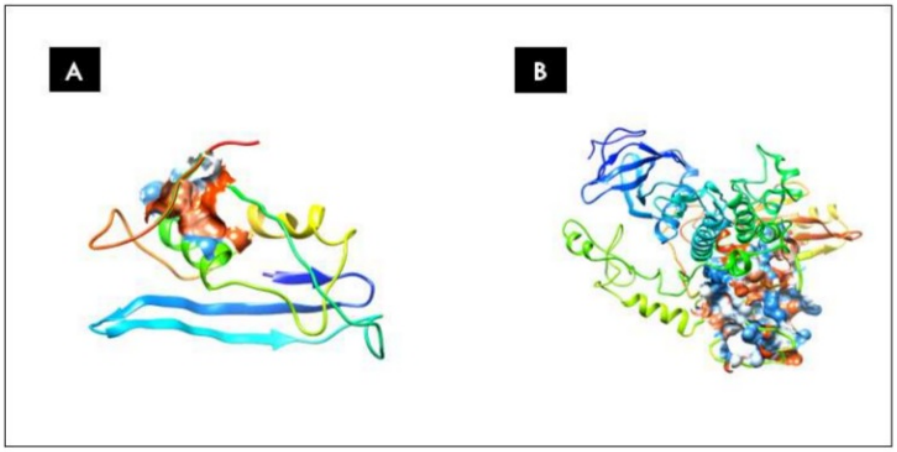

Figure 3. Binding site analysis of PepYLCV-BC1 and Pepper-SnRK1.

Binding site prediction of [A] PepYLCV-BC1 [B] Pepper-SnRK1. Binding sites were shown in colored pockets, hydrophobic [red] and hydrophilic [blue]. CASTp analysis of PepYLCV-BC1 showed that highly potential binding sites within the alpha-helix region in the C-terminal domain, and Pepper-SnRK1 within the Ubiquitin-associated domain and kinase-associated domain. This result presenting the similarity of interaction, both in computation and experiment.

3.3. Protein-protein interaction

The protein-protein analysis showed the interaction of PepYLCV-BC1 and Pepper-SnRK1 was located near to the predicted binding site [Figure 4].

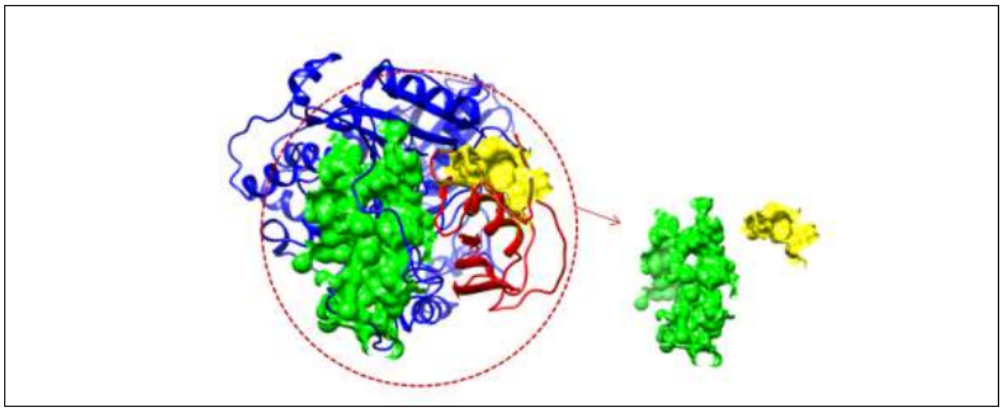

Figure 4. Docking of PepYLCV-BC1 and Pepper-SnRK1 Protein.

Protein-protein interaction of PepYLCV-BC1 [red] and Pepper-SnRK1 [blue]. Binding sites were shown in colored pockets, PepYLCV-BC1[yellow] and Pepper-SnRK1 [green]. PatchDock and FireDock analysis showed that interaction of PepYLCV-BC1 and Pepper-SnRK1 located in the predicted binding site. This similar result between binding site prediction and protein interaction indicating the accuracy of protein-protein interaction in nature.

4. Conclusion

Our findings provide an alternative approach to predict begomovirus and pepper interactions in silico. Both of binding site prediction and docking analysis could predict potential interaction regions. Our results have shown the C-terminal domain PepYLCV-BC1 interacts with Pepper-SnRK1 Ubiquitin-associated domain and kinase-associated domain, which also within the C-terminal domain. This result could be useful in virus suppression by knocking out via the CRISPR/Cas9 method.

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