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Artificial intelligence (AI)-based protein modeling for the interpretation of grapevine genetic variants

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Abstract

Genetic variants known to produce single residue missense mutations have been associated with phenotypic traits of commercial interest in grapevine. This is the case of the K284N substitution in VviDXS1 associated with muscat aroma, or the R197L in VviAGL11 causing stenospermocarpic seedless grapes. The impact of such mutations on protein structure, stability, dynamics, interactions, or functional mechanism can be studied by computational methods, including our pyDock scoring, previously developed. For this, knowledge on the 3D structure of the protein and its complexes with other proteins and biomolecules is required, but such knowledge is not available for virtually none of the proteins and complexes in grapevine. Fortunately, the possibility of modeling proteins and complex structures with Artificial Intelligence (AI)-based methods like AlphaFold2 and AlphaFold2-Multimer will facilitate the application of this approach to proteins and complexes without available structure. Moreover, we are developing new methods based on AI to combine AlphaFold models, molecular dynamics (MD), pyDock energy scoring, and CCharPPI descriptors to predict the impact of protein mutations at the molecular level. As a case study, we have modelled the impact of the R197L seedlessness-associated substitution in VviAGL11. This protein is a homo-dimeric transcription factor that interacts with VviMADS4 dimeric protein to form a functional hetero-tetramer. Structural modeling of this complex provides insights into the functional mechanism of this protein and the role of the mentioned mutation. This protein modeling approach could be extended for grapevine mutation analysis at the genomic level.

Keywords: AI-based modeling, Seedless grapes, Protein-protein interactions, Mutation impact analysis, Protein structure