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Peer Review

# Review of: "Can AI Modelling of Protein Structures Distinguish Between Sensor and Helper NLR Immune Receptors?"

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As is apparent from the title and abstract, this paper represents an effort to demonstrate how Alphafold3 can be used to identify protein functions, even in cases where the proteins lack canonical diagnostic motifs.

I approached this paper as someone working as an outsider to the use of modeling. This paper is generally clearly presented. Admittedly, I did not test the scripts for myself, but rather relied on what the authors presented.

This paper demonstrates how AF3 can distinguish the functions and provide likely 3-D structures for plant proteins serving as receptors (sensors) and enactors (helpers) in anti-pathogen defenses. It seems, though, that their protocols work best (or solely) when it is already known that the sensors and helpers are paired. When two molecules have been paired through functional assays, or found to fulfill the 3 criteria stated in the last part of the Results section, this program can reveal which is a sensor and which is not; which forms a funnel structure and which does not. It did not appear that the program could scan an entire proteome for a partner protein for a given resistance molecule. That may be the next step the authors will work on. I would also have been interested to know whether the predictive scores for sensor/helper pairs in the inflammasomes of animals were similar to those of the plant proteins analyzed here.

Although the paper was grammatically well done, I thought the phrase “such as helpers” (pg 2, line 3) was obscure, and that the phrase “of NLR” on line 7 of the same page could be improved by the insertion of “an” before the noun.



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## Declarations

**Potential competing interests:** No potential competing interests to declare.