

Peer Review

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

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The paper "Can AI Modelling of Protein Structures Distinguish Between Sensor and Helper NLR Immune Receptors?" uses the structural prediction approach AF3 to classify paired NLR proteins into sensor or helper categories based on predicted structural characteristics. They observed higher AlphaFold 3 confidence scores for helper NLRs than for sensors. In the case study, the paper found that AF3 can differentiate between putative sensors and helpers even when both proteins lack non-canonical domain annotations. Although the paper is well presented, it lacks detailed information regarding the higher AF3 confidence scores of the helper than the sensor. What are the possible reasons or properties of the helper NLRs for gaining a higher pTM score than the sensor NLRs? Is this related to sequence similarity or some other reasons? In my opinion, this information provides weight to the paper.

The section "Helper AF3 structures form funnel-shaped structures unlike sensors" is very well explained. However, the paper is clear, very informative, and helpful in further studies of host-pathogen interactions using structural properties. The information is also useful for developing new machine-learning methods for the classification of the NLRs.

## Declarations

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