



## **Forecasting binding affinity of paratope-epitope surfaces with a novel decision tree framework**

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Human metapneumovirus (hMPV) poses serious risks to pediatric, elderly, and immunocompromised populations. Traditional antibody discovery pipelines require 10–12 months, limiting their applicability for rapid outbreak response. This project introduces ImmunoAI, a machine learning framework that accelerates antibody discovery by predicting high-affinity candidates using gradient-boosted models trained on thermodynamic, hydrodynamic, and 3D topological interface descriptors. A dataset of 213 antibody–antigen complexes was curated to extract geometric and physicochemical features, and a LightGBM regressor was trained to predict binding affinity with high precision. The model reduced the antibody candidate search space by 89%, and fine-tuning on 117 SARS-CoV-2 binding pairs further reduced Root Mean Square Error (tRMSE) from 1.70 to 0.92. In the absence of an experimental structure for the hMPV A2.2 variant, AlphaFold2 was used to predict its 3D structure. The fine-tuned model identified two optimal antibodies with predicted picomolar affinities targeting key mutation sites (G42V and E96K), making them excellent candidates for experimental testing. In summary, ImmunoAI shortens design cycles and enables faster, structure-informed responses to viral outbreaks.

**Keywords:** *hMPV, AI/ML, Drug Design, Gradient-Boosted*



## References

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