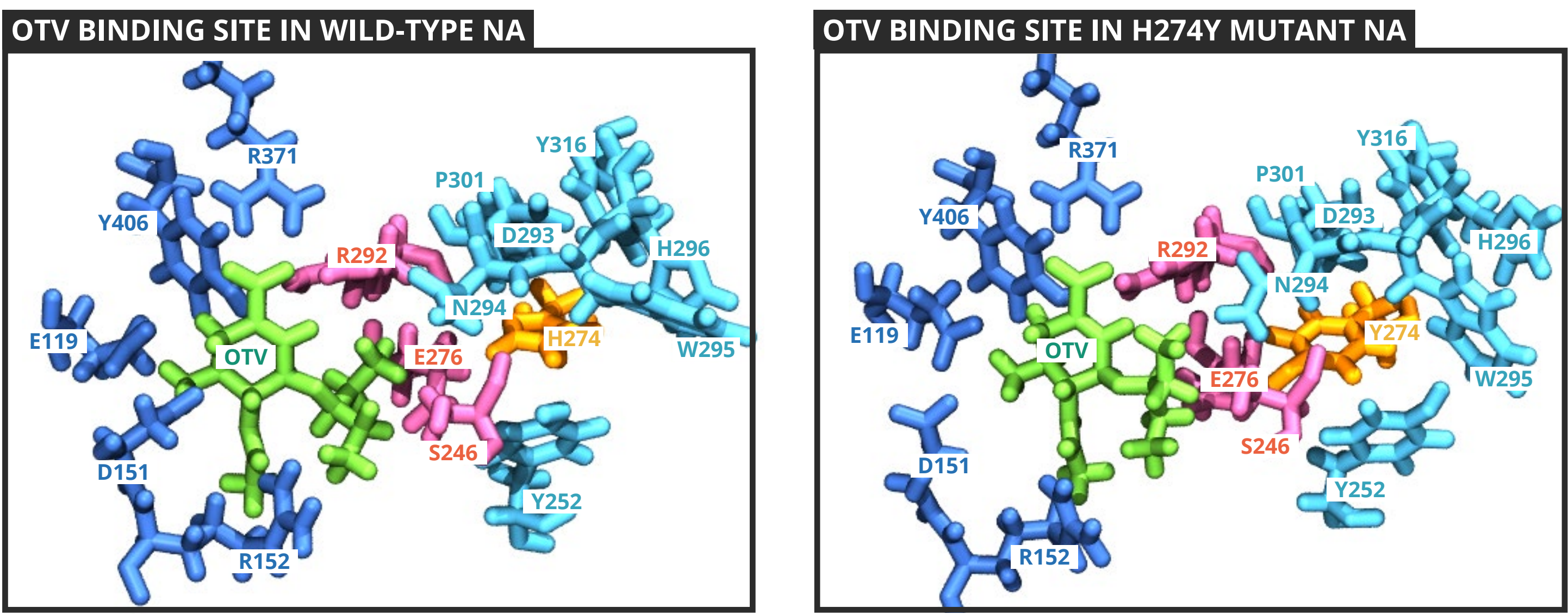


# Dynamic residue interaction network analysis of the **oseltamivir binding site** of N1 neuraminidase and its **H274Y** mutation site conferring drug resistance in **influenza A virus**

## BACKGROUND

Oseltamivir (OTV)-resistant influenza virus exhibits His-to-Tyr mutation at residue 274 (H274Y) in N1 neuraminidase (NA). However, the **molecular mechanisms by which the H274Y mutation in NA reduces its binding affinity to OTV have not been fully elucidated.**

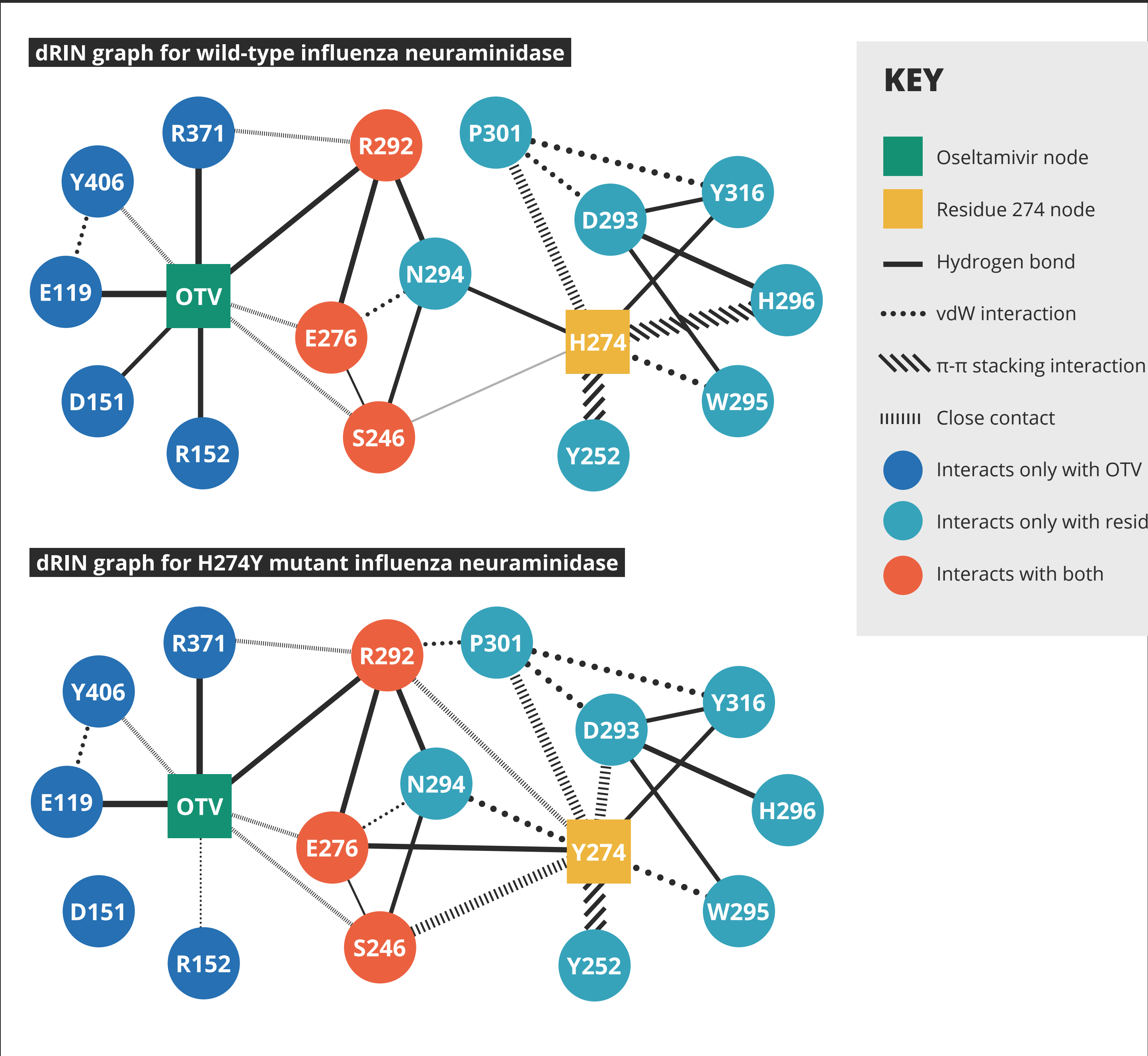


## METHODS

In this study, we used **dynamic residue interaction network (dRIN) analysis based on molecular dynamics simulation** to investigate the correlation between the OTV binding site in NA and its H274Y mutation site.

## RESULTS

dRIN analysis revealed that the **OTV binding site and H274Y mutation site of NA interact via the three interface residues connecting them.** H274Y mutation significantly enhanced the interaction between residue 274 and the three interface residues in NA, thereby significantly decreasing the interaction between OTV and its surrounding loop 150 residues. Thus, we concluded that **such changes in residue interactions could reduce the binding affinity of OTV to NA, resulting in drug-resistant influenza viruses.**



## CONCLUSION

Using dRIN analysis, **we succeeded in understanding the characteristic changes in residue interactions due to H274Y mutation, which can elucidate the molecular mechanism of reduction in OTV binding affinity to influenza NA.** Finally, the dRIN analysis used in this study can be widely applied to various systems such as individual proteins, protein-ligand complexes, and protein-protein complexes, to characterize the dynamic aspects of the interactions.

### DYNAMIC FLUCTUATIONS NEAR THE OTV BINDING SITE

