electrostatic interactions. As shown in (Figure 61) , the pyridine ring protonated nitrogen was one time bound with the Asp855 and Asn842 side chains and another time was bound to the Thr845 hydroxyl group (which is involved in the usual water-mediated hydrogen bond). In the first mode, which is more favorable (has less binding energy), the 2-methyl indoline ring was placed in the hydrophobic specificity pocket, making extensive van der Waals interactions with the surrounding residues. Hence, these compounds are thought to have what it takes to be good binders for the EGFR-kinase enzyme.

AZ-4 had the best score among 2-methylindoline compounds (-8.3 Kcal/mol).

AZ-4 also had an electrostatic interaction with the ATP-binding site of the EGFR kinase domain with additional electrostatic interaction (Figure 61).

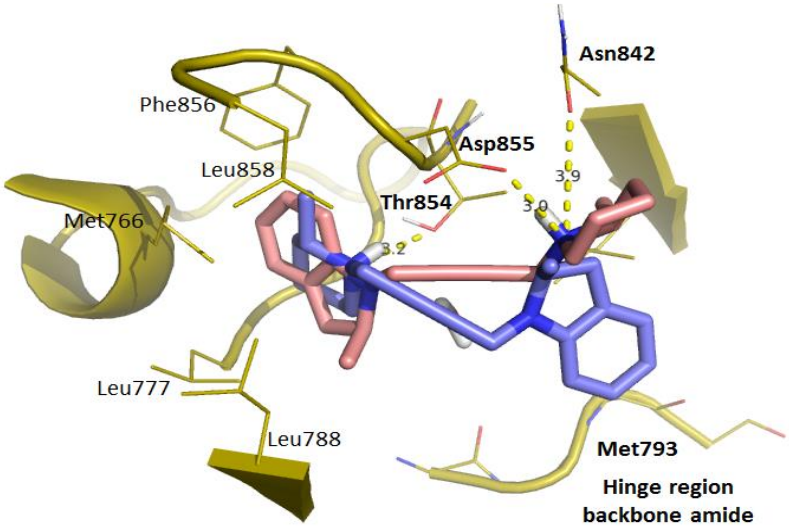

Figure 29: Shows multiple binding modes demonstrated by AZ4 (blue or pink sticks) in the ATP-binding site of the EGFR kinase domain (gold). The picture was generated by PyMol.[9] Electrostatic interactions are shown as yellow dotted lines. Some protein chains are not shown for clarity.