***A computational model of human PFK1 binding sites for two selected compounds***

The cmpd No. 9 interacts with the PFK-P/PFK-M binding site through a combination of hydrophobic interactions with Tyr64, Arg97, and Phe101 and multiple hydrogen bonds involving residues such as Gly34, Arg102, Gly127, Ser130, and Arg219 (**Fig. 4, above**). The ligand cmpd No. 30 forms a stable complex with the PFK-L isoform through multiple non-covalent interactions: hydrophobic interactions with Arg97, extensive hydrogen bonds involving residues Gly34, Gly127, Gly129, Ser130, Ser173, Arg219, and Arg310, and a significant π-cation interaction with Arg97 (**Fig. 4, below**). These interactions jointly stabilize both ligands within the protein binding site and contribute to the overall stability of the ligand-protein complexes.

The model with a modified ATP binding site, where arginine at position 102 was substituted for threonine, was generated by using the most probable rotamere obtained from the Dunbrack database ([http://dunbrack.fccc.edu/bbdep2010/](http://atpscan.global.hornetsecurity.com?d=AVOuKSlWPgoxVt0OkeJg9Jq0DGbDk3aLYCtkzli68Bk&f=svFvsyjZ8o8SyvUMVIo08fggGXzqTZe3m8SCOz-a26_5njr8jXiQtTq5wZDP9zpk&i=&k=yqjz&m=i25az-E-TMAOhydCg5KTfFB9QwSg-Narw8_IRJM5XKgBLvBHjtJqcDF9xe9mwfUoTEhWLLeszEeXkf_fBV5v0wGSFRlhIyliqb0t2mB6ekL11jvM4A9uH700d_oVbWnr&n=BJa6adQuBCWHngxOlr0IRS3u54BCuofp1TYa52pgv3o27mvjS0G_J7KL1MTbyzOF&r=I64dTuajV8A-aPgYJVXfqUT-KnQhZ6wOIZiNork1tKBH5Qw6fpxsd77NdYG1c5ee&s=5aa7fbb5b6f7d6c4554705962329b9410f75b502def3ccc7c9e641ca829ce20a&u=http%3A%2F%2Fdunbrack.fccc.edu%2Fbbdep2010%2F)) that exhibited no steric clashes.