

Supplementary Video. In this schematic movie, apo FGFR1 (left panel) demonstrates rapid P-loop dynamics, while apo FGFR2 (right panel) displays less P-loop motion. Upon reversible binding of the inhibitor (0:20 seconds) to FGFR1, the P-loop motion is significantly slowed, resulting in an extended P-loop conformation that disfavors formation of a covalent bond between the inhibitor and the P-loop cysteine. In FGFR2, inhibitor binding does not significantly alter the P-loop dynamics, allowing the inhibitor and P-loop cysteine to achieve sufficient proximity to form a covalent bond.