Supporting Information of

Molecular Mechanism Exploration of Potent Fluorinated PI3K Inhibitors with a Triazine Scaffold: Unveiling the Unusual Synergistic Effect of Pyridine-to-Pyrimidine Ring Interconversion and CF_3 Defluorination

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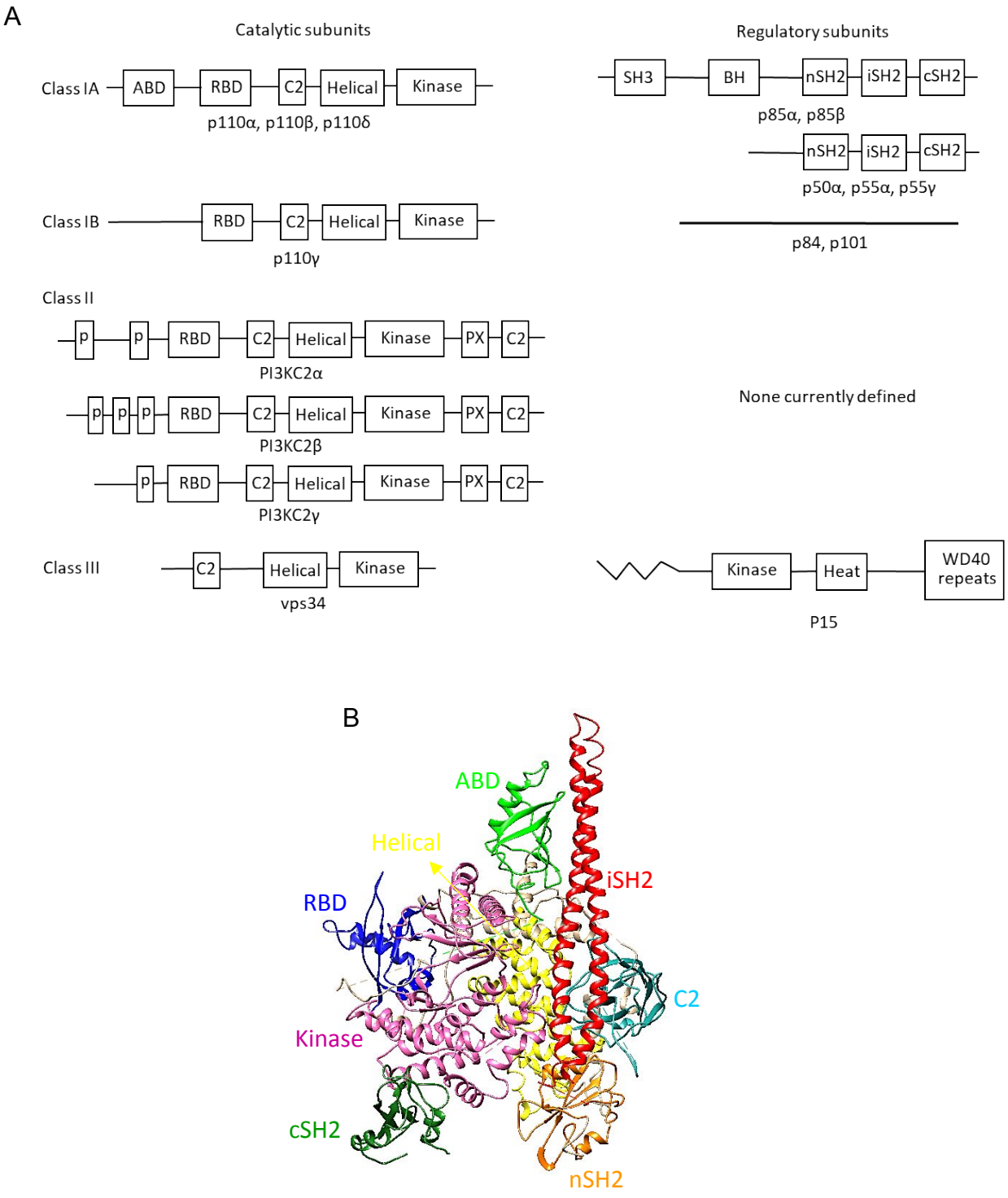

Figure S1. (A) Domain schematic of the Classes-I to III PI3K. The core region of catalytic subunits belonging to class I, II, and III PI3K comprises a C2 domain, helical domain, and kinase domain, but vary in other regions of the enzyme. The domain structure of the Class IA regulatory subunits has been specified, while the domain structure of Class IB regulatory subunits has not been clearly defined. For the Class II PI3K, no regulatory subunits have been provided and p15 is the regulatory subunit of the Class III PI3K. (B) Ribbon diagram of the p110α/cniSH2 heterodimer created from multiple structures, each domain is colored and labeled separately.

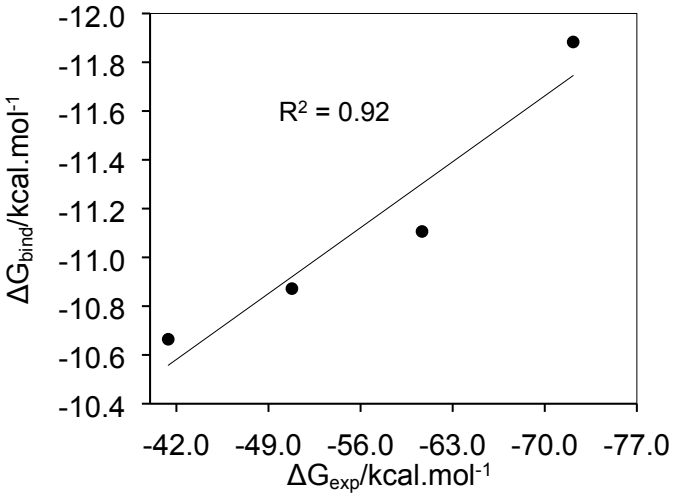

Figure S2. Correlation coefficient (R^2) values plotted for the experimental binding free energies (ΔG_{exp} in kcal.mol^{-1}) were estimated using the equation $-RT\ln(K(i))$ versus the binding free energies predicted with MM/GBSA (ΔG_{bind} in kcal.mol^{-1}).