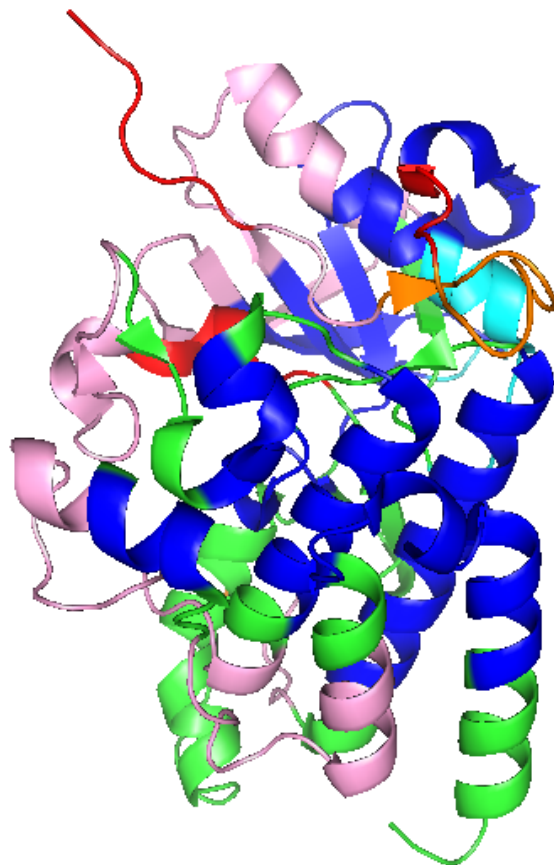


Can a Truncated Domain Truly Represent a Whole Enzyme?

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Ion Cyclotron Resonance User Program



The enzyme at left is the primary drug target for treatment of abdominal cancer. After some months, the molecule typically mutates, and drugs are no longer as effective. By observing changes in the surface exposure of various parts of the molecule on binding of drugs, we can establish the effect of the mutation, as a guide to future design of drugs to overcome it.

Gajiwala, K. S.; Wu, J. C.; Christensen, J.; Deshmukh, G. D.; Diehl, W.; DiNitto, J. P.; English, J. M.; Greig, M.; He, Y.-A.; Jacques, S. L.; Lunney, E. A.; McTigue, M; Molina, D.; Quenzer, T. A.; Wells, P. A.; Yu, X.; Zhang, Y.; Zou, A.; Emmett, M. R.; Marshall, A. G.; Zhang, H.-M.; Demetri, G. "KIT Kinase Mutants Show Unique Mechanisms of Drug Resistance to Imatinib and Sunitinib in Gastrointestinal Stromal Tumor Patients," *Proc. Natl. Acad. Sci. U.S.A.* **2009**, *106*, 1542-1547.