1080-92-36 **Yi Mao*** (maoyi0@gmail.com), 3720 15th Ave NE S220, Seattle, WA 98195. *Dynamical Basis for Drug Resistance of HIV-1 Protease.*

Background: Protease inhibitors designed to bind to protease have become major anti-AIDS drugs. Unfortunately,the emergence of viral mutations severely limits the long-term efficiency of the inhibitors. The resistance mechanism of these diversely located mutations remains unclear.

Results: Here I use an elastic network model to probe the connection between the global dynamics of HIV-1 protease and the structural distribution of drug-resistance mutations. The models for study are the crystal structures of unbounded and bound (with the substrate and nine FDA approved inhibitors) forms of HIV-1 protease. Coarse grained modeling uncovers two groups that couple either with the active site or the flap. These two groups constitute a majority of the drug-resistance residues. In addition, the important residues identified by the dynamical changes in binding and the results agree well with the complete mutagenesis experiment of HIV-1 protease.

Conclusions: The dynamic study of HIV-1 protease elucidates the functional importance of common drug resistance mutations and suggests a unifying mechanism for drug-resistance residues based on their dynamical properties. The results support the robustness of the elastic network model as a potential predictive tool for drug resistance. (Received December 11, 2011)