SUPPORTING INFORMATION

Title: Chemometrical Identification of Mutations in HIV-1 Reverse Transcriptase Conferring Resistance or Enhanced Sensitivity to Arylsulfonylbenzonitriles

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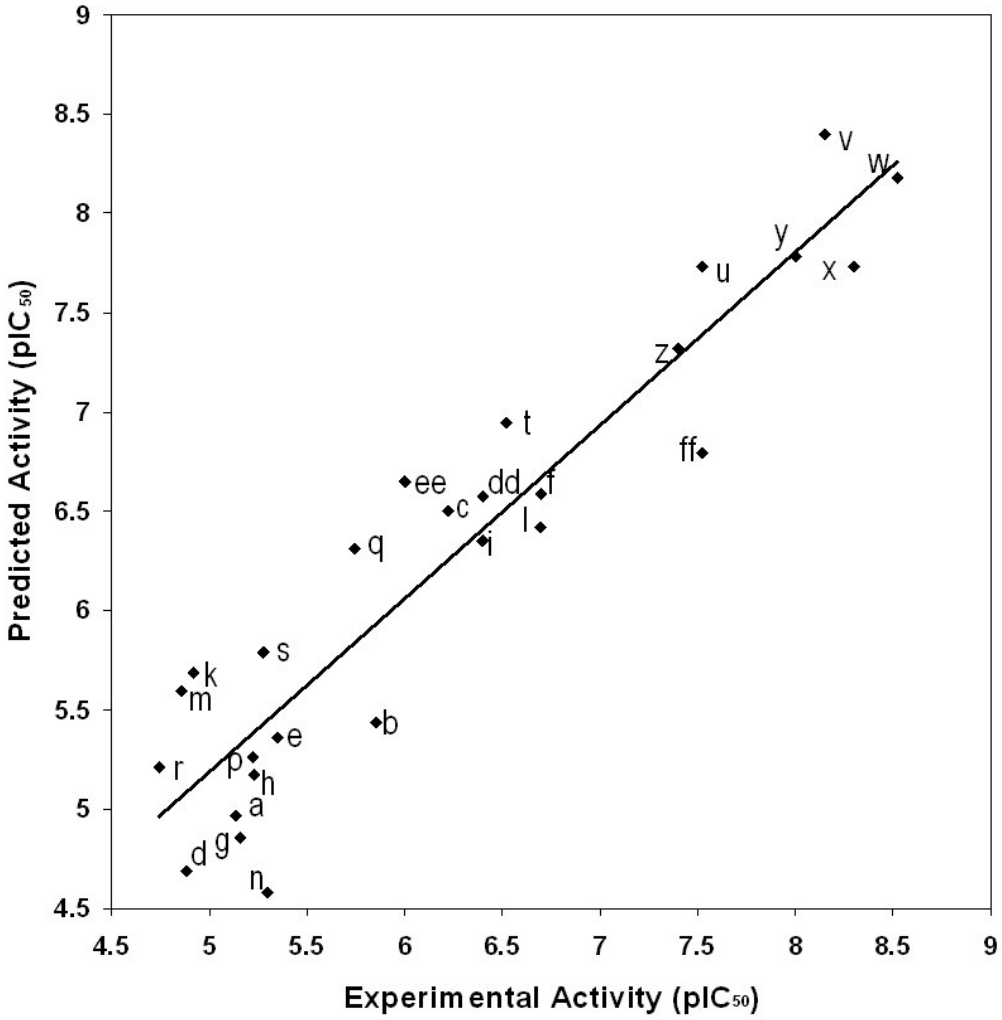

Figure 1. Correlation between experimental and predicted activities (pIC_{50} values) for the whole set containing the 27 arylsulfonylbenzonitriles studied.

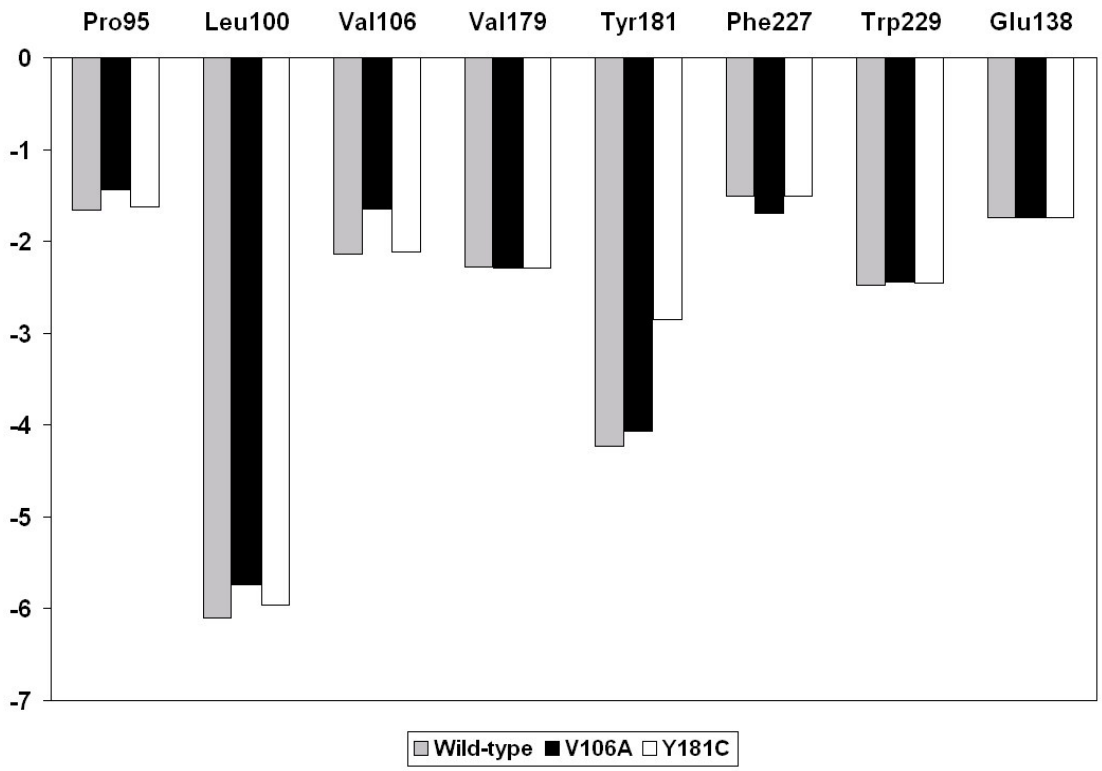

Figure 2. AMBER van der Waals interactions between compound **v** and selected amino acids in HIV-1 RT, as calculated for the wild-type enzyme and the V106A and Y181C mutants.

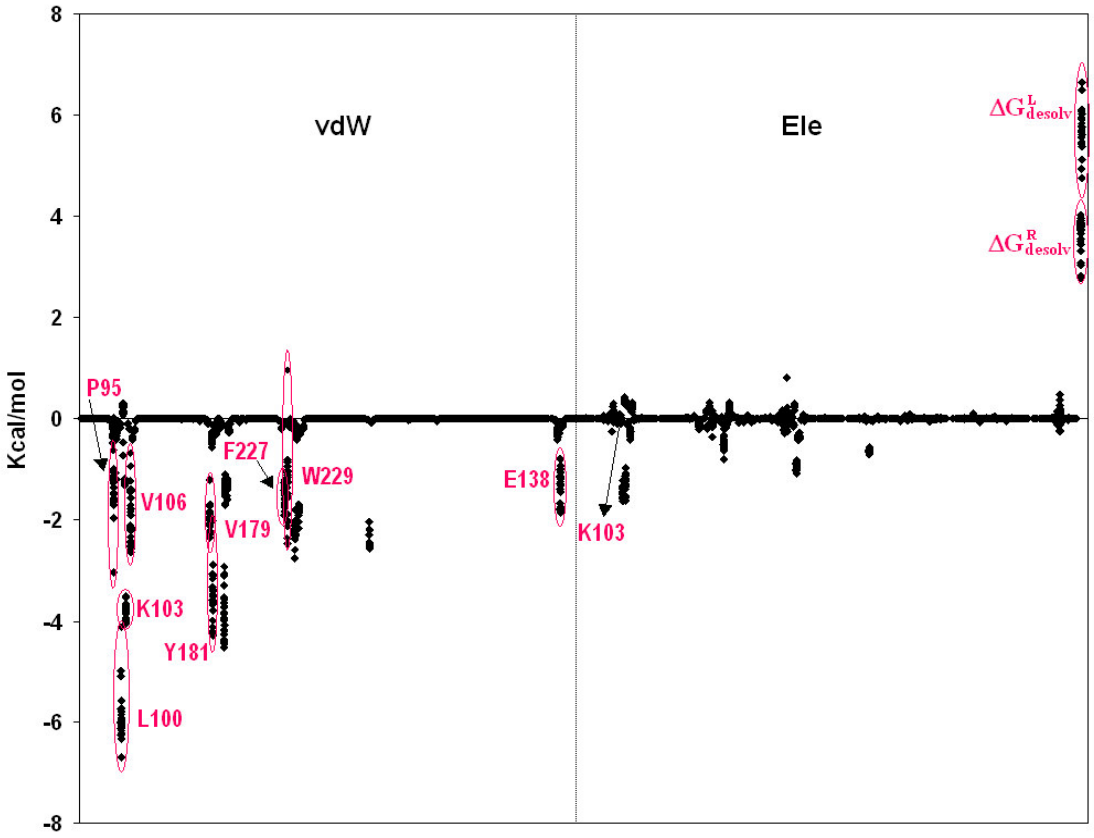

Figure 3. Interaction energy variables that enter the PLS analysis leading to the COMBINE model for the whole set of 2-amino-6-arylsulfonylbenzonitriles studied. Each diamond represents a value from the energy matrix. On the horizontal axis, the variables are ordered sequentially and correspond to van der Waals (left-hand side) and electrostatic (right-hand side) interactions between the ligands and the protein residues included in the analysis (p66 subunit: 4-11, 85-122, 147-247, 260-276, 305-329, 338-354, and 372-389; p51 subunit: 14-62 and 119-149). Residue-based partitioning of the vdW interaction energies was achieved with the ANAL module in AMBER. Encircled and labeled in red are those interaction energy variables that are discussed in the text.

Table 1. Evolution of the Chemometric Indices[a] as the Number of Principal Components in the COMBINE Models for the 2-amino-6-arylsulfonylbenzonitriles is Increased.

25 compounds	# PC	r^2	q^2	SDEP
	1	0.835	0.747	0.594
	2	0.899	0.854	0.452
	3	0.950	0.887	0.398
	4	0.961	0.881	0.408
	5	0.967	0.837	0.477
27 compounds	# PC	r^2	q^2	SDEP
	1	0.818	0.702	0.635
	2	0.884	0.801	0.520
	3	0.944	0.838	0.469
	4	0.959	0.851	0.450
	5	0.962	0.815	0.502

[a] For internal validation the inhibitors were assigned randomly to one of five groups of approximately the same size, each group in turn was excluded from the analysis, and the whole procedure was repeated 20 times. This procedure is more stringent than the more commonly used leave-one-out method.