

A comparison of HIV-1 drug susceptibility information as provided by two phenotypic drug resistance assays

**M. Van Houtte¹, K. Van Der Borgh¹, G. Picchio²,
T. Pattery¹, P. Lecocq¹ and L. Bachelier³**

¹Virco BVBA, Mechelen, ²VircoLab, Inc. Raritan, NJ, and ³VircoLab, Inc. Durham, NC



Introduction

- **Four assays that provide phenotypic drug susceptibility information**
 - Antivirogram (Virco, Mechelen, Belgium)
 - PhenoSense (Monogram Biosciences, S. San Francisco, CA, USA)
 - vircoTYPE HIV-1 (Virco, Mechelen, Belgium)
 - Phenoscript (Viralliance, France)
- **Very few comparative data between the assays exist**

Study Objectives

- **To compare vircoTYPE HIV-1-derived phenotypic drug susceptibility data with PhenoSense-derived phenotypic drug susceptibility data measured on the same set of viral isolates**

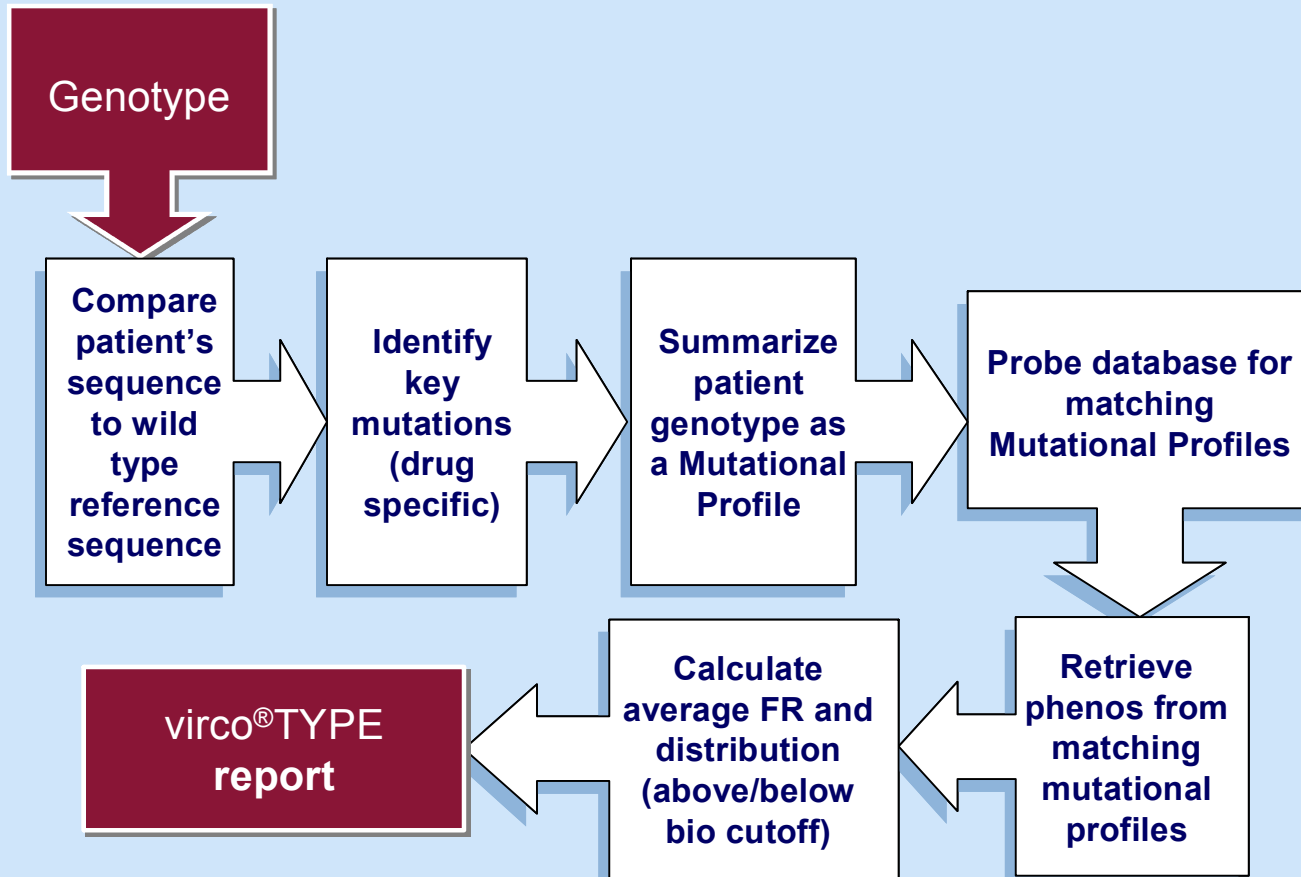
Source Data

- **Data set in Stanford's database containing, for the same viral isolates:**
 - Genotypic sequence information
and
 - Phenotypic susceptibility data (FC in IC_{50}) as measured by the PhenoSense in vitro drug resistance test

Methods (1)

- **Between 183 and 501 isolates were available for the comparisons for all antiretroviral drugs, except for tenofovir and atazanavir.**
- **Genotypic information linked to each isolate was used to obtain a predicted phenotype using the *Virtual*Phenotype bio-informatics tool.**

VirtualPhenotype prediction tool

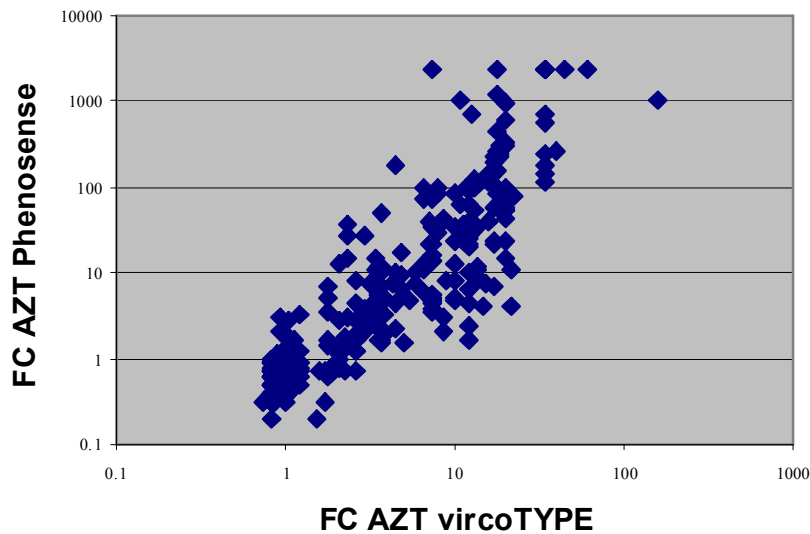


Methods (2)

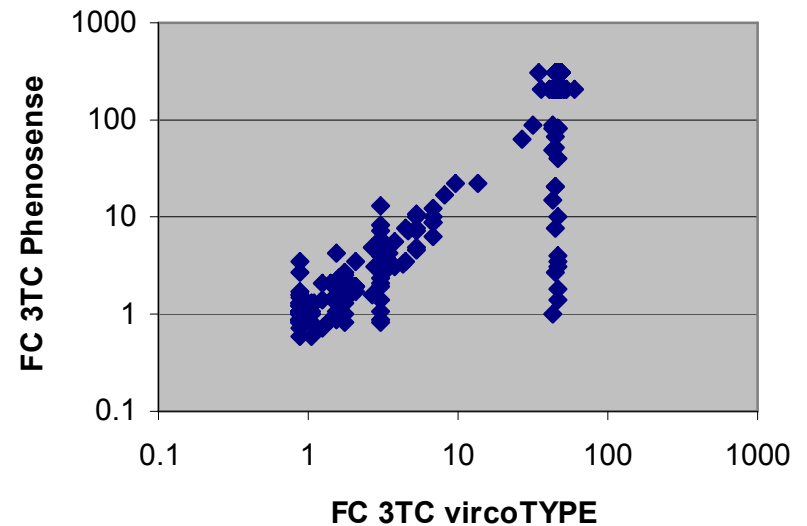
- FC values of the two assays plotted
- Pearson's correlation coefficients between the FC of two assays calculated
- Percentage agreement in susceptibility calls between vircoTYPE HIV-1 prediction and PhenoSense value using BCOs and CCOs
- Analysis of discordant calls by taking the ratio of vircoTYPE FC to PhenoSense FC. A ratio of ≤ 0.4 or ≥ 2.5 was considered a discordance.

PhenoSense FC values plotted against vircoTYPE FC values

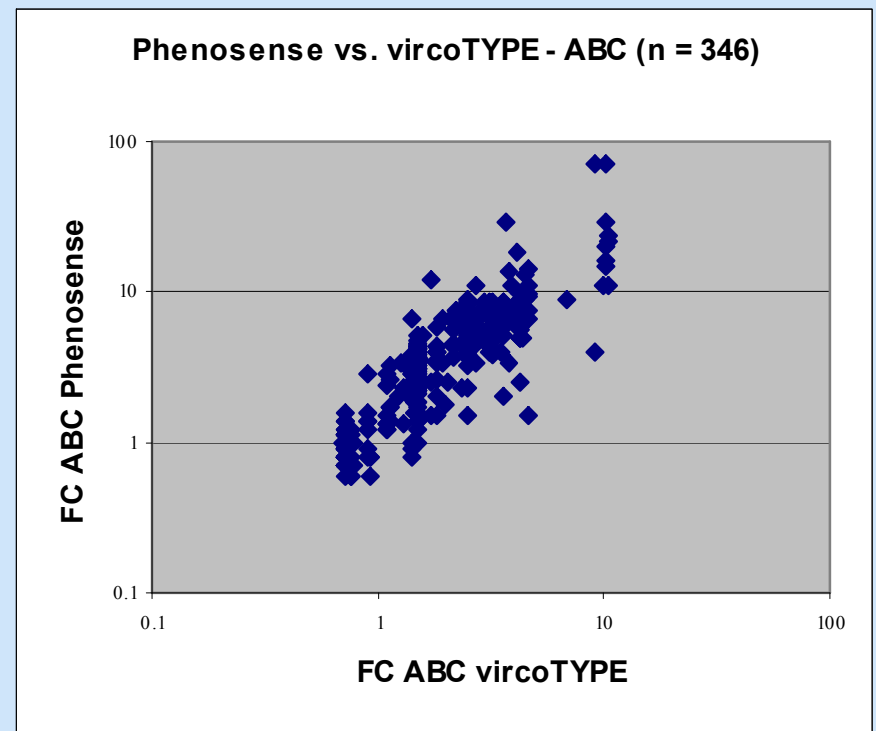
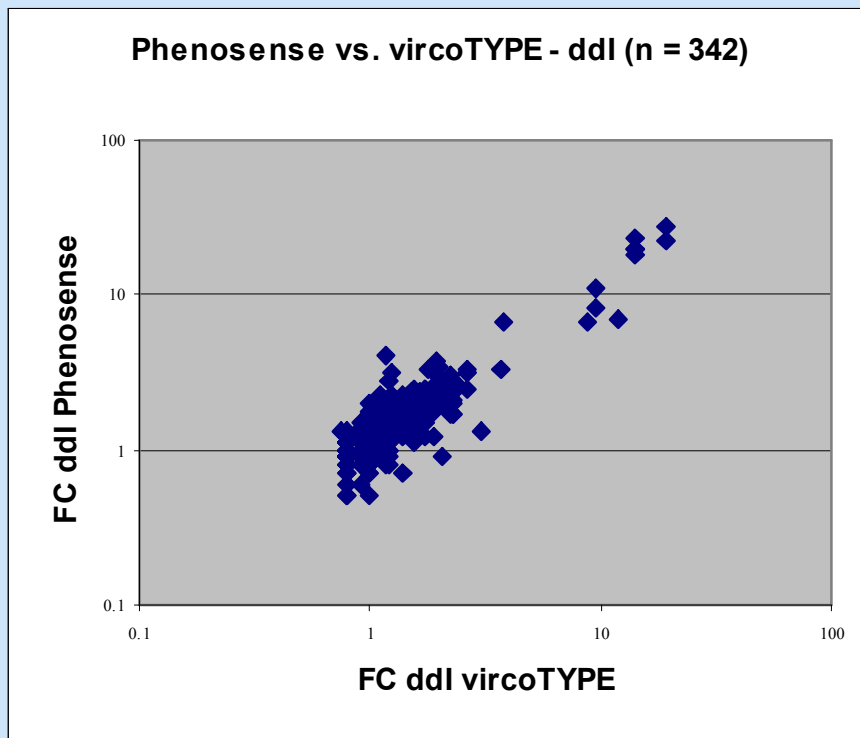
Phenosense vs vircoTYPE - AZT (n = 348)



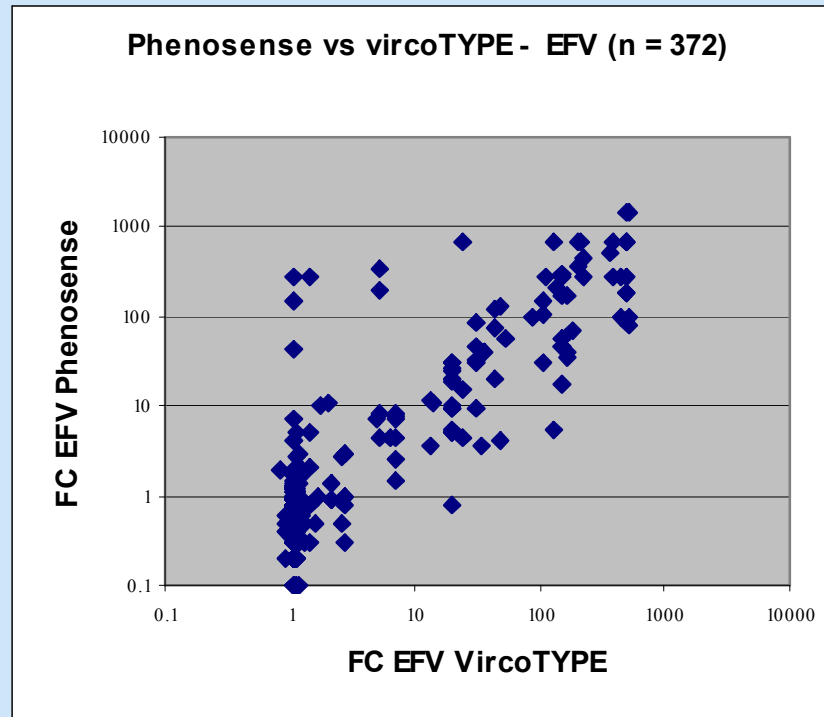
Phenosense vs. vircoTYPE - 3TC (n = 353)



Phenosense FC values plotted against vircoTYPE FC values

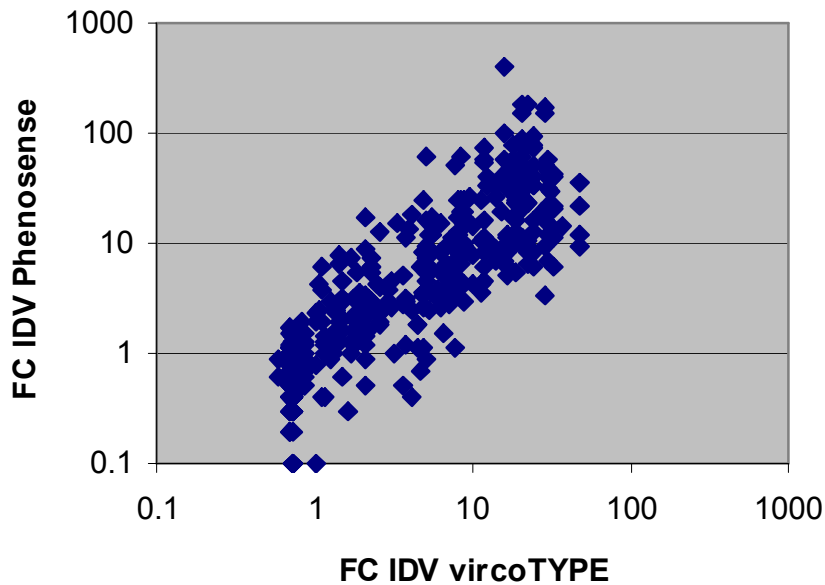


Phenosense FC values plotted against vircoTYPE FC values

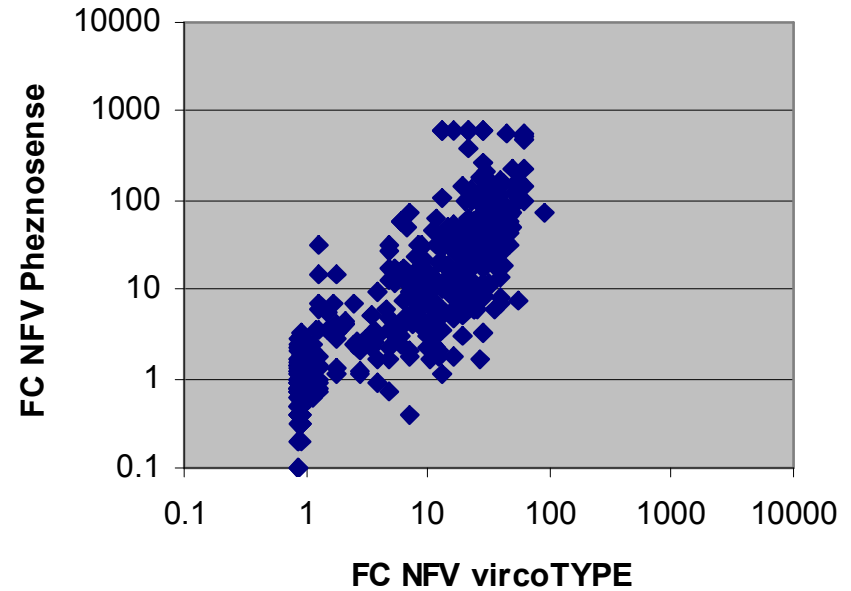


Phenosense FC values plotted against vircoTYPE FC values

Phenosense vs. vircoTYPE - IDV (n = 484)

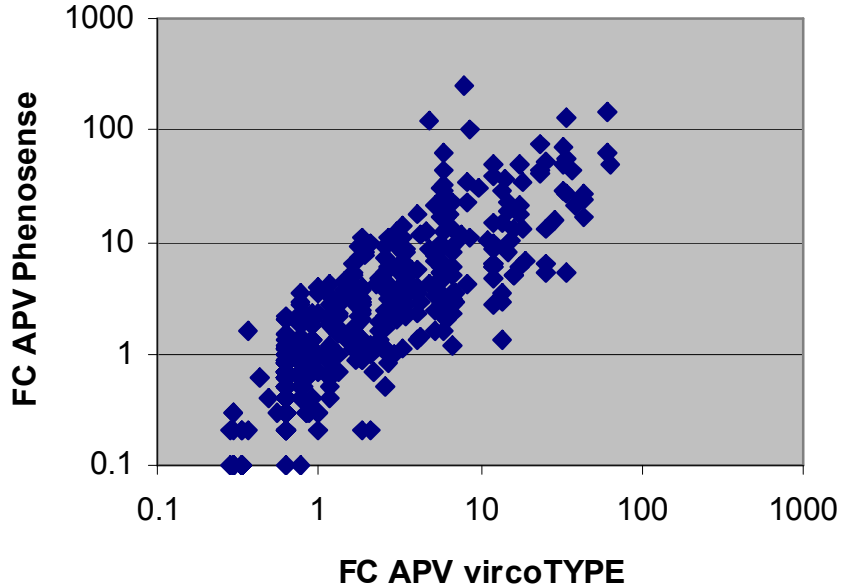


Phenosense vs. vircoTYPE - NFV (n = 516)

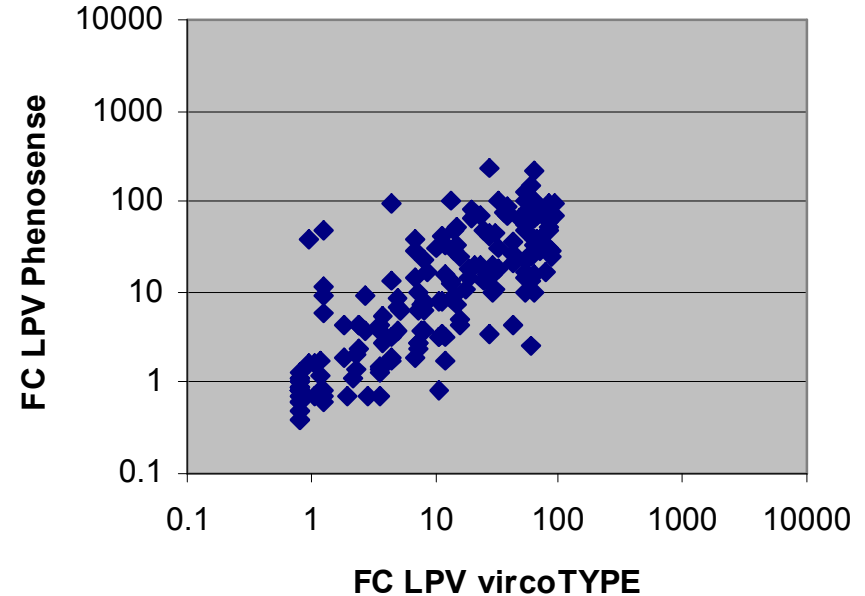


Phenosense FC values plotted against vircoTYPE FC values

Phenosense vs. vircoTYPE - APV (n = 493)



Phenosense vs. vircoTYPE - LPV (n = 185)



Correlation between Phenosense and vircoTYPE HIV-1 FC values

Drug Class	Drug	Pearson's Correlation Coefficient	N
NRTI	AZT	0.91	273
	3TC	0.98	296
	ddl	0.91	277
	ddC	0.89	252
	D4T	0.87	282
	ABC	0.90	285
NNRTI	NVP	0.91	366
	DLV	0.85	358
	EFV	0.89	347
PI	IDV	0.89	447
	IDV/r		447
	RTV	0.91	421
	NFV	0.87	477
	SQV	0.86	452
	APV	0.86	447
	LPV	0.84	147
Mean	----	0.9	----

Concordance between vircoTYPE and PhenoSense calls

Drug Class	Drug	Clinical or Biological Cut-offs		Concordance	No. of discordant calls with VT/PS FC ratio ≤ 0.4 or ≥ 2.5	No. of PS-Resistant Samples ^b	N
		virco [®] TYPE HIV-1	PhenoSense [™]				
NRTI	AZT	2.7	1.9	92.3	11 (4.0)	132	273
	3TC	1.1	3.5	87.2	3 (1.0)	197	296
	ddl	1.3	1.7	79.1	0 (0)	73	277
	ddC	---	na	---	---	---	252
	D4T	1.1	1.7	89	3 (1.1)	89	282
	ABC	2.1	4.5	89.8	9 (3.2)	97	285
NNRTI	NVP	5.2	2.5	92.9	13 (3.6)	120	366
	DLV	7.7	2.5	92.5	12 (3.4)	73	358
	EFV	3.4	2.5	95.4	16 (4.6)	92	347
PI	IDV	2.1	2.1	91.9	14 (3.2)	229	447
	IDV/r	4.1	10	84.3	20 (4.5)	118	447
	RTV	2.4	2.5	94.8	12 (2.9)	199	421
	NFV	2.3	2.5	92.2	25 (5.2)	295	477
	SQV	1.7	1.7	91.2	20 (4.4)	205	452
	APV	1.8	2	88.1	27 (6.0)	189	447
	LPV	10	10	89.1	12 (8.2)	71	147
Mean	----	----	----	90	13 (3.7)	----	----

Conclusions

- **The plots and the correlation coefficients, as well as the level of concordance in the susceptibility calls indicate good agreement between phenotypic resistance measured by vircoTYPE HIV-1 and Phenosense assays.**

Conclusions

- **Despite the fact that the PS assay and VT assay use different approaches to obtain phenotypic information, this study suggests that both assays correlate well and they provide, on most occasions, similar interpretations of resistance across the drugs investigated.**
- **This information will be of value to physicians who may currently use these assays interchangeably.**

Acknowledgements

- **Virco Lab Ops Team**
- **Virco Bioinformatics Team**
- **P. Alen**
- **M. Tuohy**

Characteristics of Data Set

	NRTIs						NNRTI			PI					
	AZT	3TC	ddl	ddC	D4T	ABC	NVP	DLV	EFV	IDV	RTV	NFV	SQV	APV	LPV
# isolates with PS results available for comparison with T**	277	297	285	257	286	290	370	364	354	466	447	501	482	464	183
# of isolates with VT quantitative prediction	273	296	277	252	282	285	366	358	347	447	421	477	452	447	147
# of isolates with VT rules-based prediction	4	1	5	5	4	5	4	6	7	19	26	24	30	17	36***
# distinct VT mutational profiles represented in group with quantitative prediction	59	53	56	62	52	60	50	49	46	129	128	153	110	108	78