ID065 Towards Better Resistance Surveillance: Clinical Performance of Short- and Long-Read NGS in HIV-1 Whole Genome Sequencing

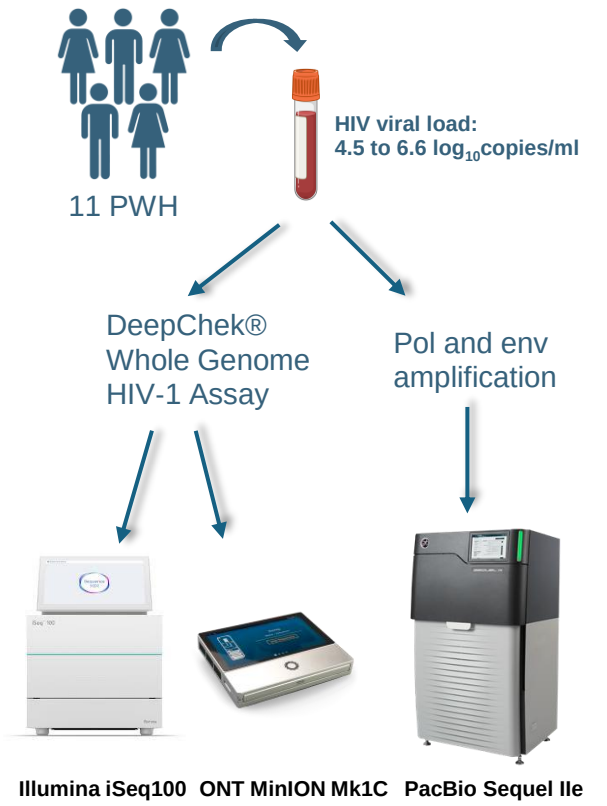
Camille Vellas[1,2]*, Amira Doudou[3], Sofiane Mohamed[3], Stéphanie Raymond[1,2], Justine Latour[1], Noémie Ranger[1], Dimitri Gonzalez[3], Pierre Delobel[2,4], Jacques Izopet[1,2]

[1]CHU de Toulouse, Laboratoire de Virologie, Toulouse, France, [2]INSERM UMR1291-CNRS UMR5051-Université de Toulouse, Toulouse Institute for Infectious and Inflammatory Diseases, France, [3]ABL Diagnostics (ABLD), France, [4]CHU de Toulouse, Service de Maladies Infectieuses et Tropicales, Toulouse, France

Introduction

Next-generation sequencing (NGS) is a powerfull approach for detecting drug-resistant variants across the HIV-1 genome, including those present at very low abundance. However, these approaches need to be well evaluated. In a previous study, we compared a short-read (DeepChek® Whole Genome HIV-1 Assay) with a long-read (PacBio SMRT) approach and observed some discrepancies, particularly in the detection of minor drug resistance mutations (DRMs)[1]. To extend this analysis, we sequenced the HIV-1 Whole Genome of 11 plasma samples using an additional long-read method: nanopore sequencing on the MinION Mk1C platform (Oxford Nanopore Technologies, ONT).

Materials and methods



Results

ID	Viral load[a]	subtype	PR[b]			RT[c]			INT[d]			ENV[e]		
			DeepChek® WG HIV-1	PacBio SMRT	ONT	DeepChek® WG HIV-1	PacBio SMRT	ONT	DeepChek® WG HIV-1	PacBio SMRT	ONT	DeepChek® WG HIV-1	PacBio SMRT	ONT
1	5.9	B	33V (99%), 62V (99%)	33V + 62V (100%)	33V (93%) 62V (92%)	None	None	None	None	None	None	43K (23%)	43K (68%)	43K (23%)
2	6.6	F1	10I (99%), 20M (98%), 36I (99%), 89M (99%)	10I + 20M + 36I + 89M (100%)	10I (97%), 20M (93%), 36I (96%), 89M (98%)	None	None	None	None	None	None	**375M (99%)**	**375M (99%)**	**375M (94%)**
3	5.8	CRF02_AG	20I (99%), 36I (99%), 63P (99%), 69K (99%), 89M (99%)	20I + 36I + 63P + 69K + 89M (100%)	20I (90%), 36I (97%), 63P (83%), 69K (96%), 89M (95%)	103R (95%), 106I (99%)	103R + 106I (100%)	103R (92%), 106I (97%)	None	***138K (13%)***	None	None	None	None
4	6.4	CRF06	16E (98%), 20I (99%), 36I (98%), 69K (99%), 77I (6%), 89M (99%)	16E + 20I + 36I + 69K + 89M (95%) 16E + 20I + 36I + 69K + 89M + 77I (5%)	16E (93%), 20I (90%), 36I (92%), 69K (90%), 77I (6%), 89M (94%)	None	None	101E (8%)	None	None	None	None	None	None
5	5.6	CRF02_AG	20I (99%), 36I (70%), 64L (99%), 69K (99%), *82A (5%)* , 89M (99%)	20I + 36I + 64L + 69K + 89M (65%) 20I + 64L + 69K + 89M (35%)	20I (86%), 36I (68%), 64L (94%), 69K (92%), *82A (5%)* , 89M (99%)	None	None	None	None	None	None	None	None	None
6	5.0	CRF02_AG	**10V (99%)**, **16E (99%)**, 20R (70%), *20T (29%)* , 36I (97%), 69K (99%), 89I (99%)	**10V** + **16E** + 20R + 36I + 69K + 89I (100%)	**10V (97%)**, **16E (82%)**, 20R (61%), *20T (28%)* , 36I (93%), 69K (96%), 89I (90%)	None	***65E (5%)*** , *101E (5%)*	***65E (9%)*** , *101E (9%)*	None	None	None	None	None	None
7	5.5	B	60E (99%), 63P (99%), 71T (12%), 77I (25%)	63P + 60E (64%) 63P + 71T (14%) 63P + 60E + 77I (9%) 63P + 71T + 77I (8%) 63P (5%)	60E (60%), 63P (93%), 71T (13%), 77I (25%)	None	None	None	None	None	None	None	None	None
8	5.0	CRF06	16E (99%), *20I (18%)* , 36I (87%), 69K (99%), 89I (100%)	16E + 36I + 69K + 89I (100%)	16E (93%), *20I (19%)* , 36I (81%), 69K (94%), 89I (64%)	None	None	None	None	None	None	None	None	None
9	5.8	CRF02_AG	20I (99%), 36I (100%), 69K (99%), 89M (99%)	20I + 36I + 69K + 89M (100%)	20I (93%), 36I (93%), 69K (94%), 89M (93%)	None	None	None	None	None	None	None	None	None
10	4.5	CRF02_AG	*10V (8%)* , 20I (100%), 36I (99%), 69K (99%), *77I (11%)* , 89M (99%)	20I + 36I + 69K + 89M (100%)	*10V (8%)* , 20I (88%), 36I (87%), 69K (93%), *77I (13%)* , 89M (95%)	108I (100%)	108I (100%)	108I (96%)	None	None	None	None	None	None
11	5.5	CRF02_AG	20I (100%), 36I (100%), 63P (99%), 69K (99%), 89M (99%)	20I + 36I + 63P + 69K + 89M (100%)	20I (90%), 36I (97%), 63P (93%), 69K (91%), 89M (94%)	None	None	None	None	None	None	None	None	None

bold: mutation with drug resistance, italic: difference between the three approaches, red: differences in drug resistance, green: differences in frequencies, + haplotype covariations. [a] log10 copies/mL, [b] protease, [c] reverse transcriptase, [d] integrase, [e] envelope.

Conclusion

Our findings indicate that the DeepChek® Whole Genome HIV-1 Assay (Illumina), PacBio SMRT, and ONT sequencing offer overall good performance for HIV-1 subtyping and DRMs detection. These preliminary findings are promising but need to be confirmed on a larger cohort of samples to assess their robustness and clinical insights.

[1] C Vellas C et al. Comparison of short-read and long-read next-generation sequencing technologies for determining HIV-1 drug resistance. J Med Virol. 2024;96(10):e29951.