

Characterization of tissue-based HIV reservoirs in the San Francisco Postmortem Systematic Investigation of Sudden Cardiac Death (POST SCD) Cohort

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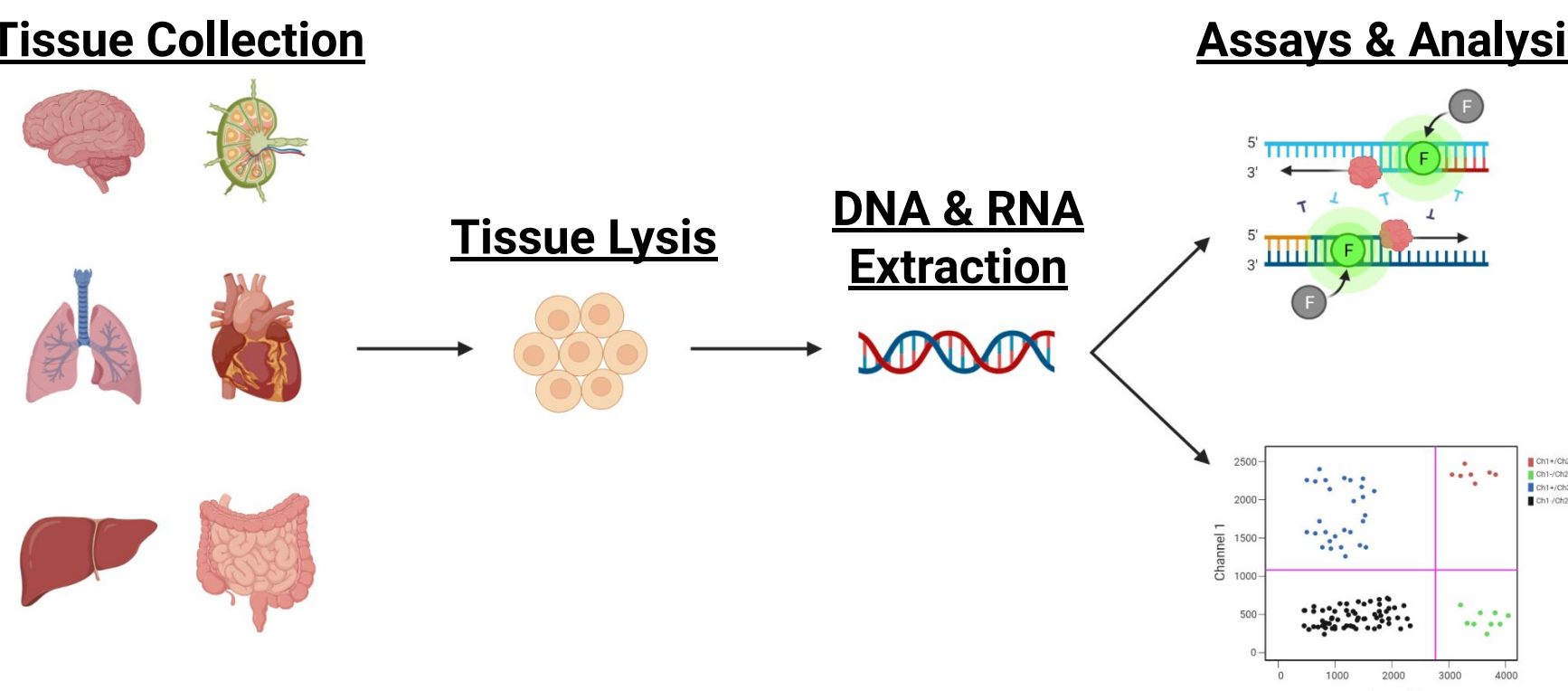
BACKGROUND

The purpose of this study is to determine the precise tissue locations of HIV reservoirs and residual viral transcriptional activity that may lead to viral recrudescence following cessation of ART, thereby generating data that can advance efforts towards HIV reservoir clearance and cure.

PRIMARY OBJECTIVES

- To measure the total burden of intact and defective proviruses and HIV transcripts across the full spectrum of different organs and tissues in vivo.
- To compare viral burdens across multiple organs and identify potential reservoirs of latently infected cells with intact HIV transcripts.

METHODS



RESULTS

- HIV RNA was detected across all organ groups studied, despite the use of suppressive ART.
- HIV intact proviral DNA was detected in all organ groups except for the liver.

DISCUSSION

- Relatively high levels of HIV RNA and DNA were detected in lymph node groups, consistent with prior reservoir studies.
- Relatively high levels of HIV RNA and DNA in the brain suggest that the CNS may be an immune privileged site that serves as a persistent reservoir of HIV-infected myeloid cells and subsequent viral replication.

This study shows evidence of HIV reservoirs and residual viral transcriptional activity in a variety of solid organs and tissues throughout the human body, despite the use of suppressive ART.

TABLE 1.

Cell-Associated HIV RNA	
ORGAN GROUPS	Average Log10 (caRNA copies per million cells)
Brain	3.16
Heart	3.05
Lung	2.43
Liver	2.45
Ileum	2.51
Colon	3.29
Total Lymph Node	3.12
Periaortic Node	5.05
Mesenteric Node	2.76
Inguinal Node	3.29

TABLE 2.

HIV DNA	All PTs			PT10 Excluded			PT10 Only		
	Int	3' X	5' X	Int	3' X	5' X	Int	3' X	5' X
Brain	3.1	2.0	3.0	ND	1.8	ND	3.1	2.8	3.0
Heart	2.0	2.8	3.8	2.0	2.8	3.8			
Lung	1.7	2.4	2.2	1.7	2.4	2.2			
Liver	ND	ND	ND	ND	ND	ND			
Ileum	3.4	2.1	3.3	3.4	2.1	3.3			
Colon	2.1	3.2	3.3	2.1	2.7	2.4	ND	4.2	4.2
Total Lymph Node	2.1	2.6	2.6	1.8	2.5	2.5	2.7	2.9	3.0
Periaortic Node	1.7	2.6	2.6	1.2	2.3	2.3	3.4	4.0	4.0
Mesenteric Node	2.0	2.1	1.5	1.9	2.1	1.3	2.1	2.2	2.4
Inguinal Node	2.5	2.6	3.4	1.4	2.3	3.3	3.6	3.5	3.7

TABLE 1.	Log10 (caRNA copies per million cells)									
	PT1	PT2	PT3	PT4	PT5	PT6	PT7	PT8	PT11	PT10
Frontal Brain	2.38	ND		ND	ND		ND	ND	ND	3.93
Left Ventricle (Heart)	2.90		ND			3.20		ND		
Lung	4.02						0.85	ND		
Liver	2.45									
Distal/Terminal Ileum	3.77	1.24	ND	ND					ND	
Sigmoid Colon		ND	ND		ND		1.01		ND	5.58
Lymph Node NOS		ND	ND			1.39	0.42			
Paratracheal Node					1.12					
Right Subclavian		ND								4.98
Left Hilar Node		ND						1.19		4.13
Periaortic Node	4.90		ND	ND	4.71		ND	ND		5.54
Mesenteric Node	5.08		ND		-0.54		ND	ND		3.73
Right Inguinal	4.60	ND		-0.08		4.28				4.38

TABLE 1 (left). Average caRNA levels by organ grouping. The table shows the average log10 transformation value of caRNA copies per million cells for each organ type. ND samples were excluded.

TABLE 2 (middle). Average HIV DNA levels by organ grouping. The table shows the average log10 transformation value of intact and defective HIV DNA copies per million cells for each organ type. Participant 10 (PT10) is the viremic control. “Int” indicates intact proviral HIV DNA, “3’ X” indicates DNA that was defective at the 3’ end, and “5’ X” indicates DNA that was defective at the 5’ end. “ND” indicates that the sample yielded no RNA, thus the log transformation was not determinable and was excluded from averages.

TABLE 3 (above). Cell-associated RNA levels across all patients and organs. The table shows the log10 transformation of caRNA copies per million cells for each sample. “ND” indicates that the sample yielded no RNA, thus the log transformation was not determinable. Participant 10 (PT10) is the viremic control.

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