Impact of hepatitis C virus (HCV) clearance on markers of immune aging and inflammation among women living with and without HIV overtime.

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Background

HIV=68,000
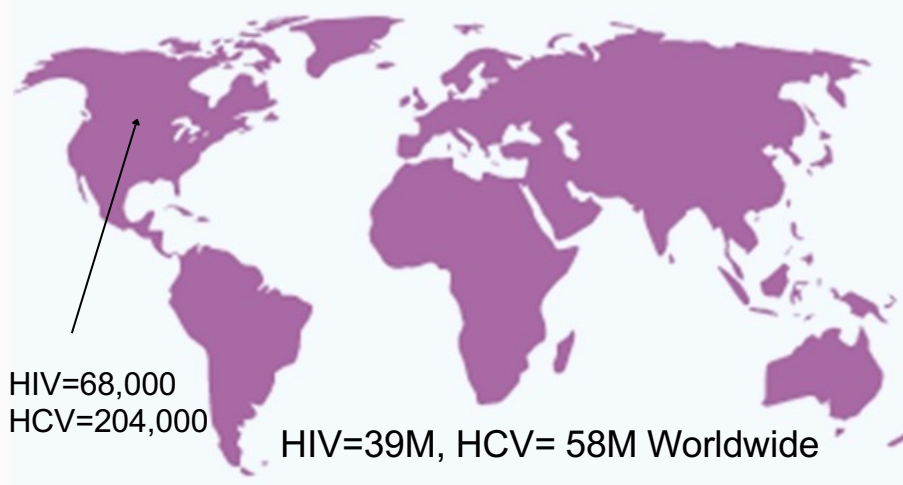HCV=204,000

HIV=39M, HCV= 58M Worldwide

Figure 1. Distribution of HIV and HCV

- Despite antiretroviral therapy (ART) and effective HIV viral suppression, people living with HIV experience **premature aging** likely linked to inflammation and immune dysfunction
- Unlike HIV, HCV can be eliminated through effective antiviral therapy, but the effect of clearing HCV on immune aging has not been described.

Objective

To characterize the effect of chronic HCV clearance on selected markers of immune aging and inflammation in women living with and without HIV

Study design

WLWH 312   WLWHV 300   WLWH 236   WLWHV 317

206 HCV+   124 HCV+

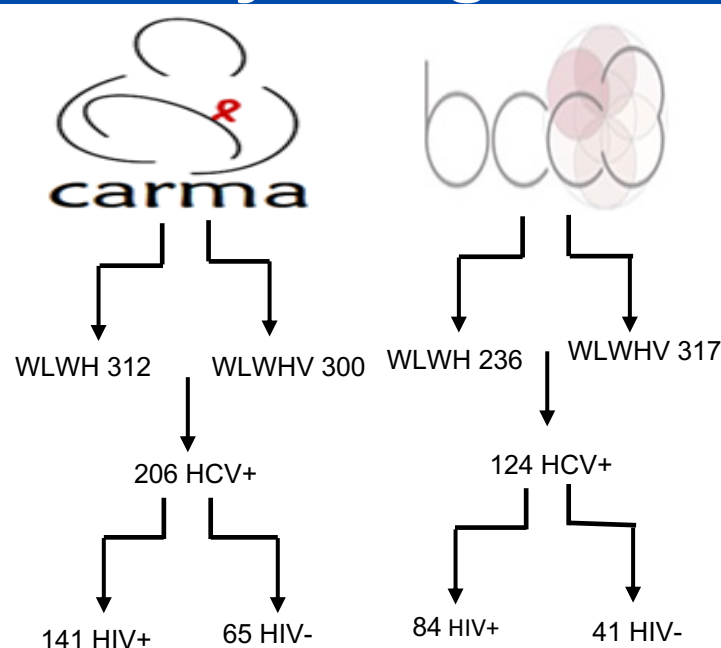141 HIV+   65 HIV-   84 HIV+   41 HIV-

Figure 2. Distribution of study participants in the CARMA and BCC3 cohorts

- This project is a longitudinal study **comparing several markers of immune aging before and after HCV clearance**, and between groups of different HIV status.

- Biospecimens pre and post HCV treatment are collected from WLWH and HIV-negative women (controls) ≥16 years enrolled in the **Children and Women AntiRetrovirals and Markers of Aging** (CARMA) cohort (2008-2018; most with multiple visits) or the **British Columba CARMA-CHIWOS Collaboration** (BCC3) cohort study (2020-ongoing; one visit each to date) .

- Participants are well matched with respect to socio-demographic characteristics which is retrieved from the REDCap database.

Methodology

Women with available biospecimen (n~30) pre- and post- HCV clearance following HCV therapy are selected. We extract plasma, extract RNA and determine HCV RNA status (pos/neg) by RT-qPCR using an in-house assay to confirm whether HCV is chronic or cleared.
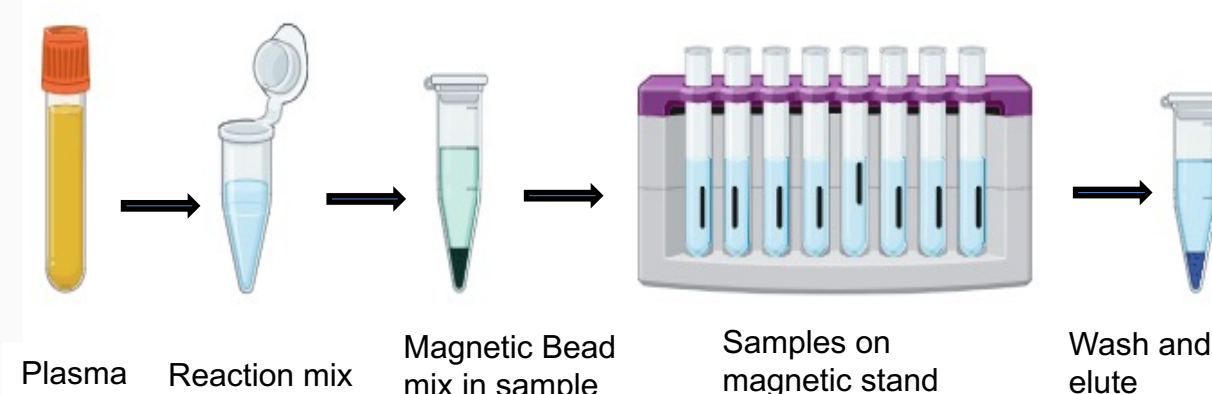
RNA extraction

Plasma   Reaction mix   Magnetic Bead mix in sample   Samples on magnetic stand   Wash and elute

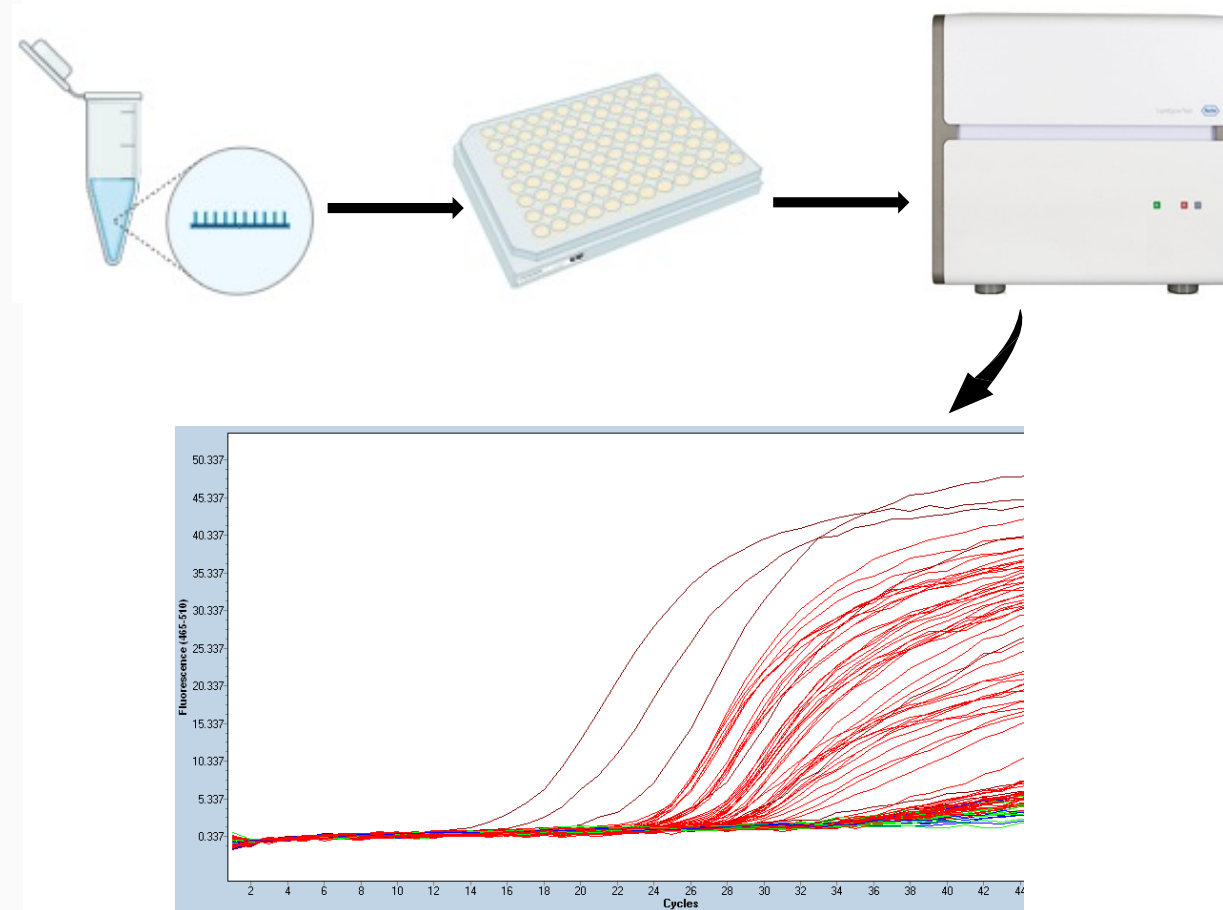**Figure 3**. HCV RNA extraction

Monoplex qPCR

Figure 4. Schematic representation of the HCV qPCR process

Table 1. Study groups

GROUPS		BASELINE		FOLLOW-UP		TARGET PER GROUP	NUMBER PER GROUP
		HIV status	HCV status	HIV status	HCV status		
STUDY	HCV clearance	Positive	Ab+ RNA+	Positive	Ab+ RNA-	~30	10
	HCV clearance	Negative	Ab+ RNA+	Negative	Ab+ RNA-	~30	0
CONTROL	Chronic HCV	Positive	Ab+ RNA+	Positive	Ab+ RNA+	~30	8
	Chronic HCV	Negative	Ab+ RNA+	Negative	Ab+ RNA+	~30	4
	No HCV	Positive	Ab-	Positive	Ab-	~30	0
	No HCV	Negative	Ab-	Negative	Ab-	~30	0

After selecting our participant for the various groups, we will proceed to investigating the various markers of immune aging and inflammation

Markers of immune aging

1. Leukocyte telomere length.
2. Mitochondrial DNA content.
Both will be measured by monochrome multiplex qPCR using DNA extracted from whole blood.
3. CD4:CD8 T cell ratio.
4. CD8 CD28-:CD28+ cell ratio.
Both will be measured by flow cytometry using live peripheral mononuclear blood cells.

Markers of inflammation and liver damage

IL-6, TNF-α, IL-10, INF-α, INF-γ, ALT and AST will be measured by mesoscale kits using plasma.

Expected results

- Chronic viral infections tend to cause immune activation, inflammation and T-cell exhaustion which tends to shorten telomere length in immune cells.
- **We anticipate that there will be an evolution in markers of immune aging and inflammation of these women from baseline to follow-up in these women.**

Significance

Since this study is looking at several markers at once, it will help draw a more complete picture of the effects of HCV clearance on immune aging in WLWH and HCV.
These findings will suggest whether HCV clearance may have longer term implications in age-related pathologies in WLWH and the importance of them clearing HCV.

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