High Frequencies of Adaptive NK Cells are Associated with Absence of Coronary Plaque in Cytomegalovirus Infected People Living with HIV

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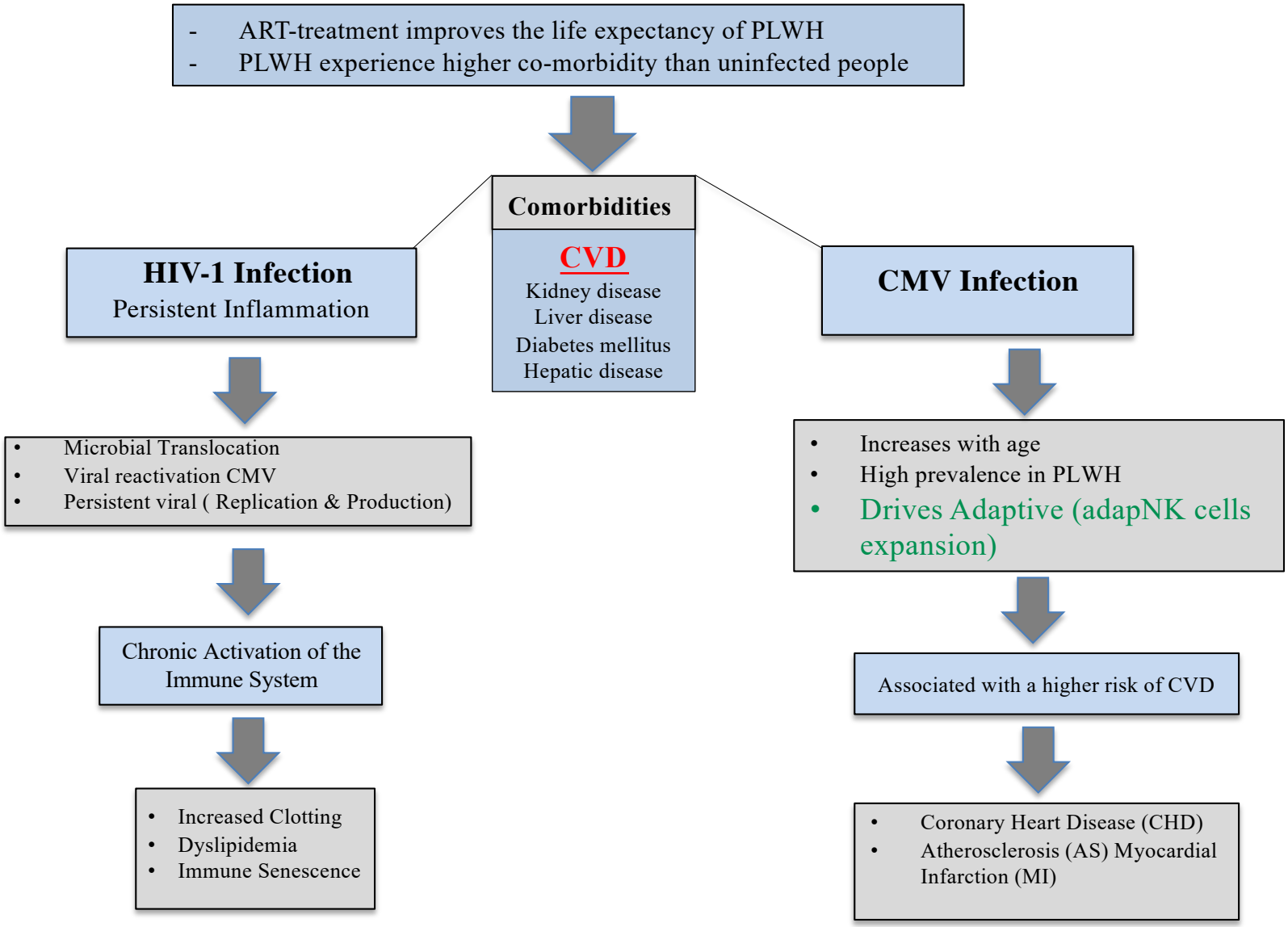
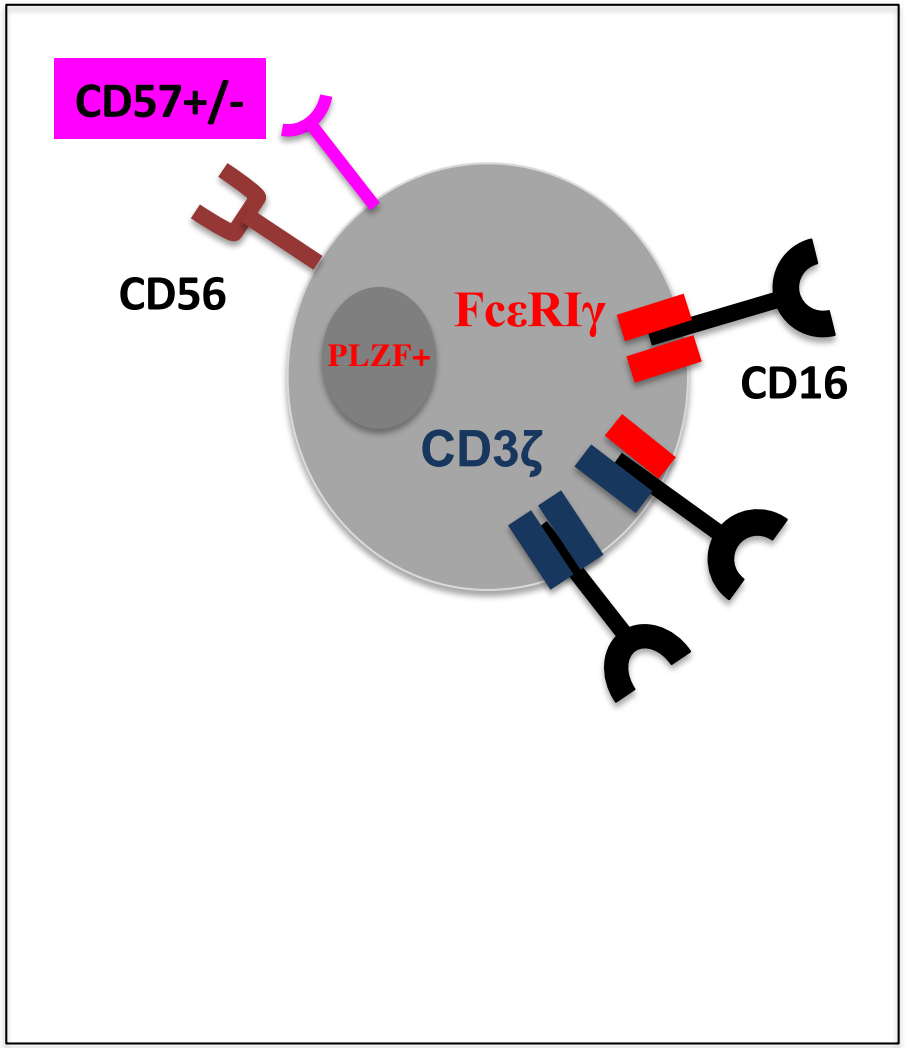
Introduction

HIV Infection and Cardiovascular Disease (CVD)



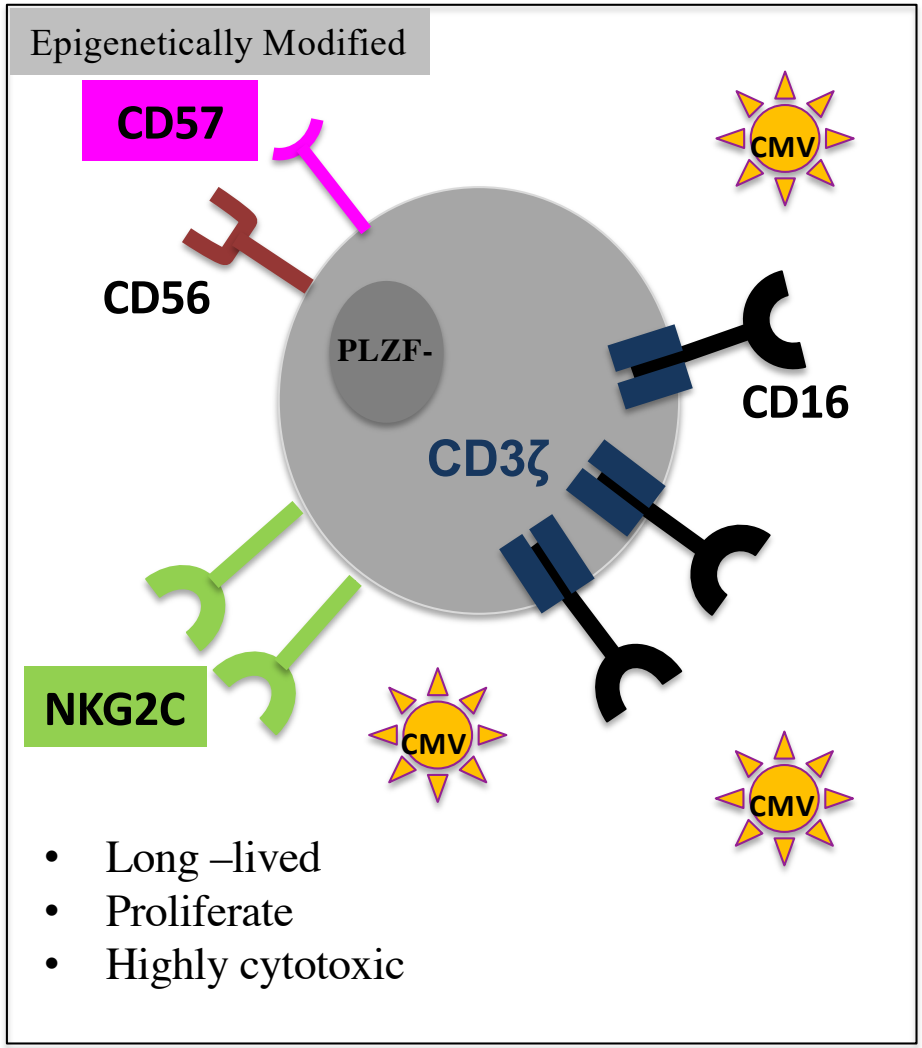
Yu Du *et al*., 2018, Haoran Wang *et al*., 2017 & Morteza Izadi *et al*., 2014 Ava Lorence *et al*., 2014 & Marcus JL *et al.,* 2016

cNK



NKG2C⁻

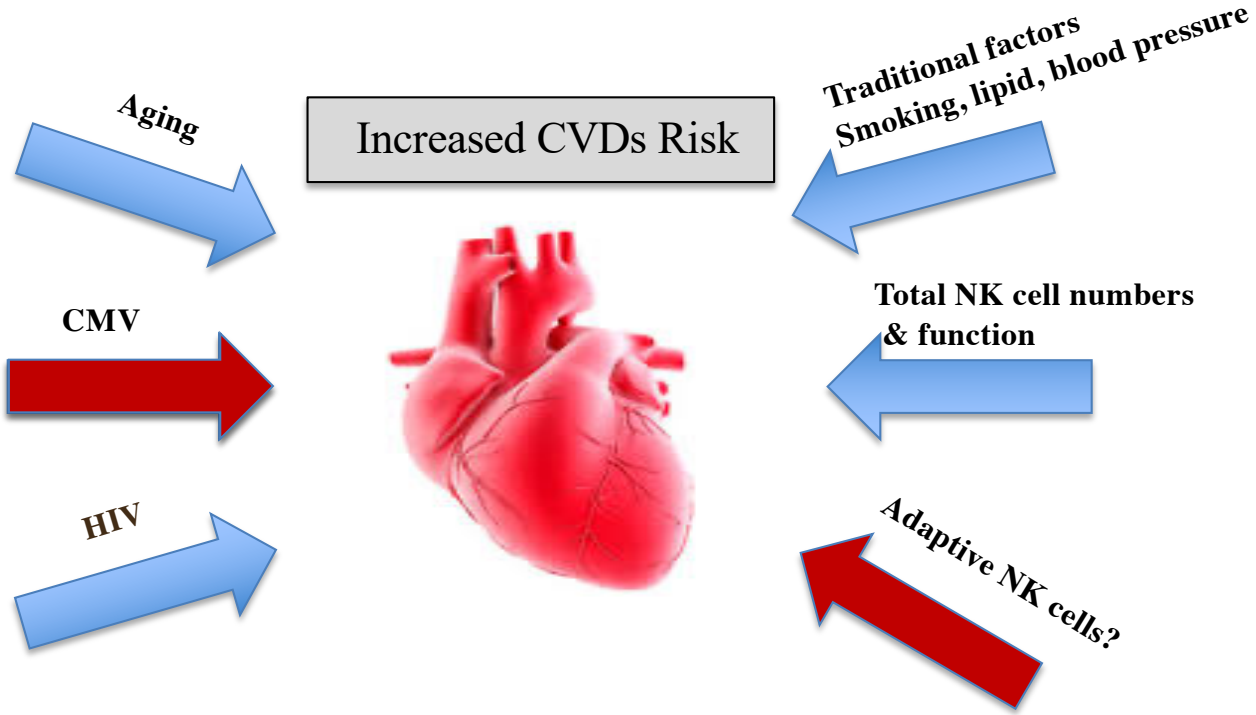
adapNK



NKG2C⁺ CD57⁺

Made by Alsulami K (information taken from Schlums H *et al.*,2015, Zhou *et al.*,2015 & D Peppa *et al.* 2018)

Rationale



Objective 1: To investigate whether adapNK cell frequency can be used as a biomarker predicting CVD outcomes

Aim-1: To determine the frequency of adapNK cells in participants of the Canadian HIV and Aging Cohort Study (CHACS) based on HIV and CMV infection status

Aim-2: To determine whether markers of CVD are worse in CMV+PLWH than in CMV mono-infected subjects enrolled in the CHACS

Bobryshev and Lord., 2005 , Martinez Rodriguez *et al*., 2013 & clerc and Rouz., 1997

Results

Table1: CHACS Study Population

Group	HIV$^+$CMV$^+$	HIV$^-$CMV$^+$	HIV$^+$CMV$^-$	HIV$^-$CMV$^-$
Males	119	28	8	15
Females	9	9	0	6
Median age (years), IQR	55.0 (50.8-60.3)	58.9 (53.0-65.7)	55.6 (51.3-57.4)	58.6 (52.8-63.9)
Total	**128**	**37**	**8**	**21**

- All CHACS participants were ≥ **40** years of age
- Median age (IQR) **55.0 (50.1- 60.8) years**
- Sample size : **194** subjects
- Infected for at least **18 years**
- Receiving antiretroviral treatment at least **15 years**

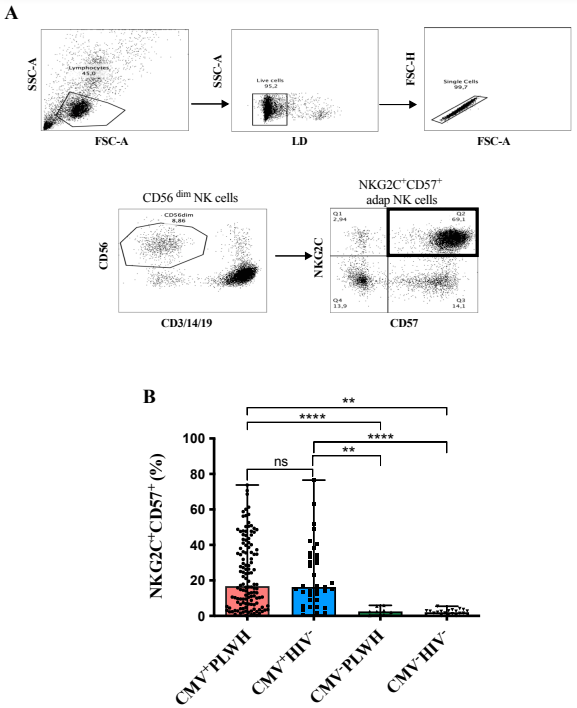


Fig1. The proportion of NKG2C$^+$CD57$^+$ adaptive NK (adapNK) cell frequency categories in total plaque volume (TPV) negative and positive CMV infected people living with human virus (CMV$^+$PLWH) and CMV mono-infected (CMV$^+$HIV$^-$) individuals.

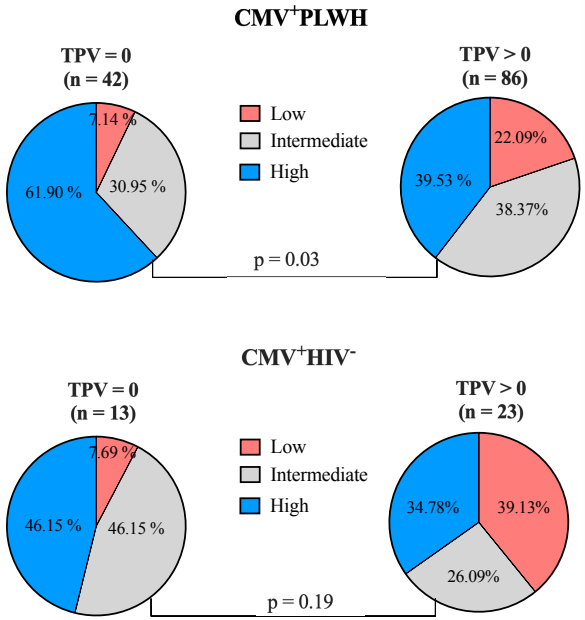


Fig 2. Frequency of AdapNK cells in CHACS Participants Stratified by Having a Negative versus Positive TPV Score

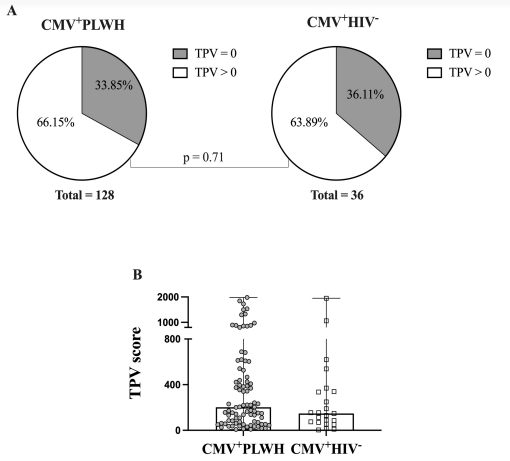


Fig 3.TPV Scores in CMV$^+$PLWH and CMV$^+$HIV$^-$ Subjects

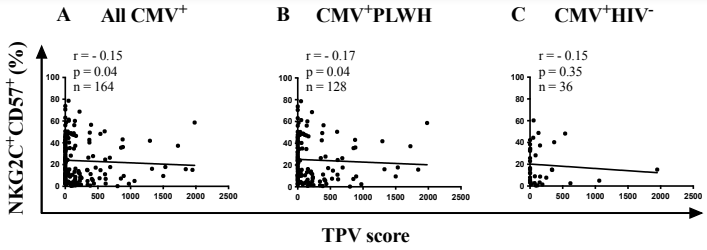


Fig 4. Correlation between TPV Scores and the Frequency of AdapNK cells in CMV$^+$PLWH and CMV$^+$HIV$^-$ Subjects

Table 1: Univariable and Multivariable Analysis of Association of AdapNK cell frequency with positive total plaque volume in CMV Seropositive Participants

Characteristics	Univariable OR (95%CI)	P value	Multivariable OR (95% CI)	P value
Adaptive NK cells frequency				
• High (>20%)	0.74 (0.56- 0.95)	**0.019**	0.75 (0.58-0.97)	**0.030**
• Intermediate (6-20%)	0.90 (0.72 – 1.14)	0.410	0.92 (0.72- 1.17)	0.509
• Low (<6%)	1.0 (ref)		1.0 (ref)	
HIV status				
• Positive	1.07 (0.81- 1.40)	0.620	1.08 (0.81-1.42)	0.582
• Negative	1.0 (ref)			
Age (per 10 years increase)	1.26 (1.09- 1.45)	**0.001**	1.23 (1.06- 1.44)	**0.006**
High blood pressure				
• Present	1.07 (0.85- 1.33)	0.56	-	-
• Absent	1.0 (ref)			
Smoking exposure (per each increase in 10 pack-years)	1.09 (1.05- 1.13)	**<0.001**	1.08 (1.02-1.13)	**<0.001**
LDL – cholesterol (1 mmol/1)	1.00 (0.91 – 1.11)	0.888	-	-
Statin use				
• yes	1.21 (0.98- 1.48)	**0.07**	-	
• no	1.0 (ref)			-
BMI (1kg/m2)	1.07 (0.81- 1.40)	0.620	-	-

Conclusion

- CMV infection drives the expansion of adapNK cells
- In this aging cohort, the frequency of adapNK cells does not differ between unlike what is observed in cohorts of younger CMV^{+}PLWH and CMV^{+} mono-infected persons wgere the % of adap NK cells is higher in CMV^{+}PLWH.
- Individuals with frequencies of adapNK cells that allow them to be classified as having a higher frequency of adapNK cells are more likely to have TPV scores = 0
- This suggests that expanded adapNK cells are associated with protection from CVD
- TPV increases with the traditional cardiovascular risk factor such as smoking and age after adjusting all variables in the model

Acknowledgments

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