

# Implications of long-term solvent use on NK activation and function: a risk factor for HIV Acquisition

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“Conflict of Interest Disclosure: I have no conflicts of interest”

# Introduction/Background

## What is Solvent Use?

- Solvents: broad group of **readily available** lipid soluble substances that's use results in psychoactive effects (Addiction Foundation Manitoba, n.d.)
- Over 1,400 products on the market (CCENDU, 2015)
  - Examples: **Lacquer thinner**, hairspray, rubbing alcohol, gasoline, ect...
  - Cost between 5 – 20 dollars
  - Globally 2% of people in drug treatment programs use solvents (United Nations Office on Drugs and Crime, 2017)

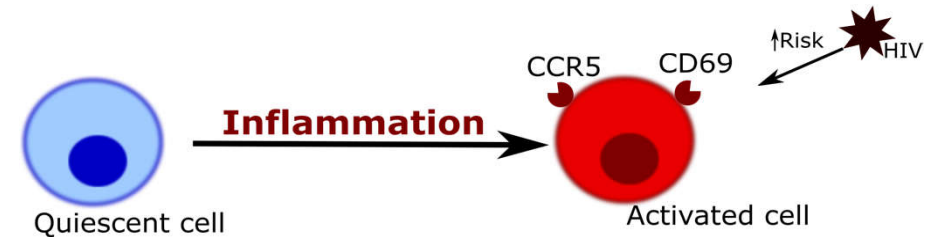
## Natural Killer (NK) cells

- CD16+CD56++ NK cells (Caligiuri et al 2008)
  - Cytokine producers
    - IFN- $\gamma$  producers in response to stimuli
    - Little to know cytotoxic abilities
- CD16++CD56+ NK cells (Caligiuri et al 2008)
  - Reduced ability to produce cytokines
  - More cytotoxic role
  - Believed to be the more mature cell type
- **Increased NK activation is associated with increased risk HIV acquisition**
  - Characterised by lower CD38 expression on NK cells (Naranbhai et al. 2012)

## Solvent use and immune activation

- Exerts pro-inflammatory effects (animal models)
  - Increased oxidative burst (Lima et al., 2015)
  - Pro-inflammatory cytokine/chemokine secretion (Soderberg, 1998)
  - Activation/recruitment of inflammatory cells (Anton & Anton, 2001)
  - Less efficient CTL response (Anton & Anton, 2001)
  - Increased vascular/mucosal permeability (Lino-dos-Santos-Franco et al., 2010)

## Immune activation and HIV



## Solvent use and infectious diseases

- Correlated with increased risk of:
  - HIV (Bell & Fowke, 2011)
  - HCV (Bell & Fowke, 2011)

**Gap in Knowledge:** what is the effect of solvent use on the immune system?

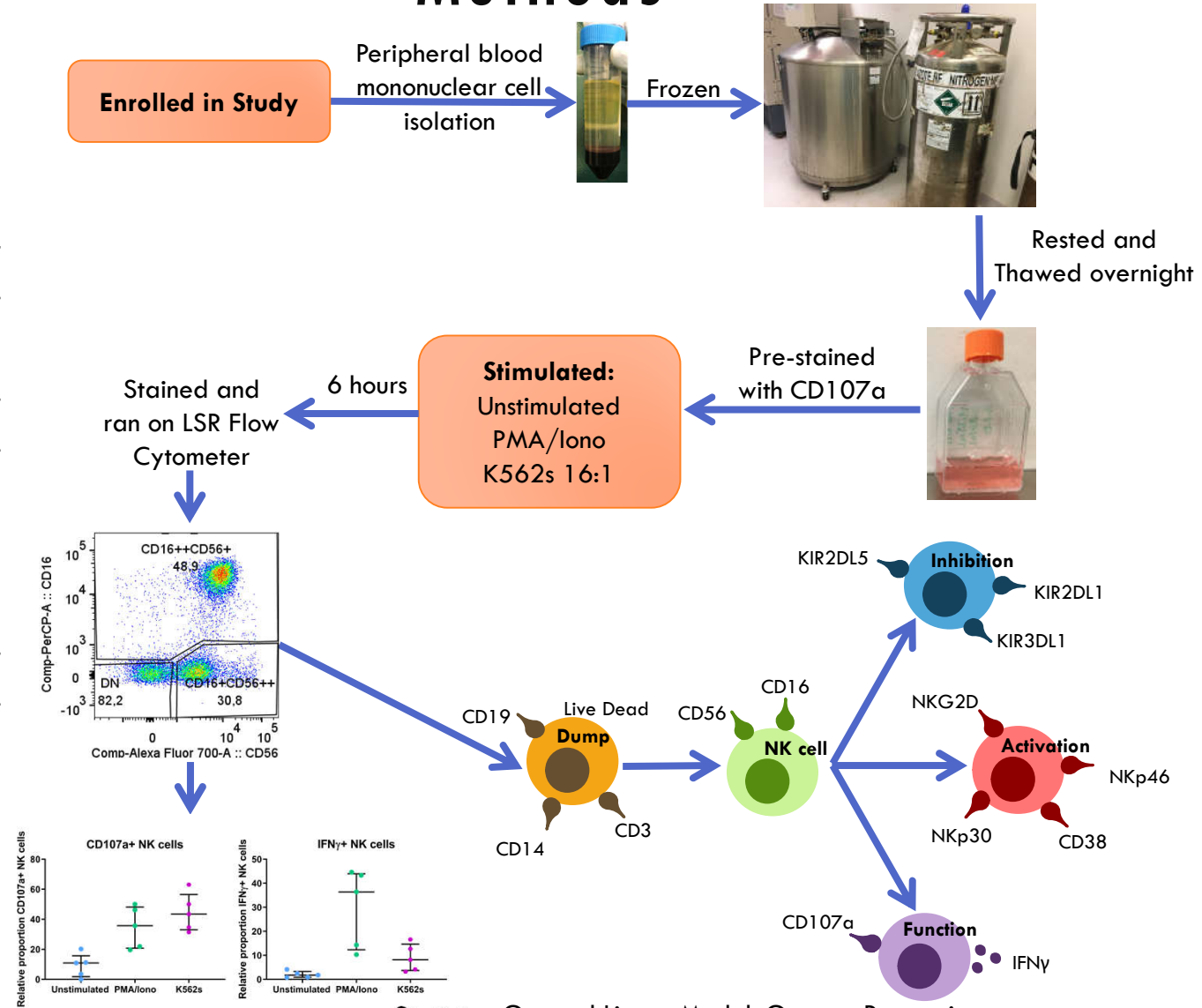
# Hypothesis: Solvent users will have greater immune activation profiles than community matched non-solvent users

## Participants (N=27)

Participants from Sunshine House Community

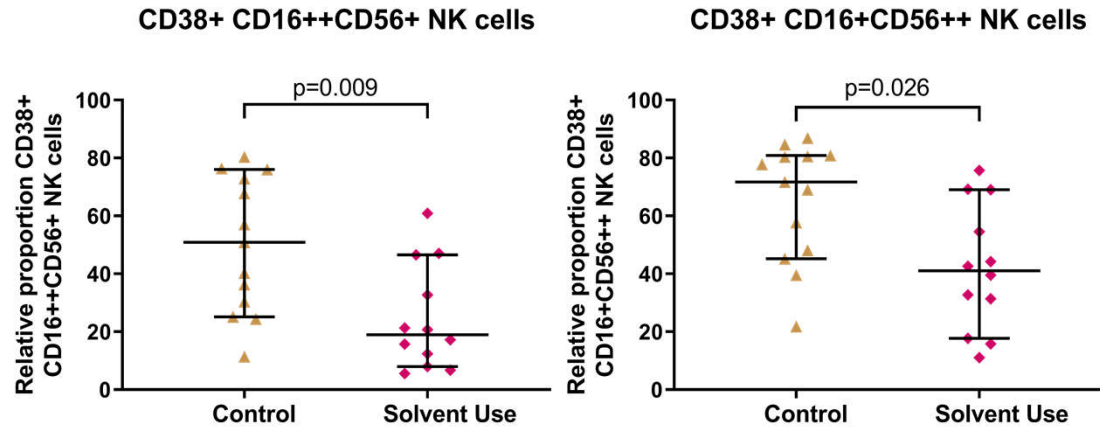
	Controls (n = 13)	Solvent Users (n = 14)	p value
<b>General Characteristics</b>			
Age (mean [SD])	44 [9.9]	46 [10]	0.560
Biological sex male (n (%))	4 (31)	10 (71)	<b>0.035</b>
<b>Behaviours</b>			
Smoke Cigarettes/Butts (n(%))	6 (46)	13 (92)	<b>0.013</b>
Smoke other substances (n(%))	8 (62)	8 (57)	0.816
Drink alcohol (n(%))	9 (69)	10 (71)	>0.999
IDU (n(%))	1 (7.7)	3 (21)	0.596
<b>Health</b>			
Ever had an STI (n(%))	6 (50)	10 (71)	0.422
Chronic Disease affecting the immune system (n(%))	8 (61)	9 (64)	>0.999

## Methods

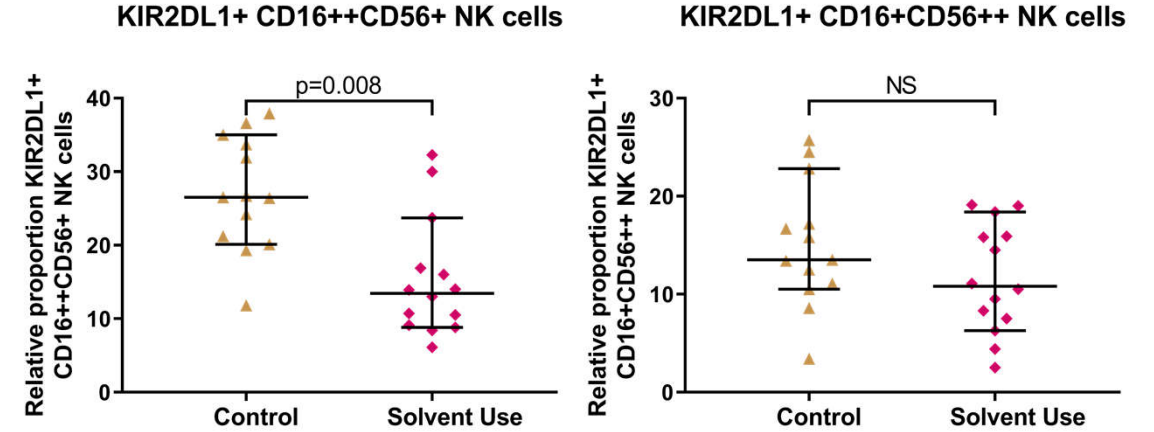


# Results: Effect of Solvent use on NK Activation and Function

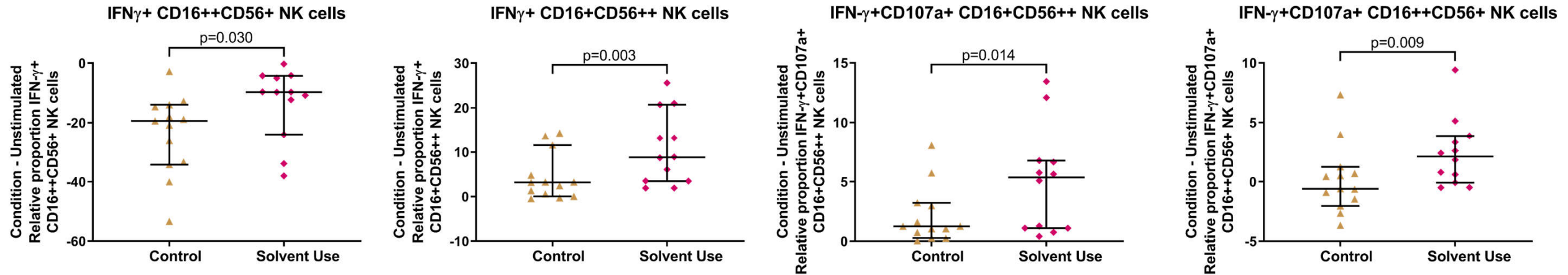
## Effect of solvent use on NK activation



## Effect of solvent use on markers of NK inhibition



## Effect of solvent use on NK function



Effect of long term solvent use on NK activation and function following 6 hour invitro stimulation assay with PMA/Ionomycin

# Conclusion and Significance

## Conclusion

- NK cells from individuals have **higher activation** levels than community matched non solvent users
- Upon stimulation these NK cells are **unable to function** to the same capacity as NK cells from community matched non solvent users

## Significance

- Phenotype of increased NK activation (CD38) has been shown to increase the risk of HIV acquisition
- Solvent users may be at increased risk of HIV acquisition due to the activation status of their innate immune system (NK cells)

## Thank you!

- Fowke lab members
- Canadian Aboriginal AIDS Network
- Sunshine House
  - Margaret Ormond
  - John Schellenberg
- Participants
- Funding Sources



Research  
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