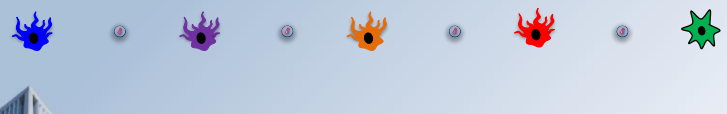
Examining the Role of Mononuclear Phagocytes in Mediating Sexual Transmission of HIV

Hafsa Rana
PhD Candidate

The Westmead Institute for Medical Research
The University of Sydney, Australia



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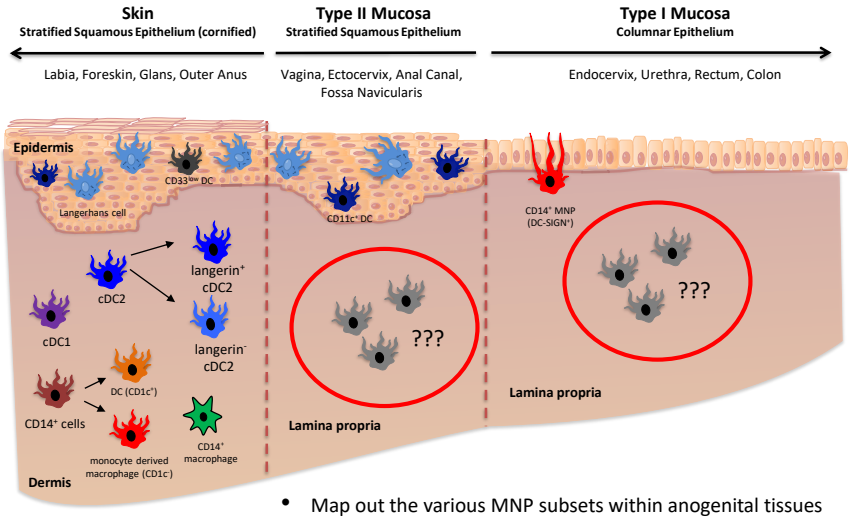
Determining the Mononuclear Phagocyte Subsets Present in Human Anogenital Tissues

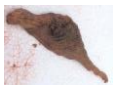


- Map out the various MNP subsets within anogenital tissues
  - Investigate the role of these cells in the transmission of HIV

Access to Human Anogenital Tissue

extensive collaborations with surgeons for access to all human anogenital tissue types

female genital tract

Labia 

Vagina 

Cervix 

male genital tract

Foreskin 

Glans 

Urethra 

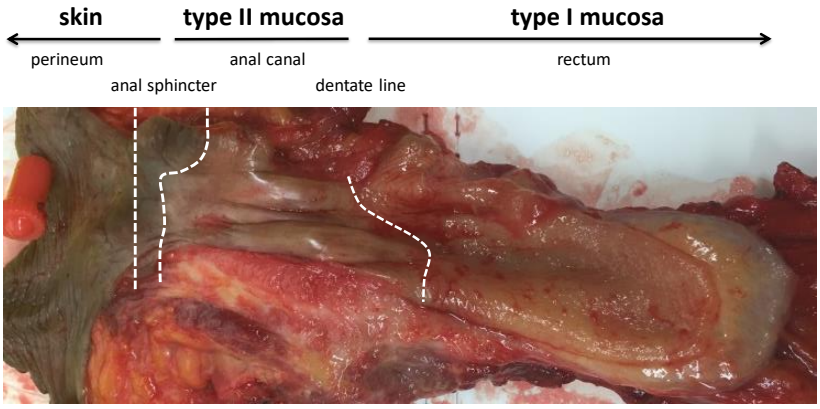
anorectal tract

Perineum

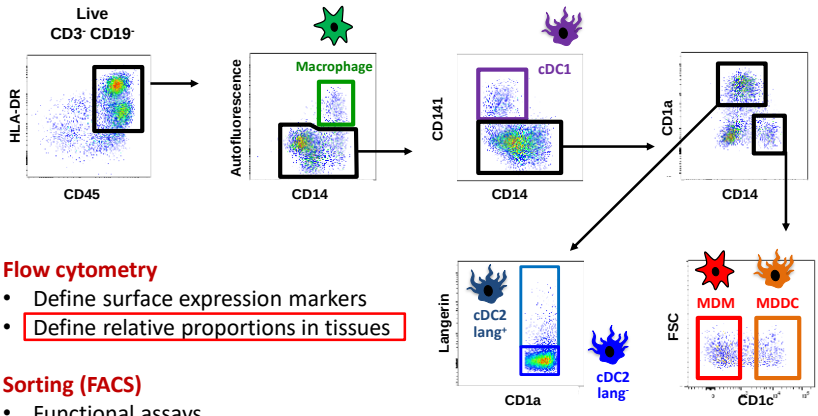
Anal Canal

Rectum

Anorectal Tissue



Dermal MNP Flow Cytometry Gating Strategy



Flow cytometry

- Define surface expression markers
- Define relative proportions in tissues

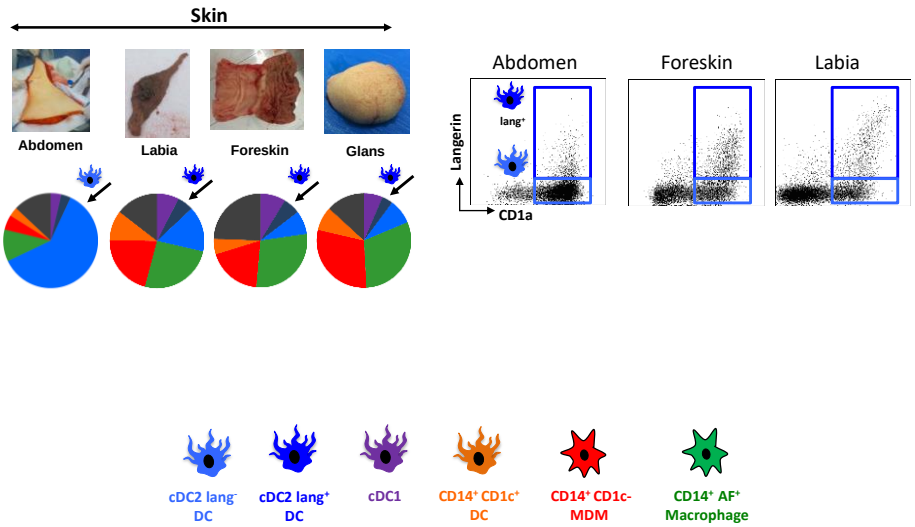
Sorting (FACS)

- Functional assays
- HIV Transfer assays

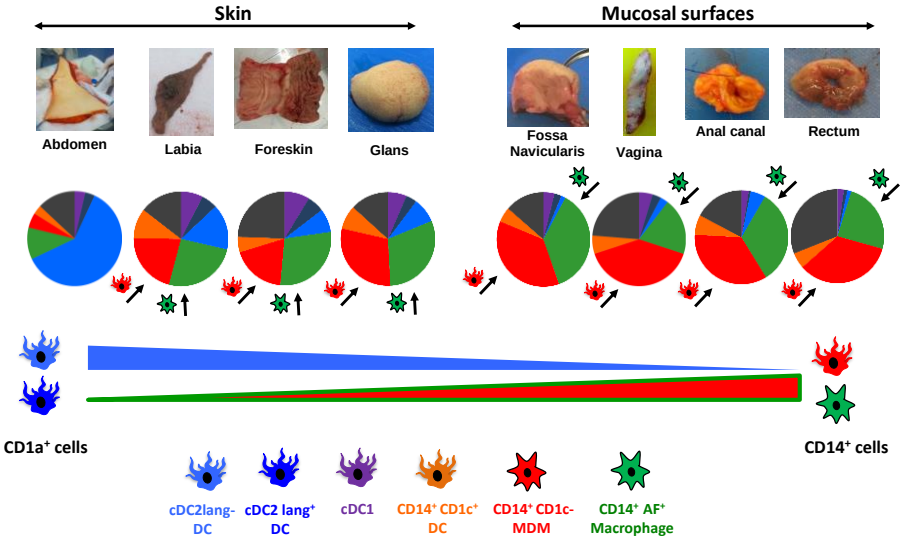
Other Panels

- Memory CD4 T Cells
- T_H cells
- Innate lymphoid cells
- B Cells

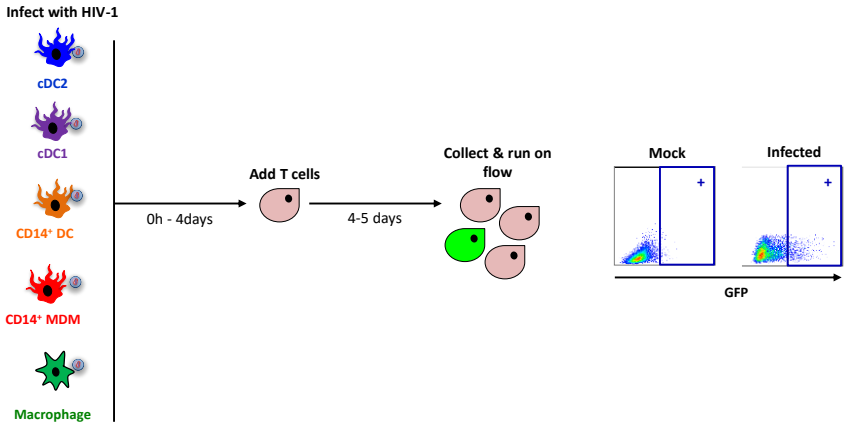
DC Subsets in Human Anogenital Tissues



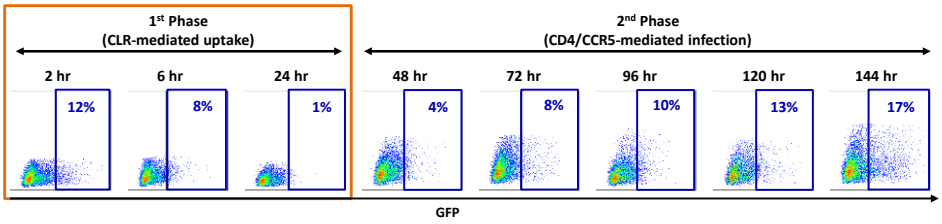
DC Subsets in Human Anogenital Tissues

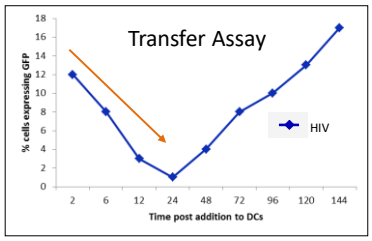


DC –T Cell HIV Transfer Assay

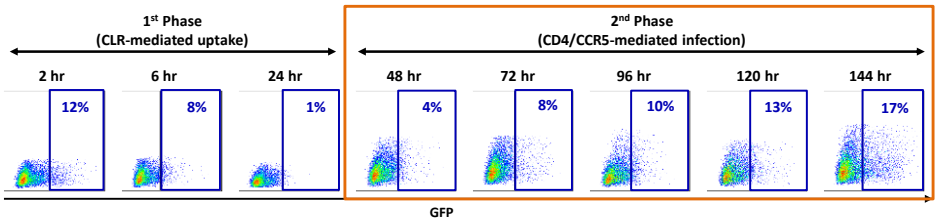


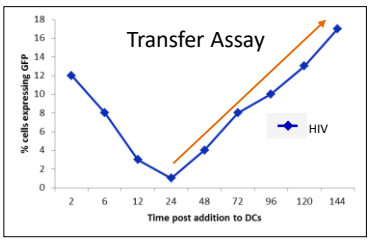
First Phase Transfer



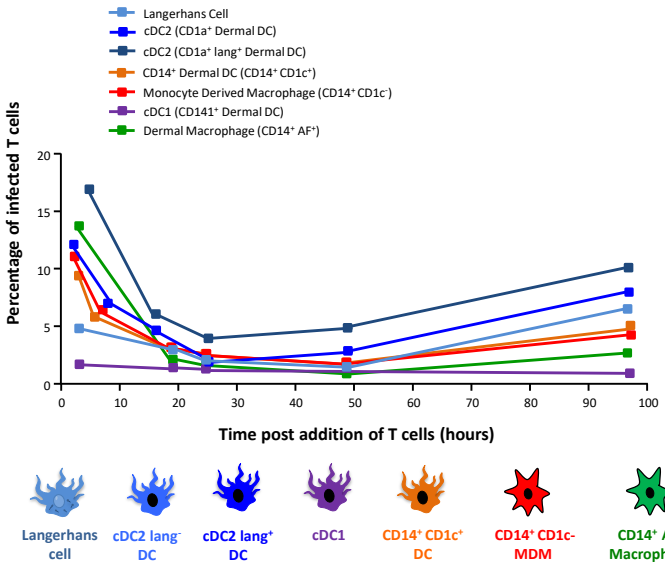


Second Phase Transfer





DC Subsets Differ in their Ability to Transfer HIV to CD4 T cells



Nasr et al., *J Immunol* 2014

Summary

1. There is considerable variation in the relative proportions of Mononuclear phagocytes found within the different tissues of the anogenital tracts
   - Lang- cDC2s dominate abdominal skin
     - Lang+ cDC2s increase in genital skin and mucosal tissues
   - Macrophages and MDMs dominate anogenital tissues
2. Majority of the subsets of MNPs are able to transfer the virus to HIV target cells in 2 phases with the Lang+ cDC2s transferring most efficiently

Significance

1. Soluble langerin has been shown to block transfer from Langerhans Cells to T cells (Nasr et al., *J Immunol* 2014)
2. Determining the receptors required for transfer provides a potential therapeutic target to inhibit viral transfer
3. Establishing which MNP populations are efficient in delivering HIV to T cells is important in the development of HIV vaccines and adjuvants

Acknowledgements

Martijn Gosselink Jake Rhodes Toby Plasto Heeva Baharlou
Chloe Doyle **Kirstie Bertram** Andrew Harman Hafsa Rana

Tony Cunningham

Najla Nasr

Plastic Surgeons
Tim Papadopoulos
Jake Lim
Laith Barnouti
Mark Kohout
Steve Merten
Gavin Sandercoe
Peter Laniewski

Colorectal Surgeons
Grahame Ctercteko
Martijn Gosselink
Kenneth Loon
Nimala Pathma-Nathan
Mark Gladman
Alan Meagher

Urologists
Ralph Cohen
Andrew Brooks
Michale Wines

University of Newcastle, UK

Muzlifa Haniffa

Rachel Botting