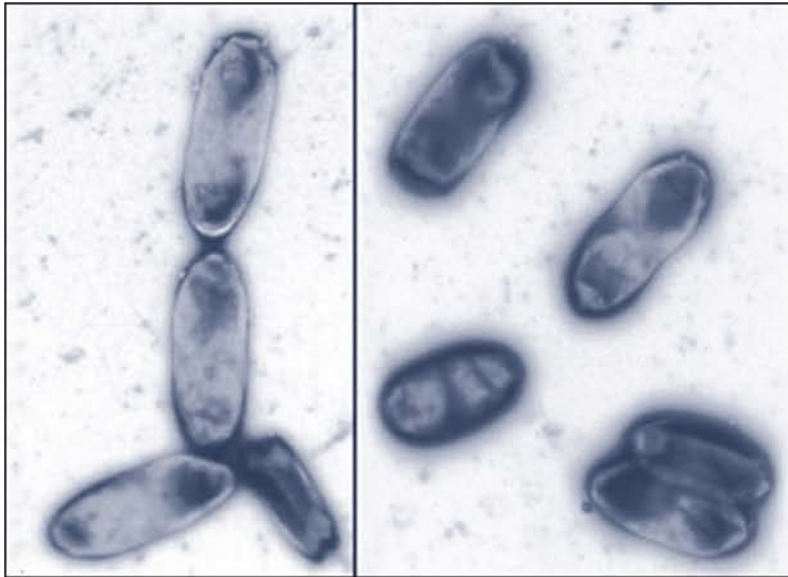






# *Haemophilus influenzae*

- Human restricted bacterial pathogen
- Can be carried by healthy individuals
- Can cause severe diseases: meningitis, sepsis, pneumonia
- Many strains have a polysaccharide capsule protecting bacteria against immune defenses
- Six serotypes of encapsulated *H. influenzae*: a-f; most virulent: Hib
- Hib was the major cause of meningitis in young children before vaccine introduction in the 1990s



Transmission electron micrographs of *Haemophilus influenzae*

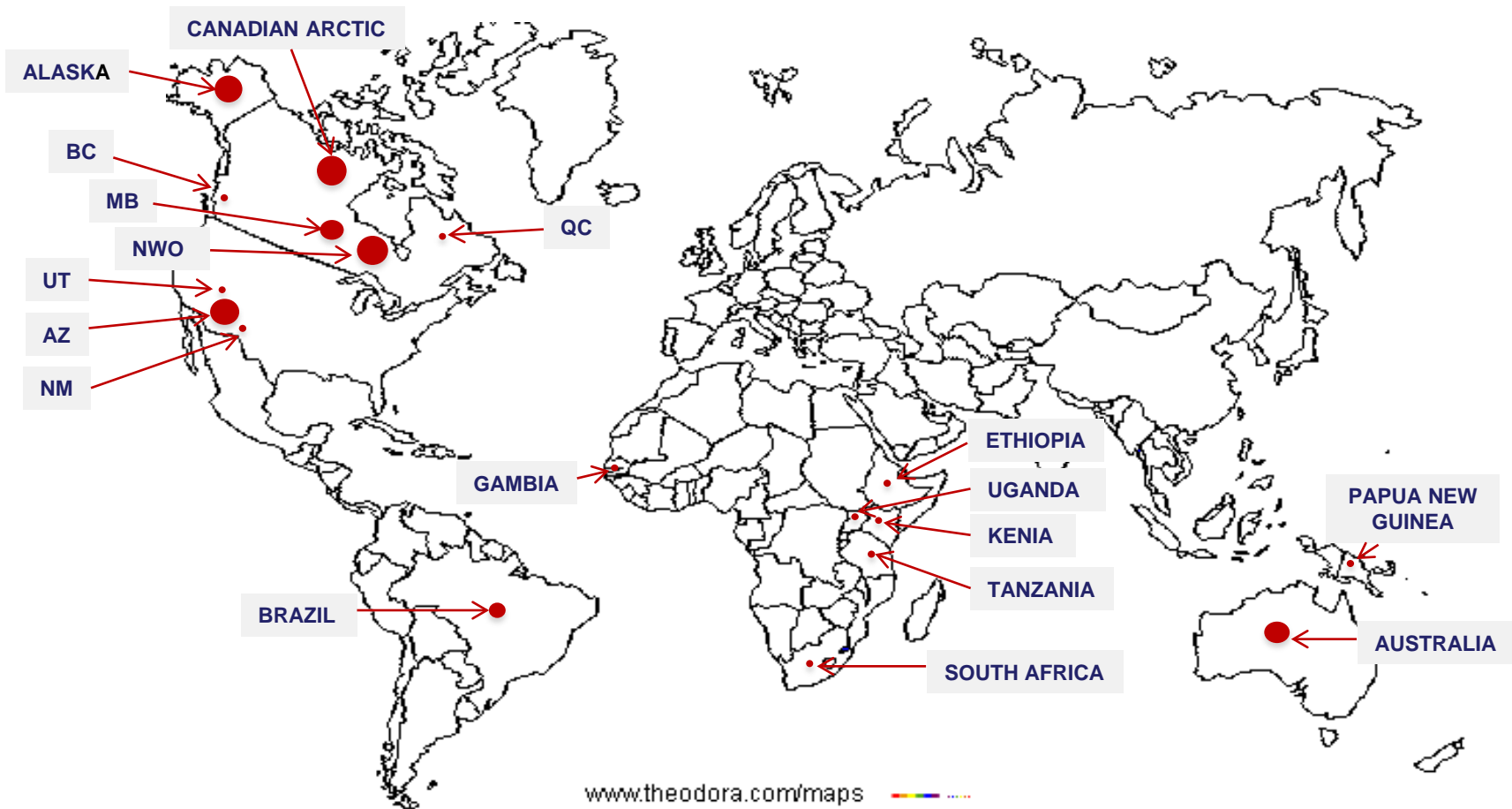
<http://www.wadsworth.org/databank/haemo.htm>



*Haemophilus influenzae* type A isolated from a child with severe blood infection

Courtesy of Dr. Raymond Tsang of the National Microbiology Laboratory

# Geographical distribution of invasive *H. influenzae* type a disease



# Children < 5 years old

Northwestern Ontario  
*H. influenzae* type **a**

Canada  
*H. influenzae* type **b**

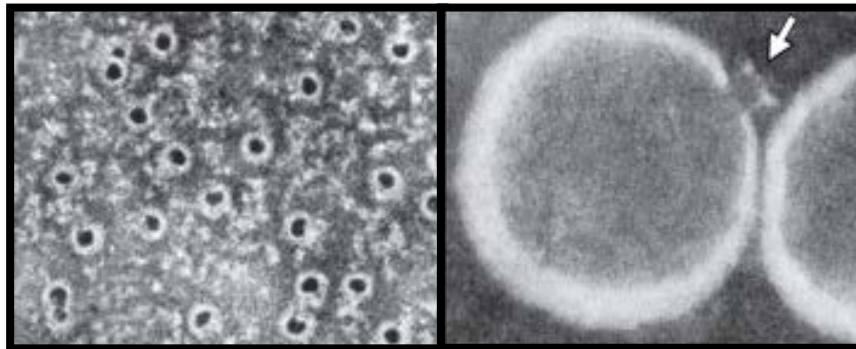
Year	2002	2004	2006	1983
Per 100,000	7.7	23.2	15.5	20

Brown et al, *Clin Inf Dis*  
2009, 49: 1240-1243

Can Dis Wkly Rep  
1986

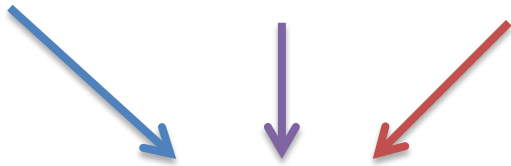
# Complement system

- System of large number of plasma proteins that react with pathogens and one another to help fight infection
- Focus on classical complement pathway
- Causes formation of membrane attack complex



# Serum Bactericidal Assay

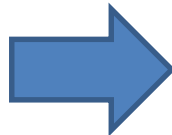
Complement    Bacteria    Serum



Serum is serially diluted  
2-fold in each well (1/8<sup>th</sup>, 1/16<sup>th</sup>)

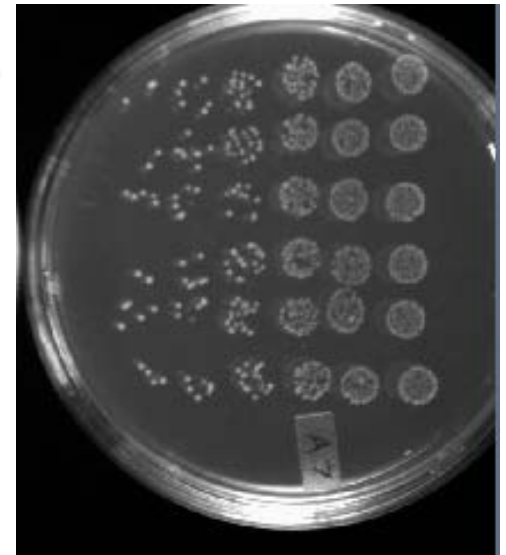


Mixture incubated  
at 37 Celsius for 1  
hour



Surviving bacteria  
plated on  
growth media

Replicates



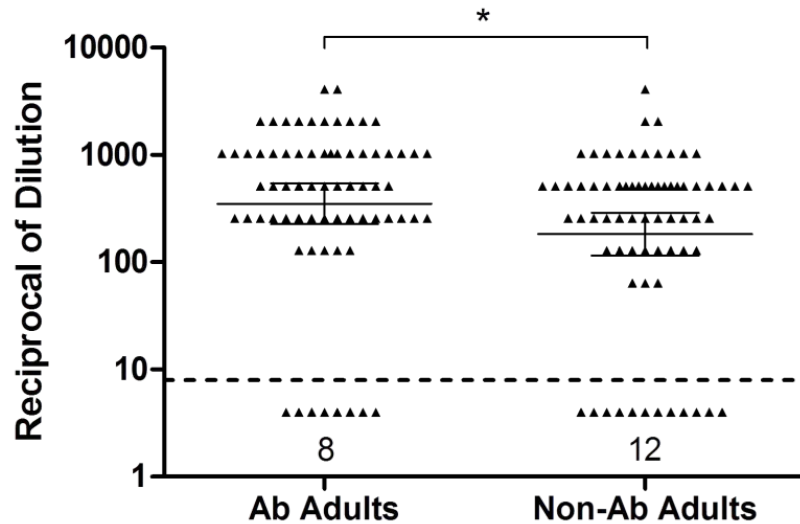
Decreasing serum concentration



# Research Question

**Is the high rate of invasive *H. influenzae* disease among First Nations People in northwestern Ontario related to a lack of protective antibody?**

# Serum Bactericidal Assay



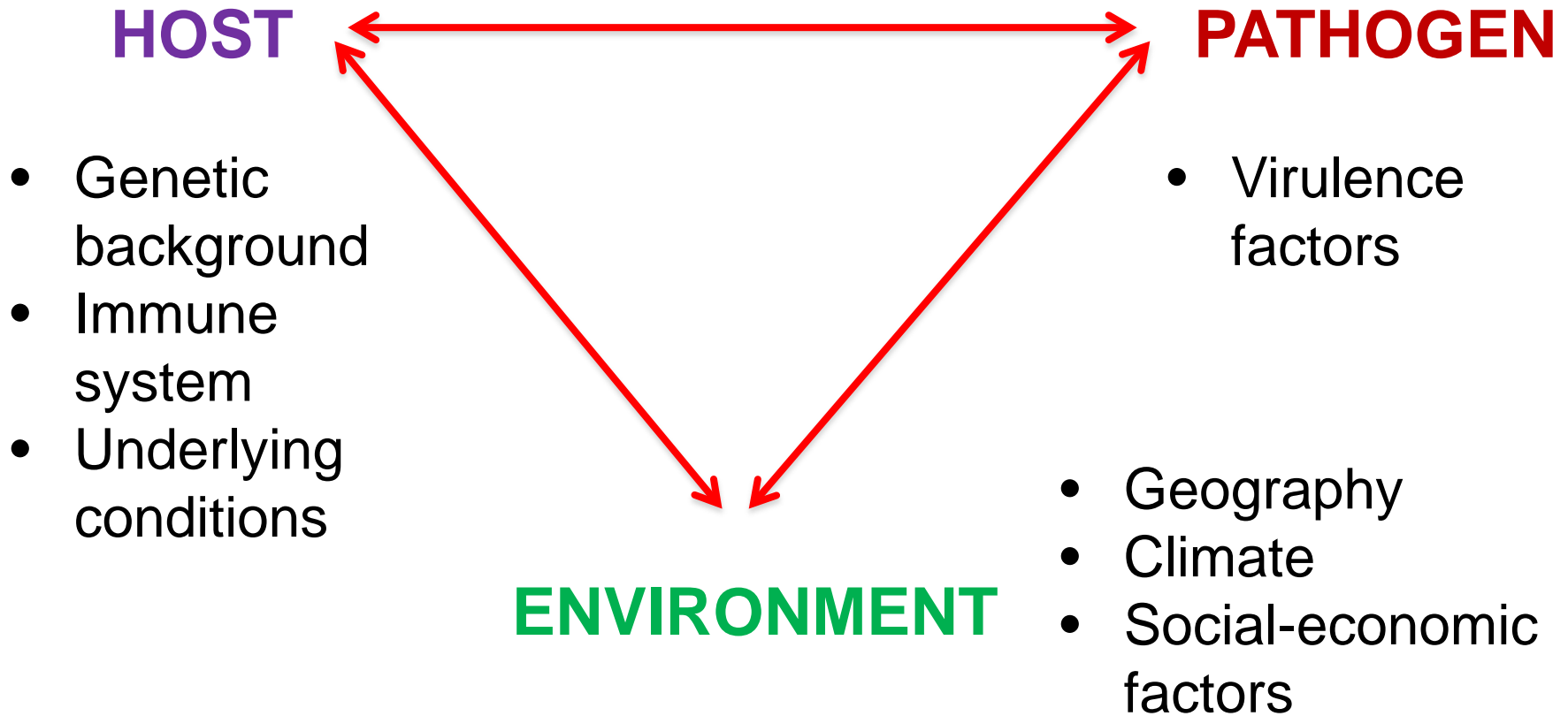
Geometric Mean Titre	351.4	182.8	p=0.0113
95% Confidence Interval	226.8-544.5	115.5-289.4	
Below Detection Limit	11%	17%	

- First Nations adults exhibited significantly higher antibody functional activity compared to their non First Nations counterparts

# Discussion

- First Nations group have significantly more potent anti-Hia antibodies compared to non-First Nations
- Implies First Nations should be *less* vulnerable to invasive Hia infection than non-First Nations
- Higher carriage rates could lead to immune boosting in the healthy and disease in the immunocompromised

# Susceptibility to infections



# Expansion of Research Program

- Naturally acquired antibody: Serum bactericidal activity of adult volunteers: First Nations communities from regions of high and low Hia incidence and non-First Nations from Kenora
- Surveillance: All *H. influenzae* isolates from Meno Ya Win Health Centre collected for analysis
- Carriage: Nasopharyngeal swabs from First Nations children 3-5 yrs from Sioux Lookout catchment area

# Naturally acquired immunity against *H. influenzae* type a



★ Asubpeeschoseewagong  
(Grassy Narrows) First Nation  
Pop: 950  
55 Serum Samples



★ Saugeen First Nation  
Pop: 725  
50 Serum Samples

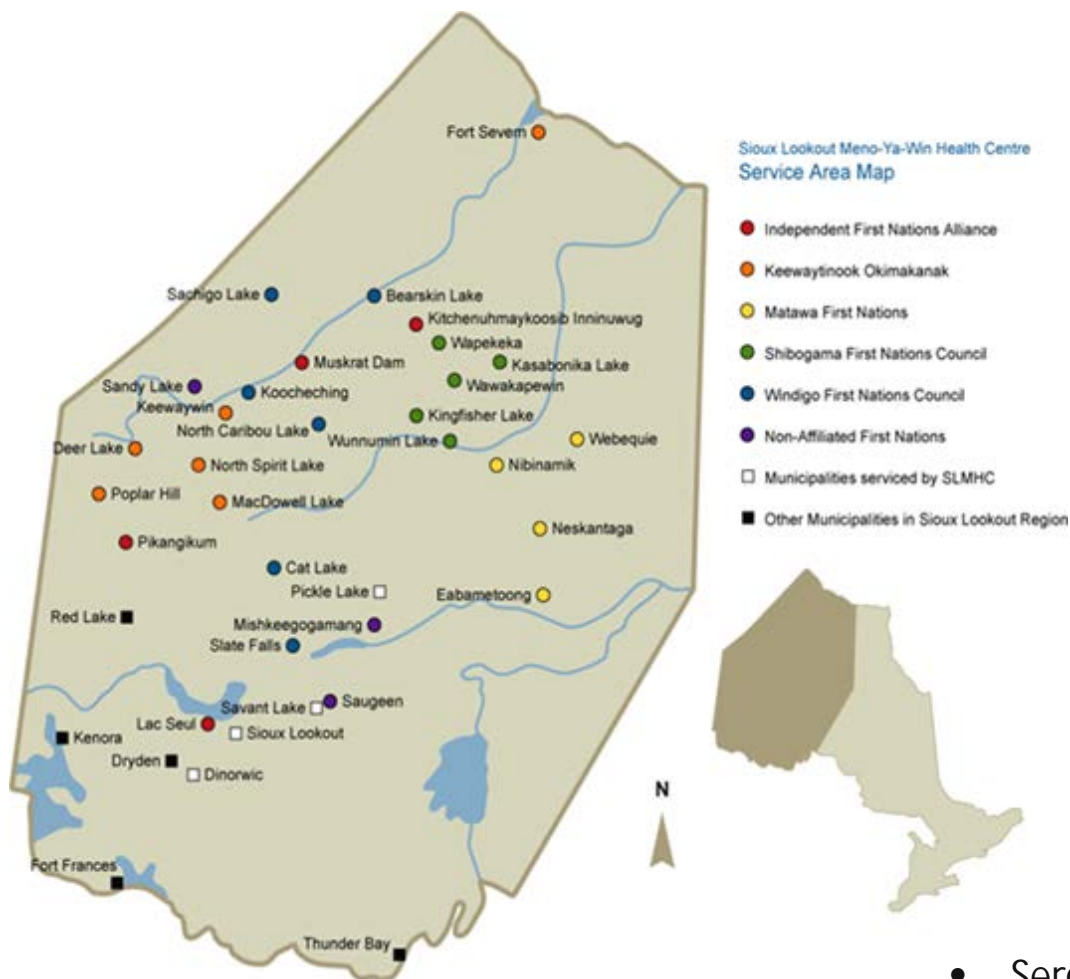


Kenora non-First Nations



<http://atlas.gc.ca>

# Meno Ya Win Health Centre: Surveillance



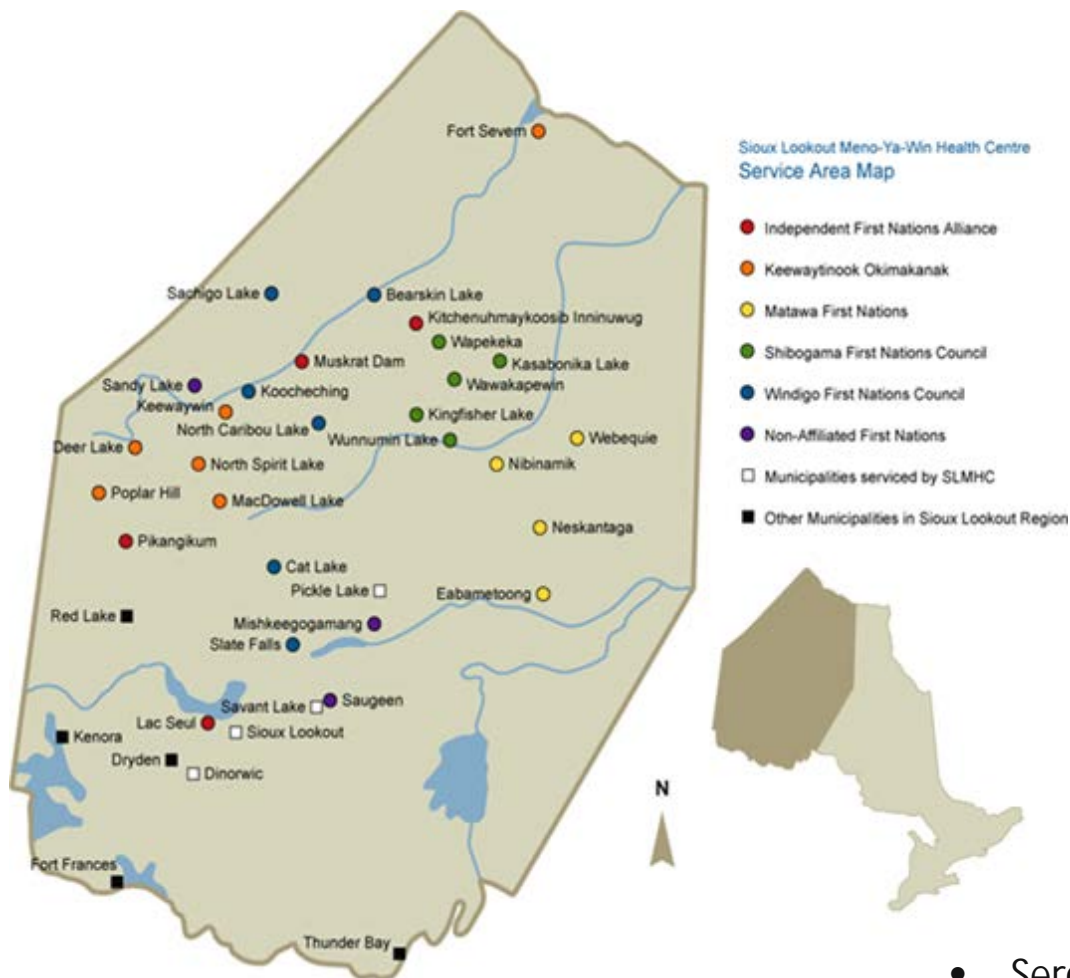
Collection of all clinical *H. influenzae* Isolates (including non-invasive)

Preliminary data (Nov 2013-Aug 2015):

Hia 6/77 (**7.8%**) of non-invasive *H. influenzae* isolates

- Serotyping
  - Clonal analysis
  - Genetic characterization
- } Raymond Tsang,  
NML

# Meno Ya Win Health Centre: Carriage



Nasopharyngeal swabs from  
First Nations children 3-5 years old

## Preliminary data

Hia 2/20 (**10%**) of swabs  
from healthy children

- Serotyping
  - Clonal analysis
  - Genetic characterization
- } Raymond Tsang,  
NML



# Future Directions

- Analyse serum samples
- Hia vaccine development SBA SOP, workshop
- Saliva IgA antibodies First Nations children

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