Infant immune responses to *B. pertussis* infection and vaccines.

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Whooping cough

- **Highly contagious respiratory infection caused by *Bordetella pertussis***
- **Estimated > 350,000 deaths worldwide annually**
- **Very severe in infants (1/10 in intensive care unit)**
- **Two types of vaccines:**
  - whole cell vaccines
  - acellular vaccines

Virulence factors of *Bordetella pertussis*

Adhesins

- **filamentous hemagglutinin (FHA)**
- pertactin
- fimbriae
- **…….**

Toxins

- **pertussis toxin (PTX)**
- tracheal cytotoxin
- adenylate cyclase toxin
- heat-labile toxin
- endotoxin (LPS)

Immunity against *Bordetella pertussis*

Humoral

High Ab levels after infection / vaccination

BUT

* **no protection of the neonate by maternal Abs**

* **no correlation between Ab levels and protection**

Cellular

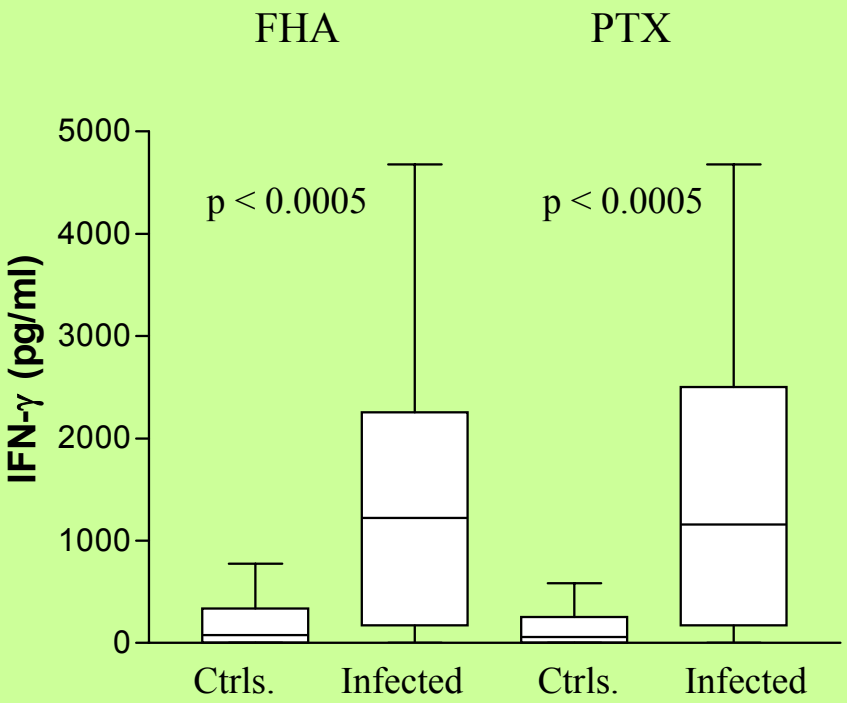
* ***murine model of respiratory infection:***
  protective role of T cells
  secretion of Th1 type cytokines

* **Th1 type cytokine secretion by T lymphocytes from convalescent children**

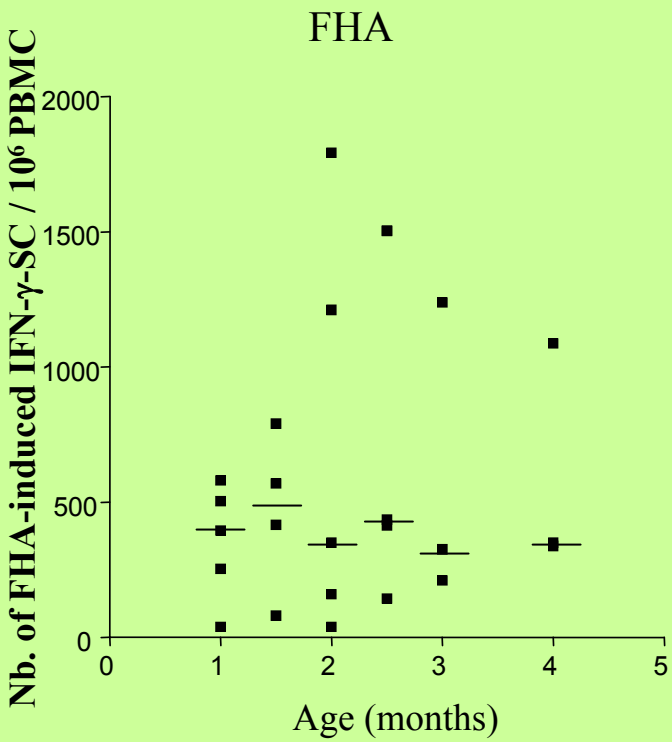
Mucosal ?

« Infants are immature in their cellular immune responses »

Acute *Bordetella pertussis* infection in 2 months old infants



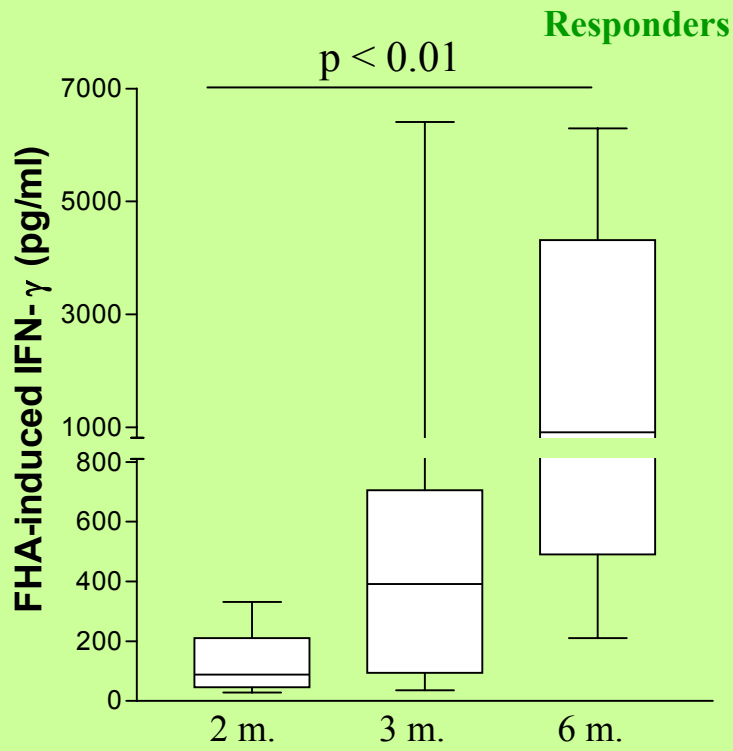
32 infected infants
age: 1 - 4 months

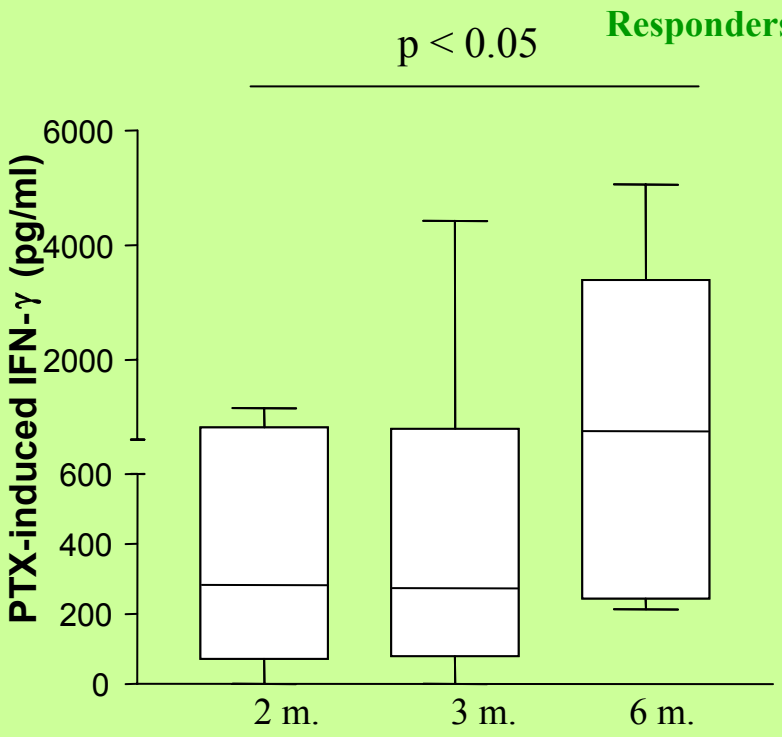


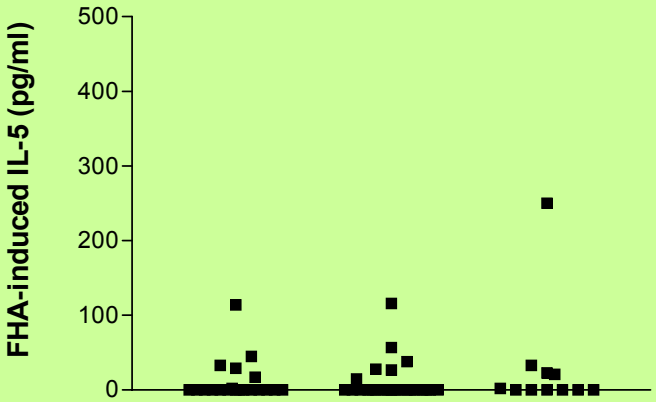
F. Mascart et al. J. Immunol. 2003; 170: 1504-9

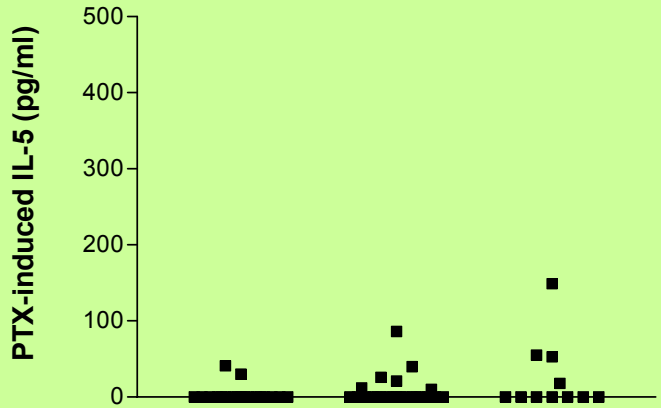
WHOLE CELL PERTUSSIS VACCINE

N = 16



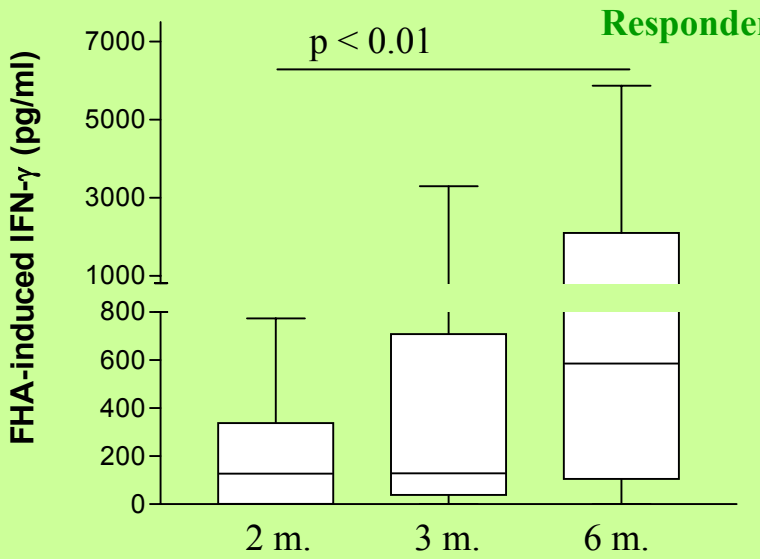


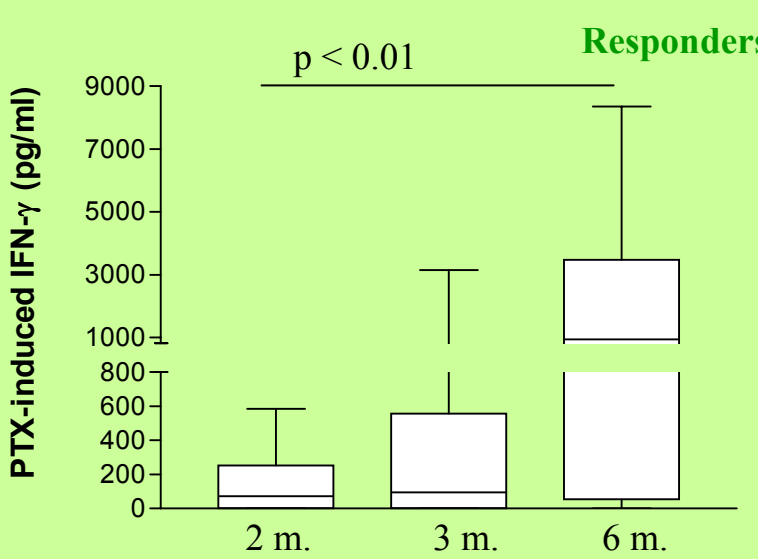


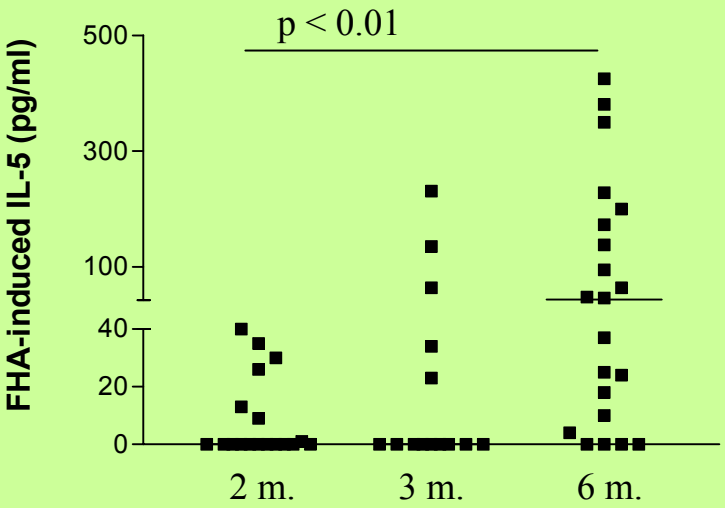


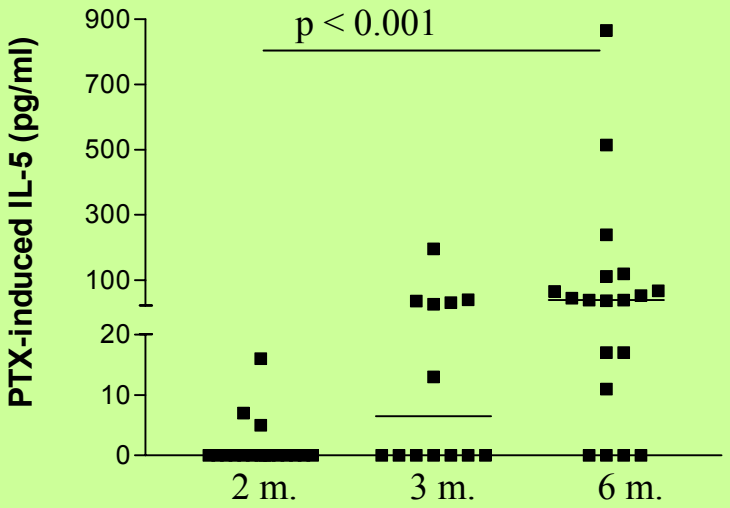
ACELLULAR PERTUSSIS VACCINE

N = 37

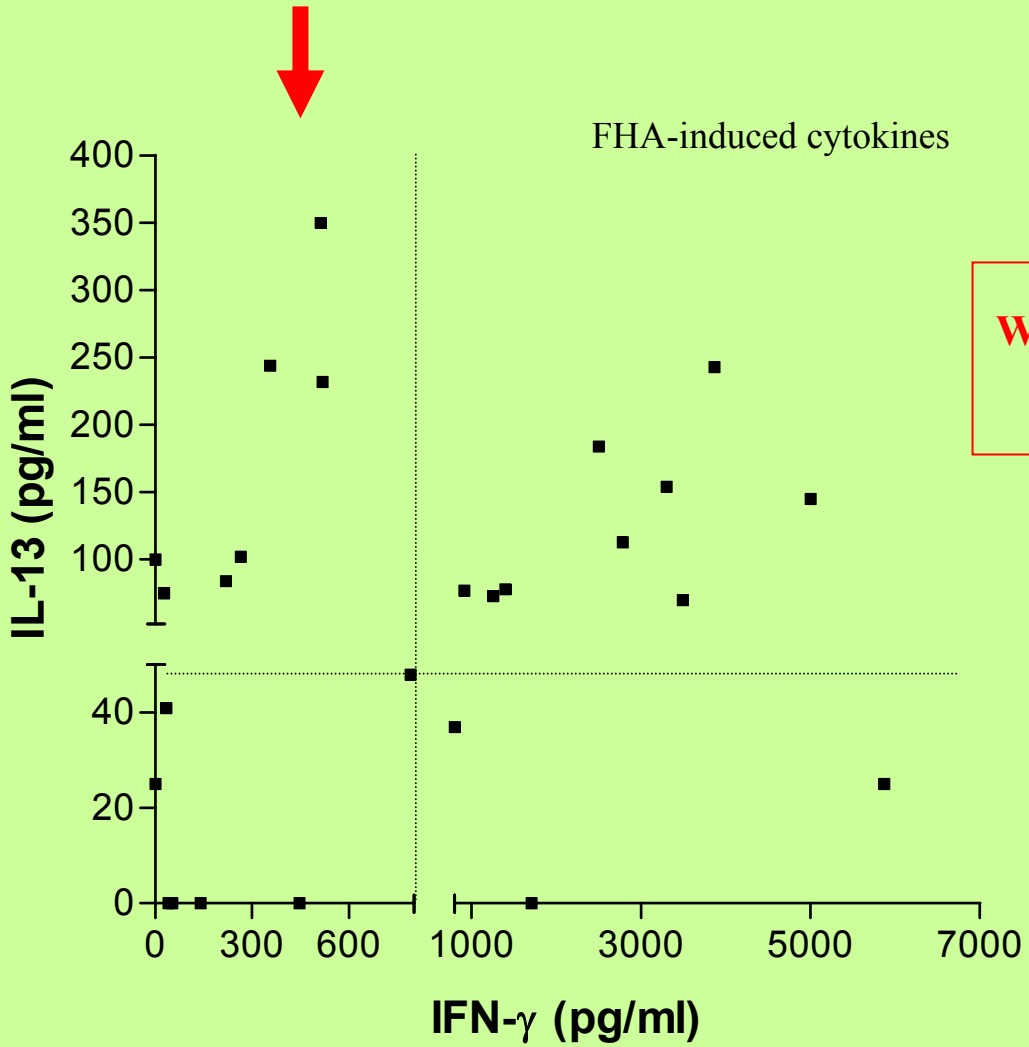








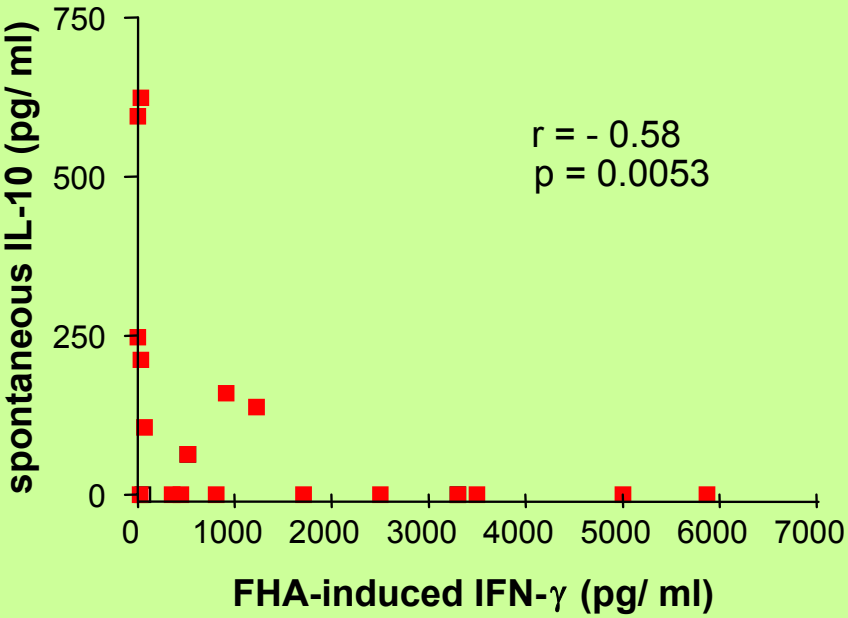
ACELLULAR PERTUSSIS VACCINE

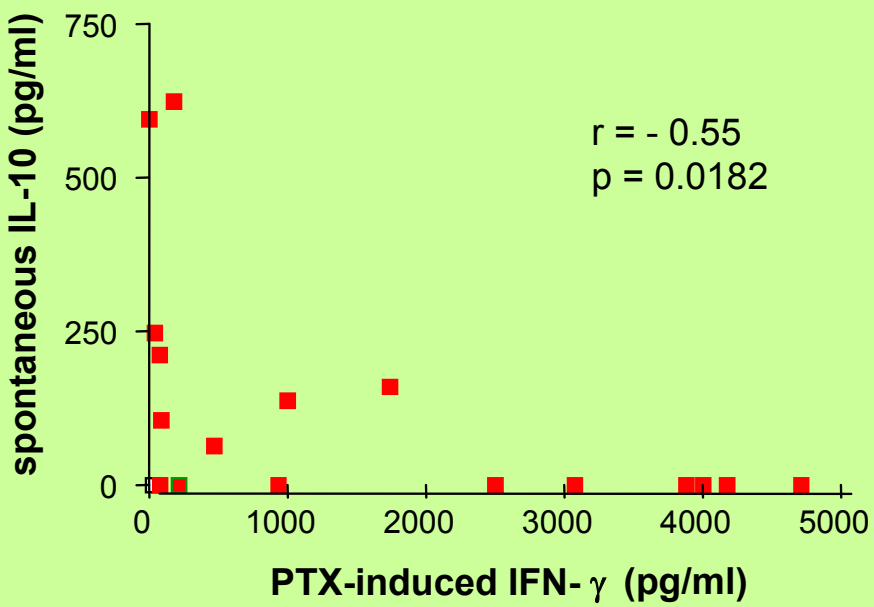


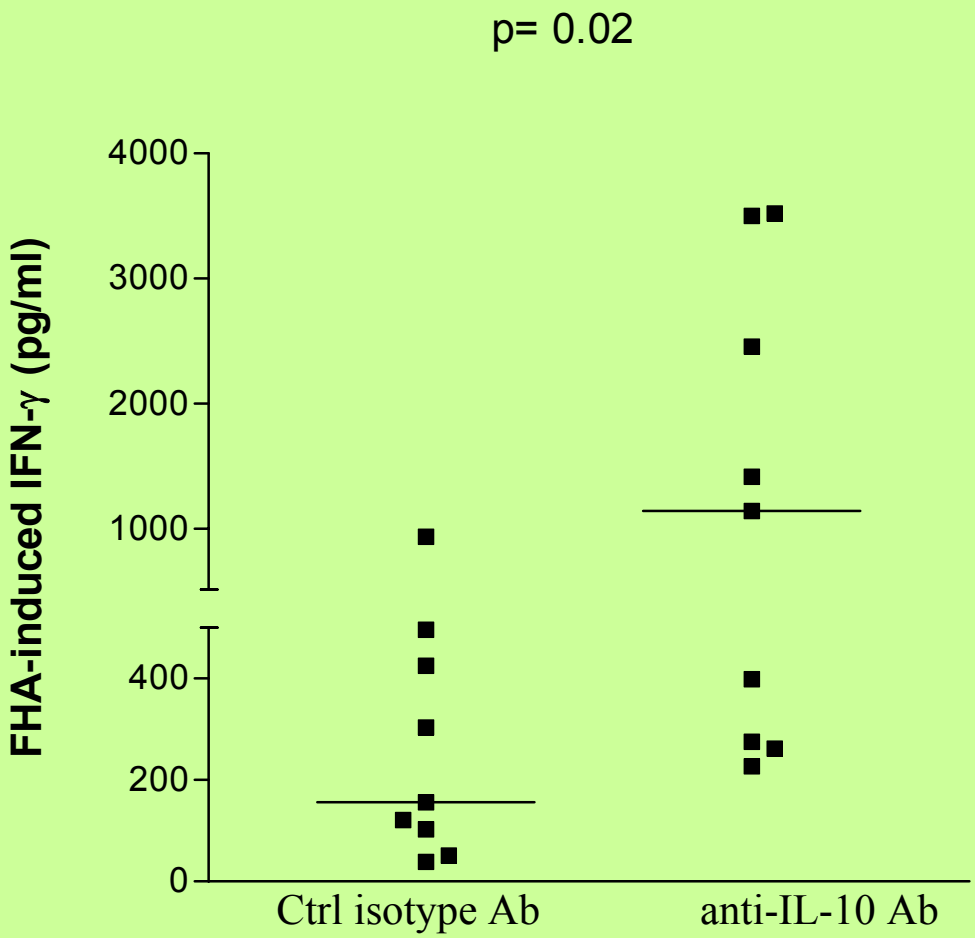
Why does an important proportion of infants not secrete IFN-γ ?

ACELLULAR PERTUSSIS VACCINE

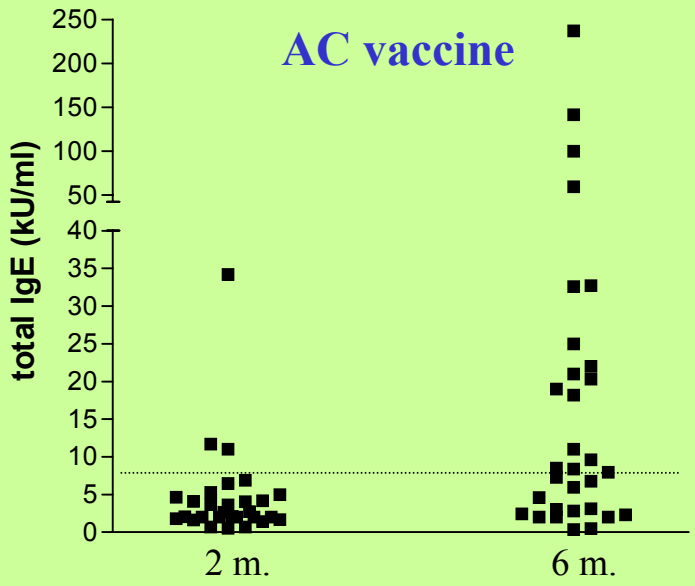
PBMC from infants who <u>do not</u> secrete IFN-γ, secrete IL-10

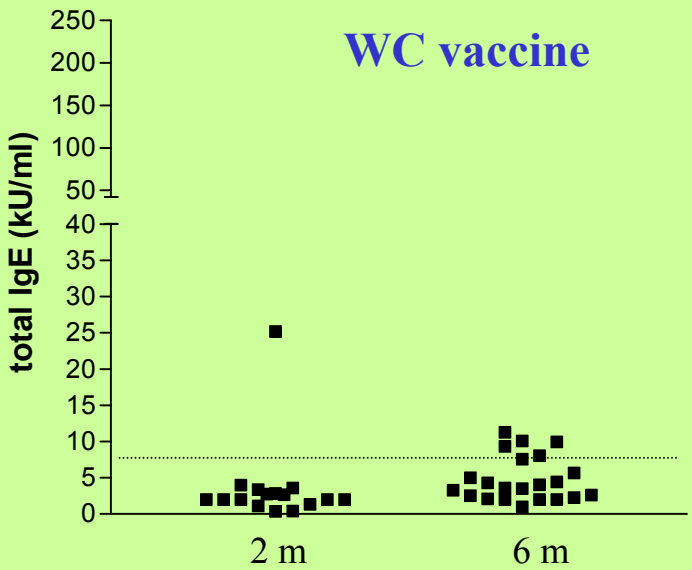


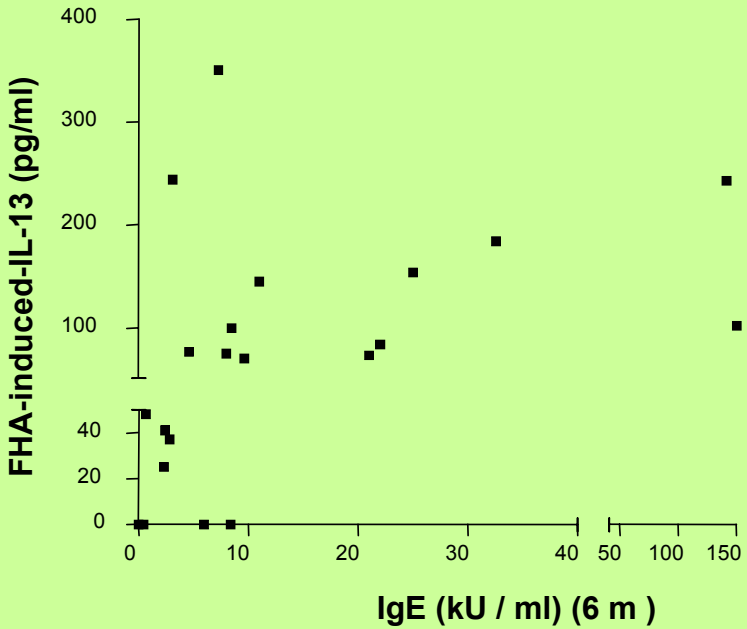



p= 0.02
FHA-induced IFN-γ (pg/ml)
4000
3000
2000
1000
400
200
0
Ctrl isotype Ab
anti-IL-10 Ab

Influence of the Th2 cytokines on other immune responses ?





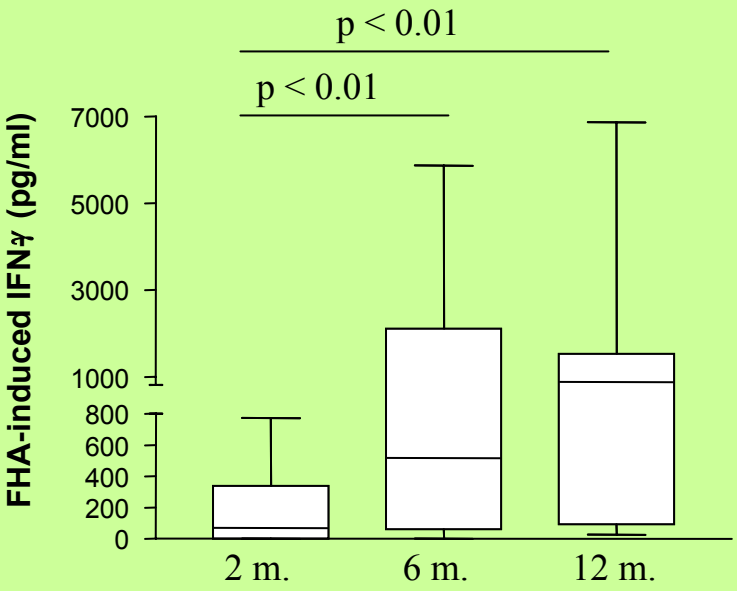


$r = 0.61$

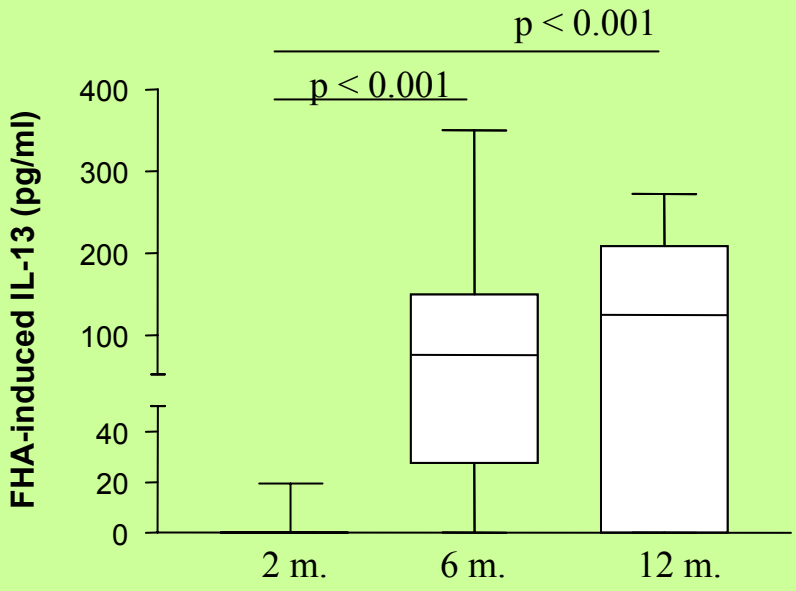
$p < 0.005$

Memory cellular immune response

IFN-γ



IL-13



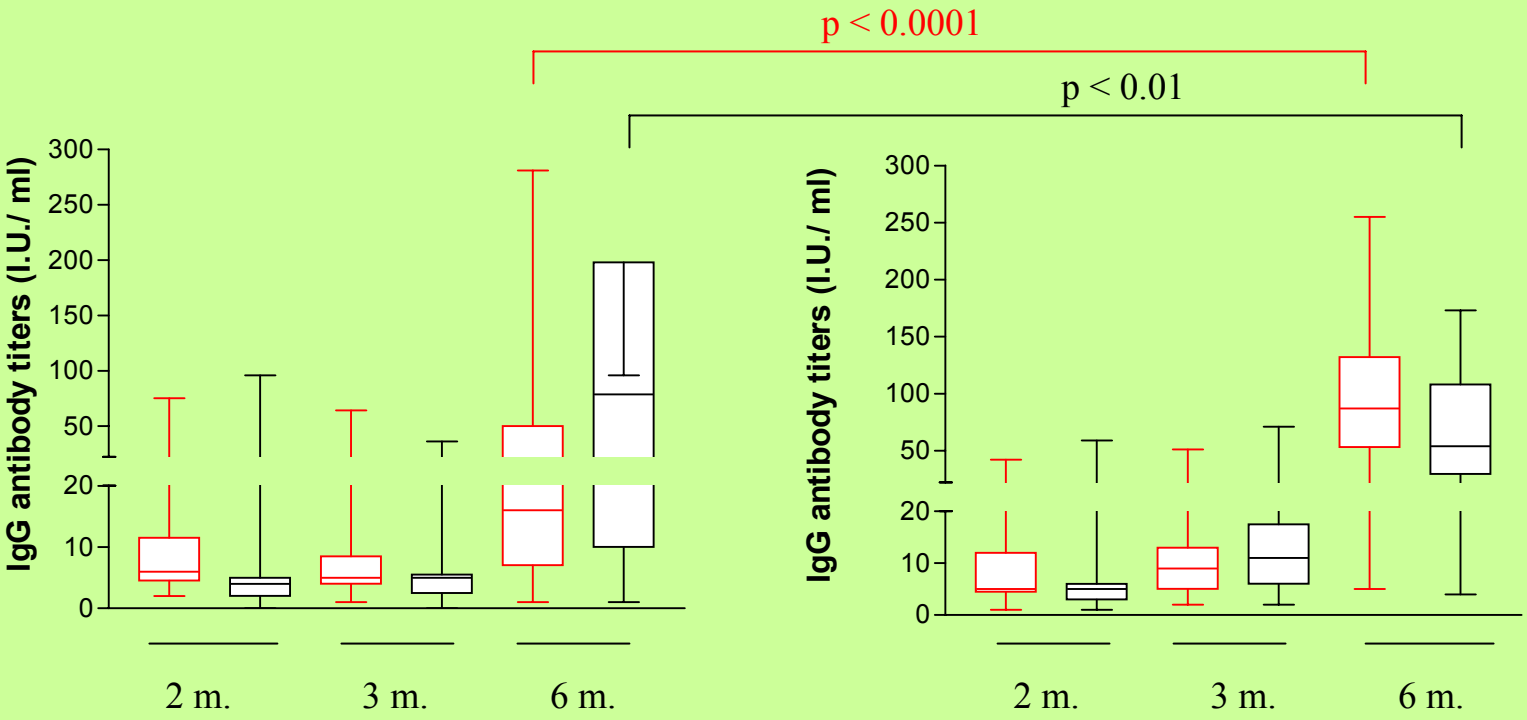
Antibody responses

Anti-FHA

Anti-PTX

Whole cell vaccine

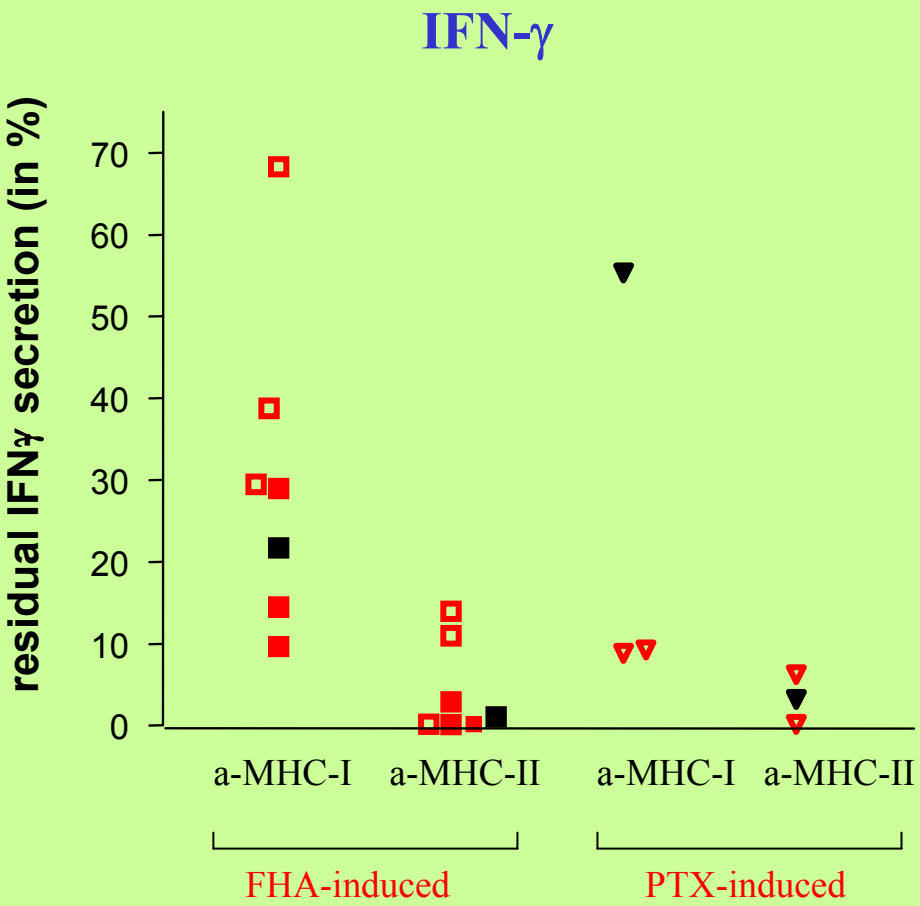
Acellular vaccine

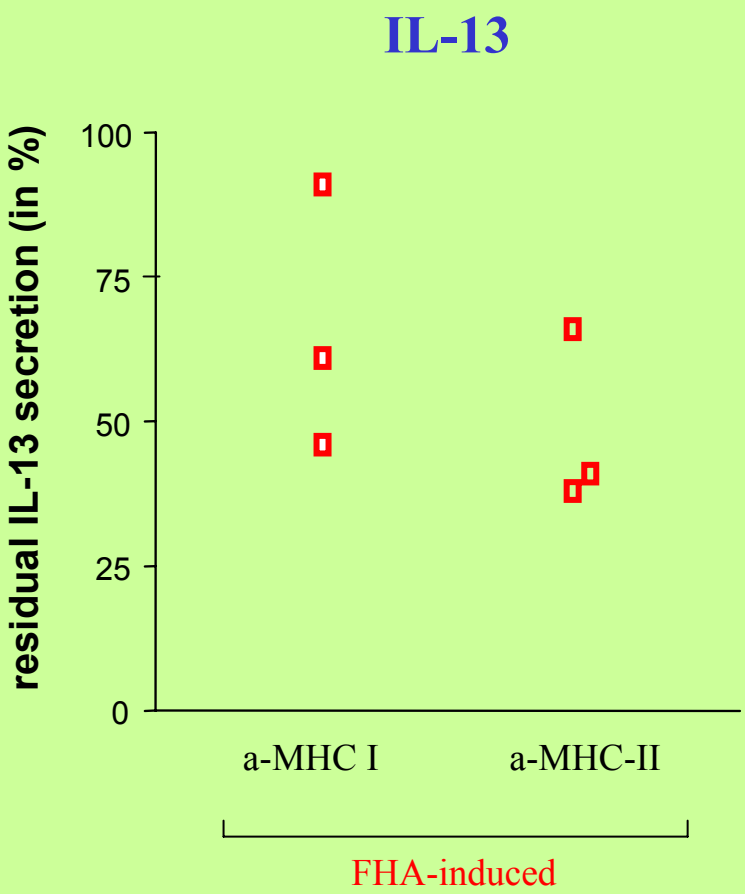


- Whole cell vaccine
- Acellular vaccine
- Acute *B. pertussis* infection

Phenotype of antigen-induced cytokine - producing cells

Effect of anti-MHC antibodies on the cytokine secretion

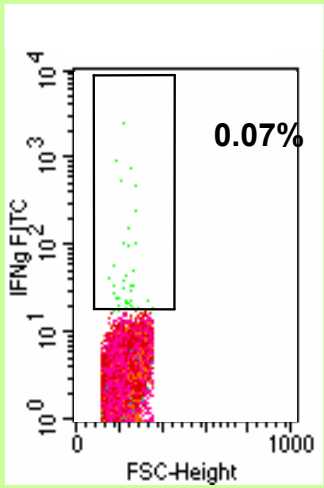




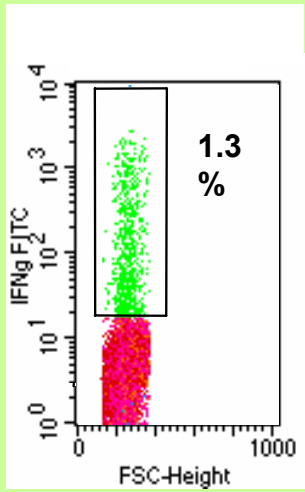
AC

Phenotype of FHA-induced IFN-γ - producing cells

Non stimulated

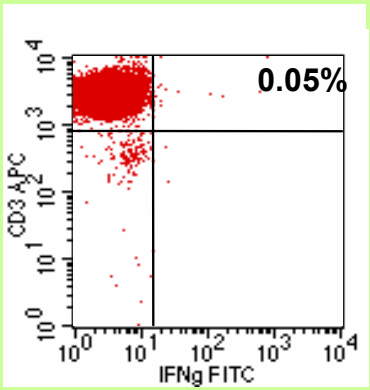


FHA

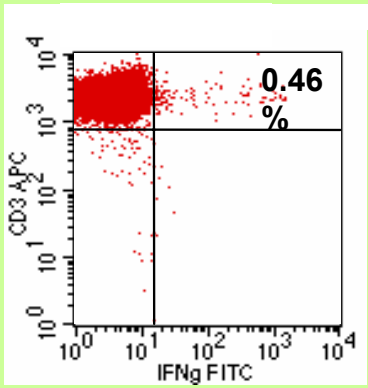


CD3+ CD4+

Non stimulated

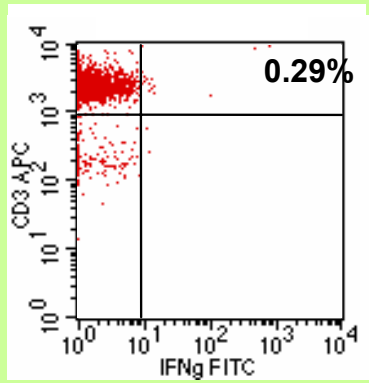


FHA

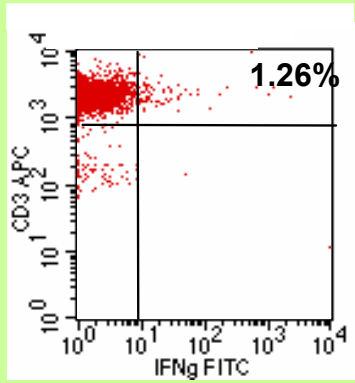


CD3+ CD8+

Non stimulated



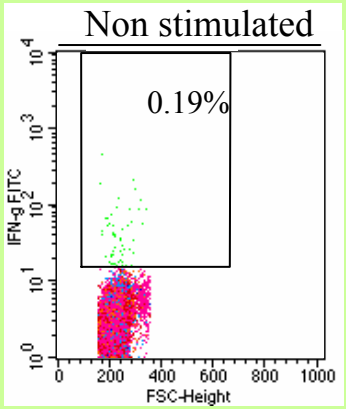
FHA

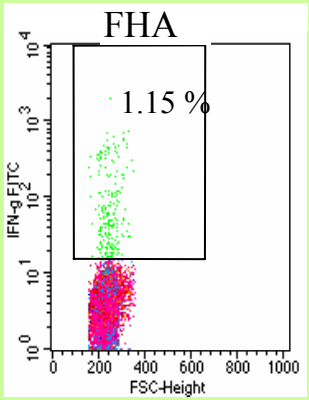


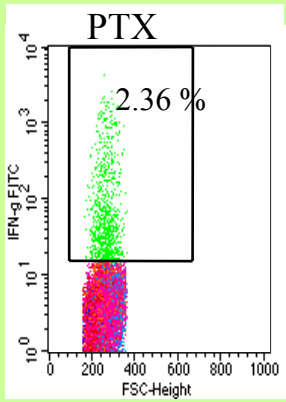
IFN-γ producing cells

Acute *B. pertussis* infection

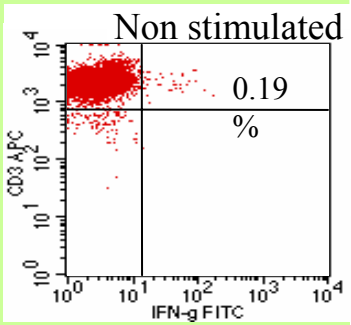
1 month-old infant

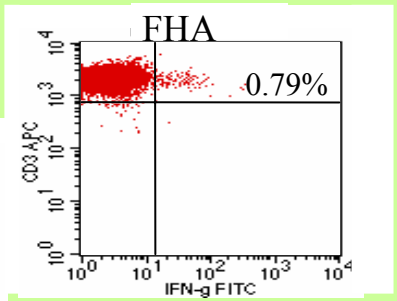


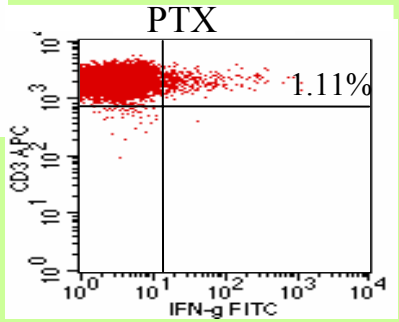




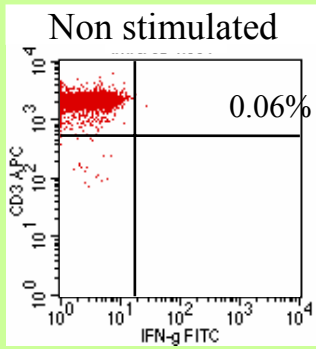
CD3+ CD4+

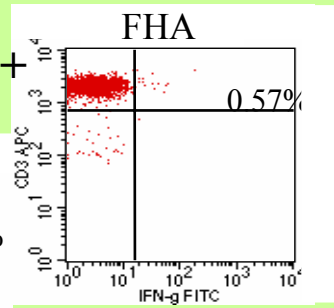


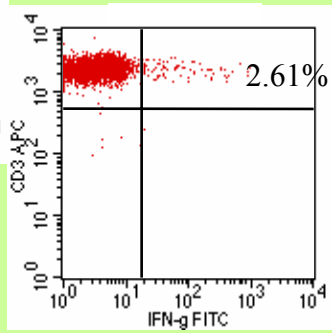




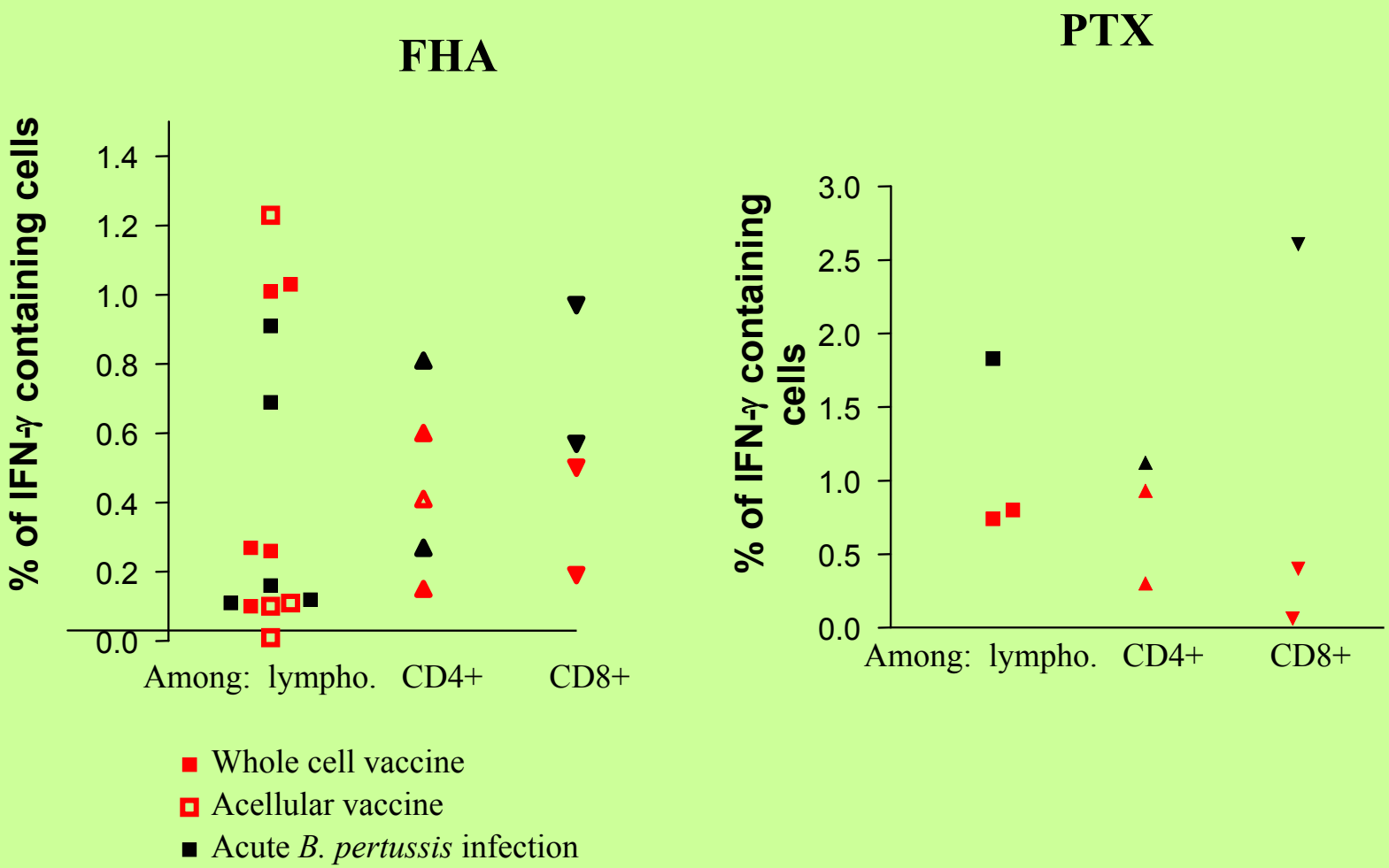
CD3+ CD8+





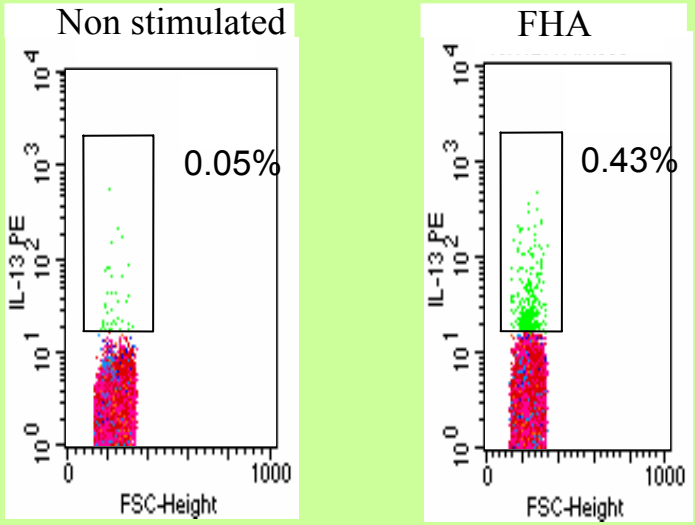


Phenotype of antigen-induced IFN-γ - producing cells

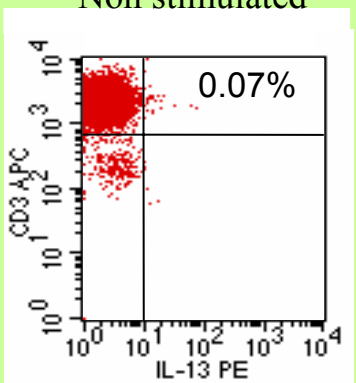


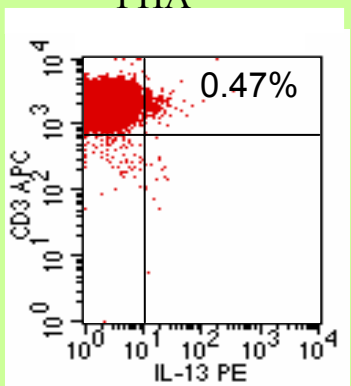
AC

Phenotype of FHA-induced IL-13 - producing cells

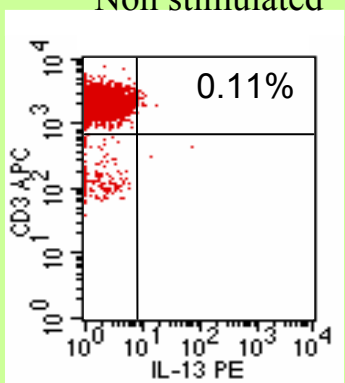


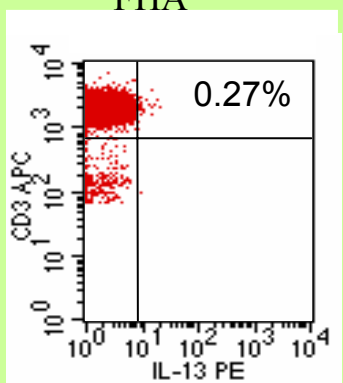
CD3+ CD4+





CD3+ CD8+





CONCLUSIONS I

Infants are able to develop a Th1-type immune response to *B. pertussis* antigens.

- 2 weeks-old infants after infection
- 6 months for most of the vaccinated infants

→ Neonatal vaccination should be possible

? Vaccines mimicking natural infection ?

⇢ Mucosal immunity ?

CONCLUSIONS II

- FHA and PTX induce IFN-γ synthesis by CD4+ and CD8+ T lymphocytes

  ⟶ role of CD8+ T lymphocytes in protection ?

- Antigen-induced IFN-γ is more frequent after the whole cell than after the acellular vaccine administration.

- Low IFN-γ response is related to high IL-10 secretion.

  ⟶ diminish IL-10 secretion ?

CONCLUSIONS III

- Antigen-induced IL-13 / IL-5 is more frequent after the AC than after the WC vaccine administration or *B. pertussis* infection.

- In infants receiving the AC vaccine, the Th2-cytokine profile is associated with hyper IgE.

⟶ long-term effects of high Th2 cytokine and IgE levels ?

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