



OUTER MEMBRANE PROTEINS BASED VACCINES AGAINST SALMONELLA

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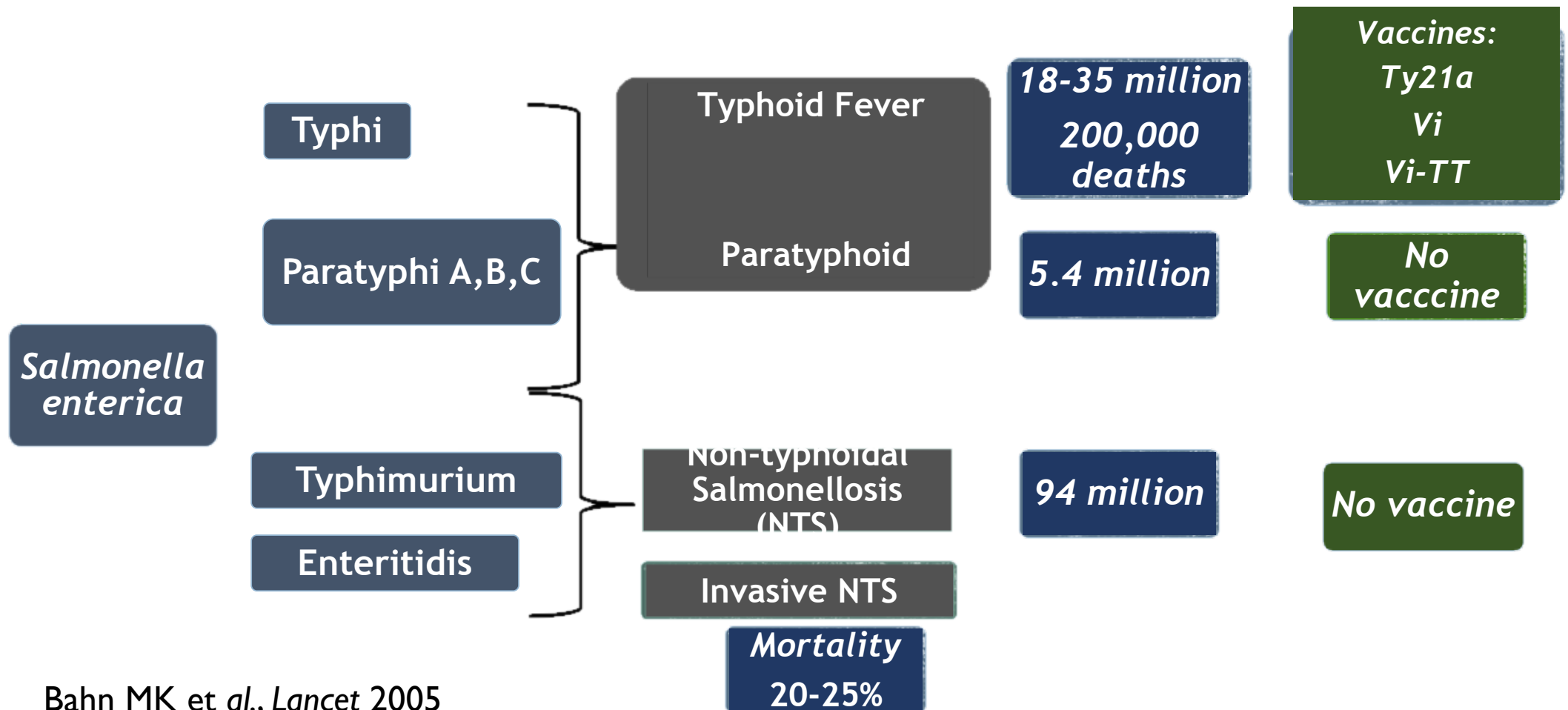
Mexican Social Security Institute (IMSS)

- Main health organisation in Mexico
- 80 million affiliates
- Large cohorts of patients
- Clinical Research
- Biobanks



1,811 Medical Facilities	
1st level Preventive medicine, first contact and family medicine	1,499
2nd level Surgical and speciality medicine	275
3rd level High specialty medicine	37

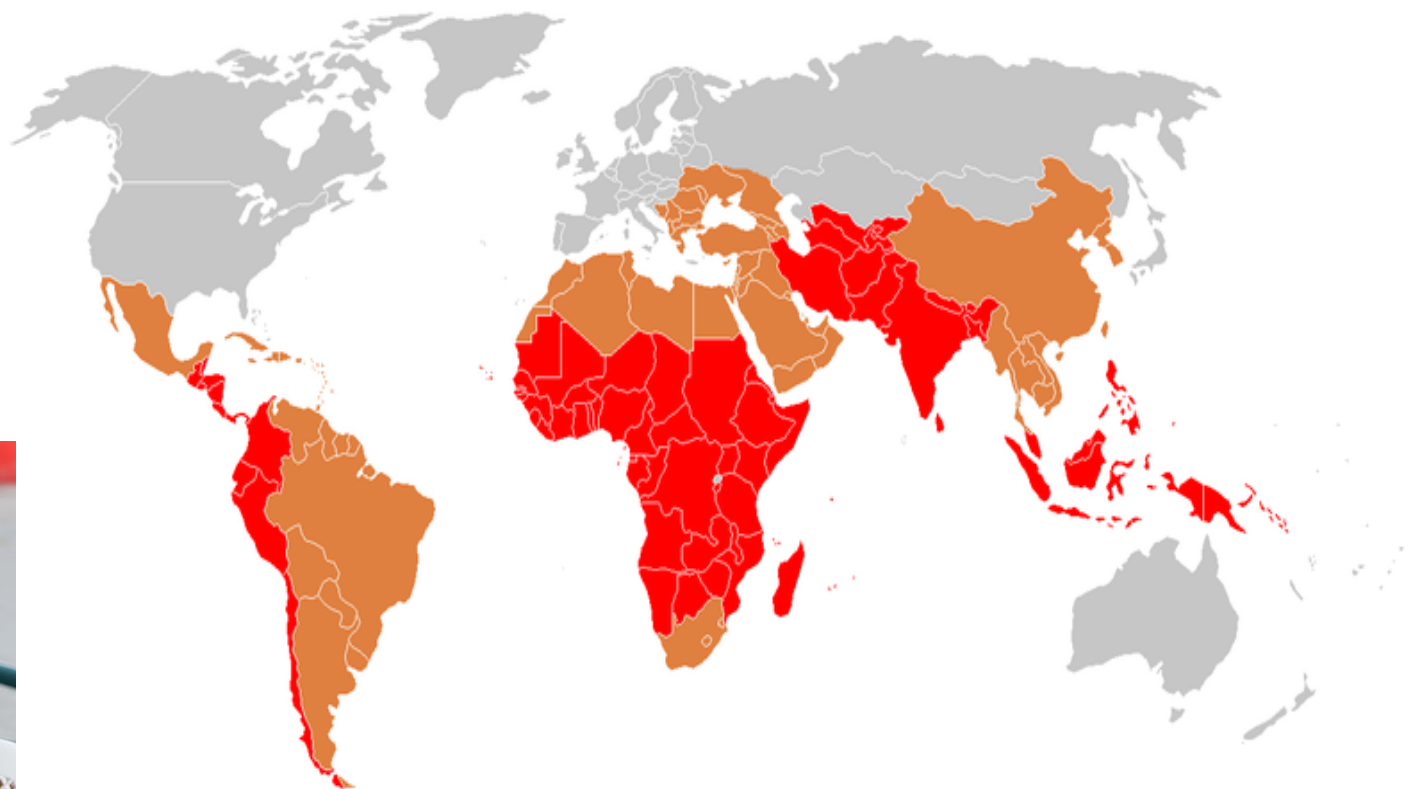
Diseases produced by *Salmonella enterica*. GLOBAL HEALTH PROBLEM



Bahn MK et al., Lancet 2005

Diseases produced by *Salmonella enterica*. GLOBAL HEALTH PROBLEM

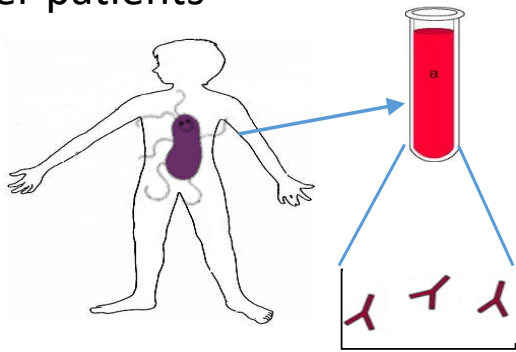
Mostly LMICs
MDR, XDR strains
WHO High priority for
Vaccine development



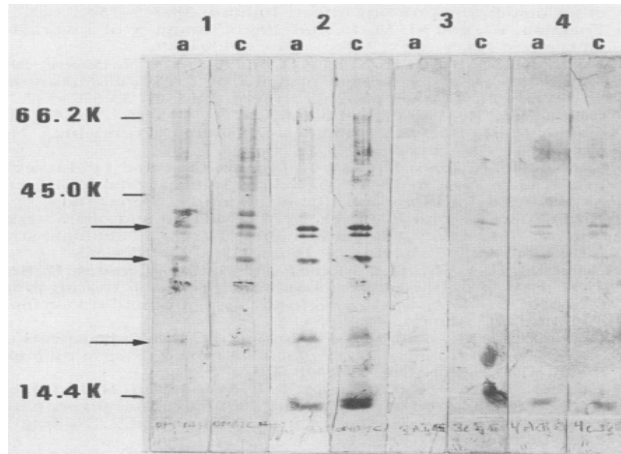
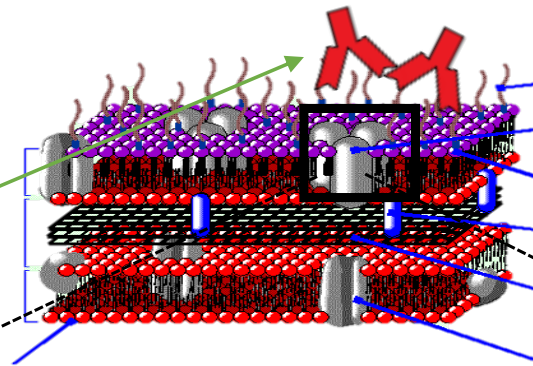
Buckle GC,. J Glob Health 2012
Majowicz, Clin Infect Dis 2010

S. Typhi porins are antigenic in Typhoid Fever patients

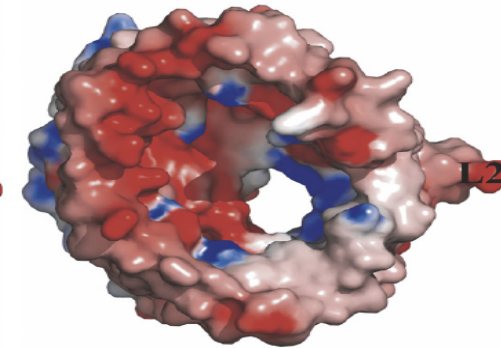
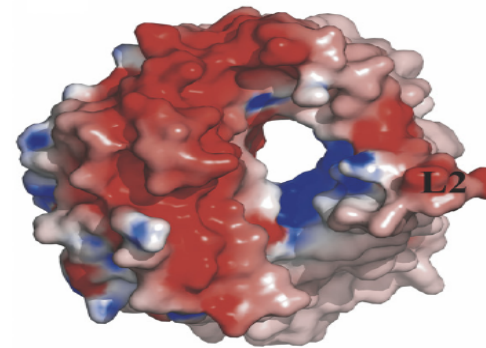
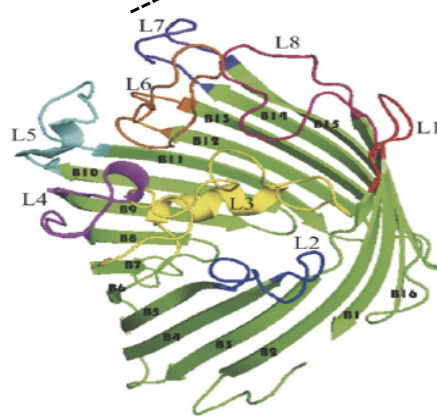
Typhoid Fever patients



S. Typhi outer membrane proteins

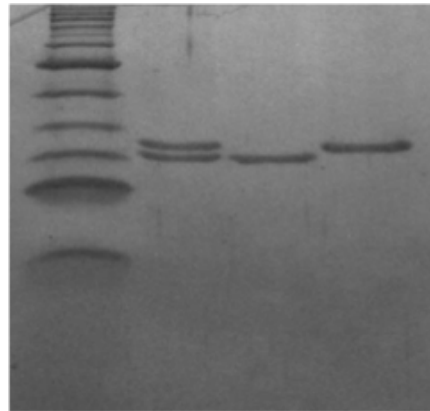
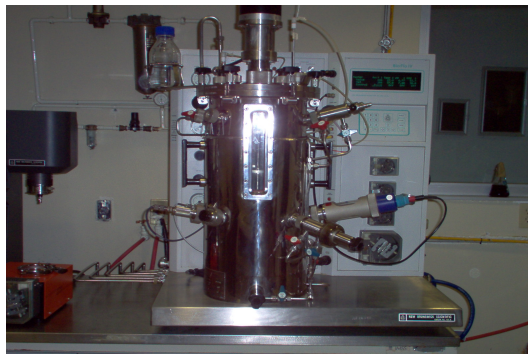


Ortiz V *et al.* J Clin Microbiol. 1989



Balasubramaniam D. *et al.* J Struct Biol 2012

S. Typhi porins are strong immunogens able to induce protection against *S. Typhi* challenge



OmpC
OmpF



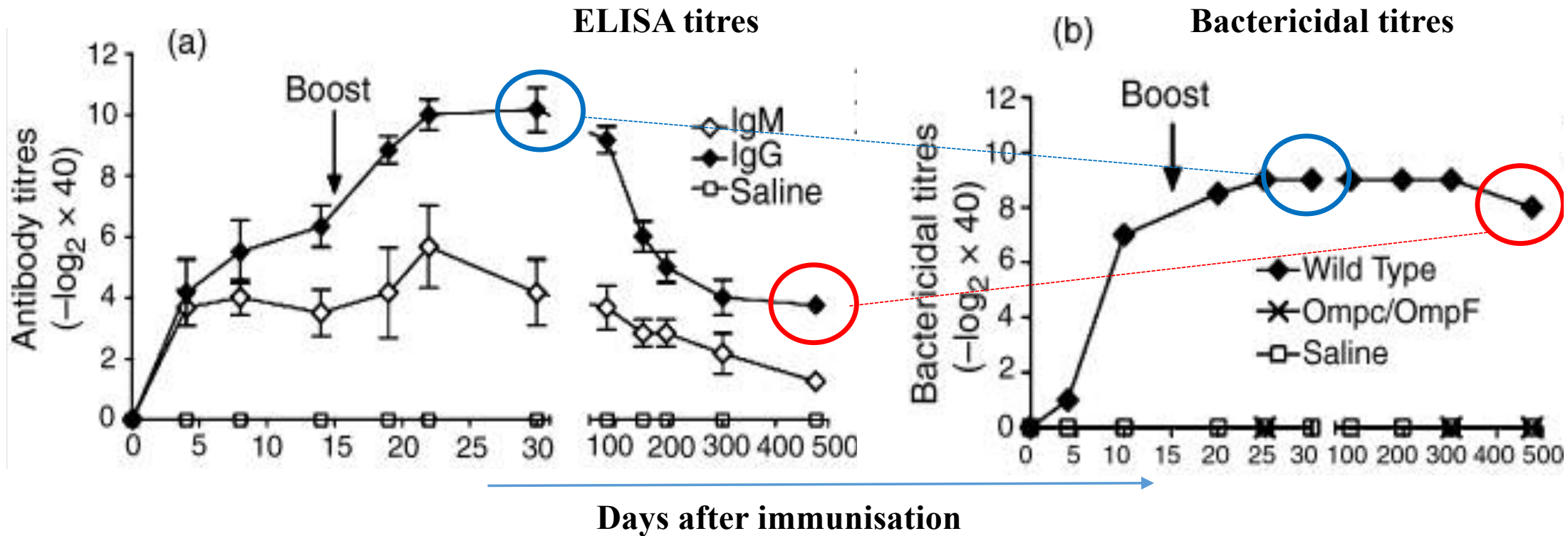
Active and passive
protection 500 DL50
S. Typhi challenge in mice

Porin specific proliferative
T cell responses in mice

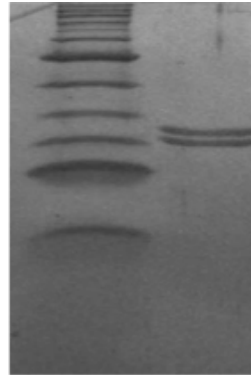
Isibasi A., *et al.* Infect and Immunity. 1988
Isibasi A., *et al.* Vaccine 1992

Gonzalez C, *et al.* Microbiol. Immunol. 1993

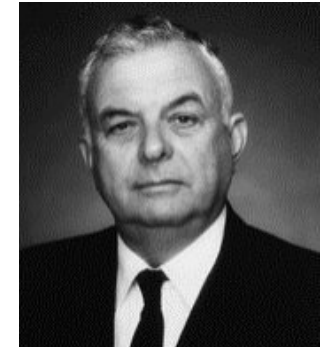
Do porins induce long-lasting protective antibody responses?



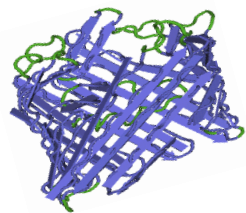
Development of Porins based experimental vaccines against Typhoid Fever



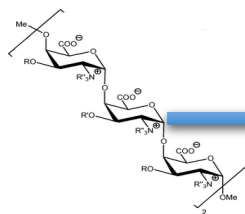
Armando Isibasi



John B. Robbins

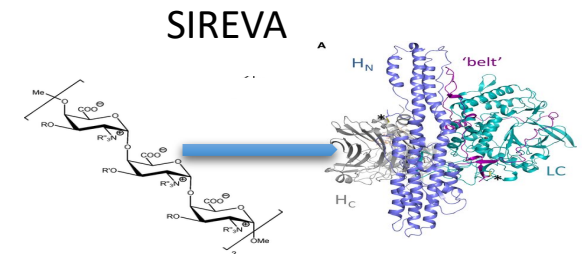
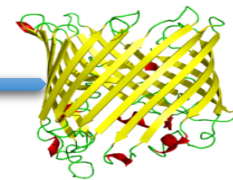


PORINS



VI-PORINS

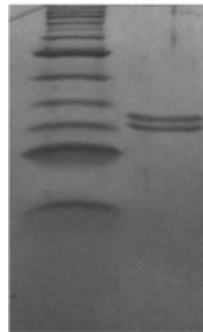
López-Macías C. 1992 BSc Thesis.
Faculty of Chemistry. UNAM



VI-TETANUS TOXOID

Rodríguez-Anguiano RE. 1999
Master Degree Thesis
Faculty of Medicine UNAM

S. Typhi porins as experimental vaccine against Typhoid Fever



ISIPOR Vaccine:

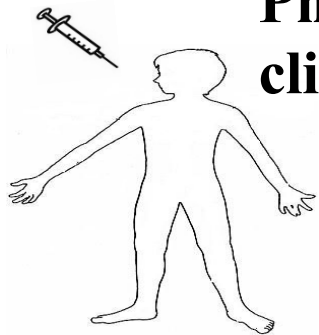
*Innocuous

*Pyrogens free

Patent No. MX346872

Safe and well tolerated vaccine

**Phase 1
clinical trial**



Immunogenic vaccine

IgM-IgG seroconversion

T cell proliferation IFN γ +

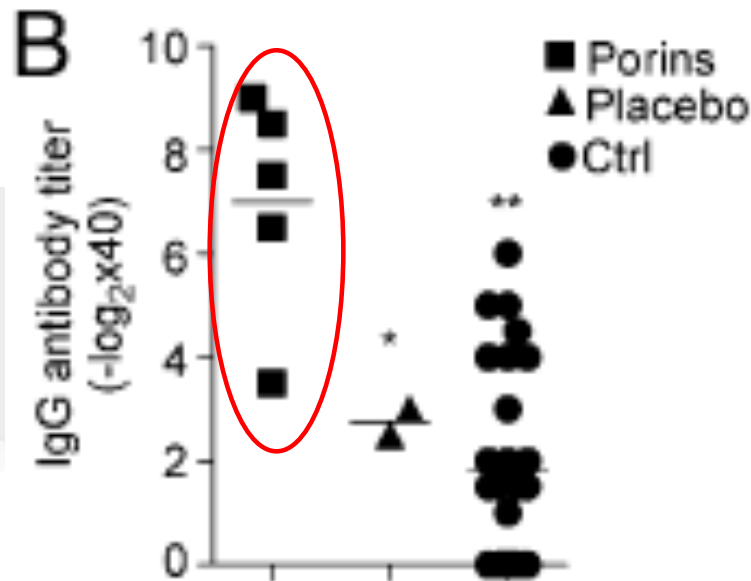
S. Typhi porins induce long-lasting IgM and IgG Ab responses in humans (11 years)



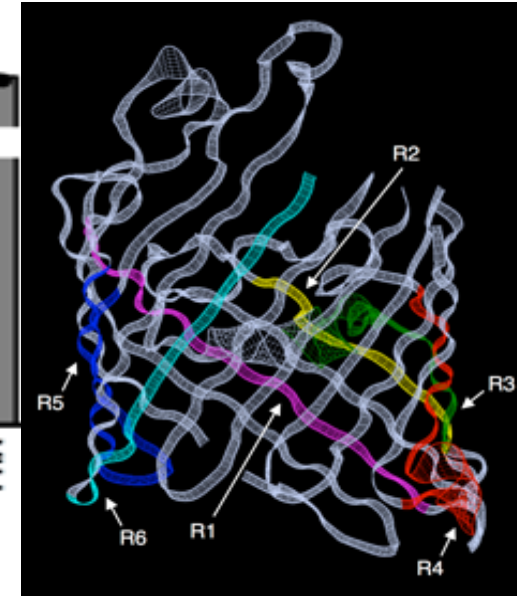
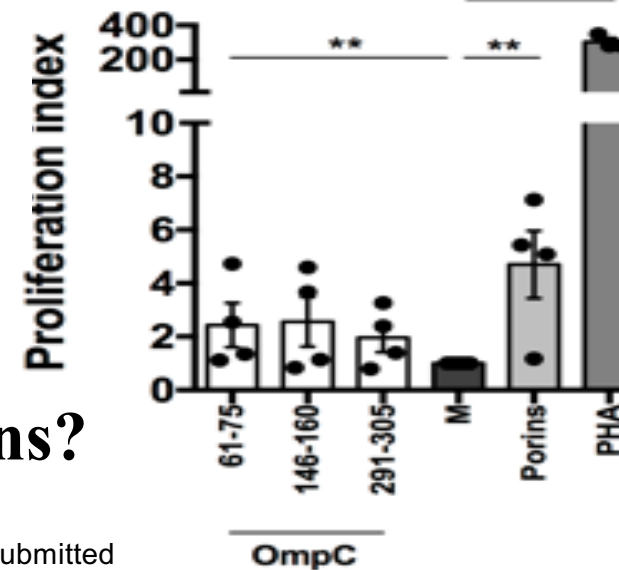
Paul Klenerman
University of Oxford UK



Prof. Burkhard Luderwig
Kantonsspital St. Gallen CH



Salmonella Porins Responses in healthy donors

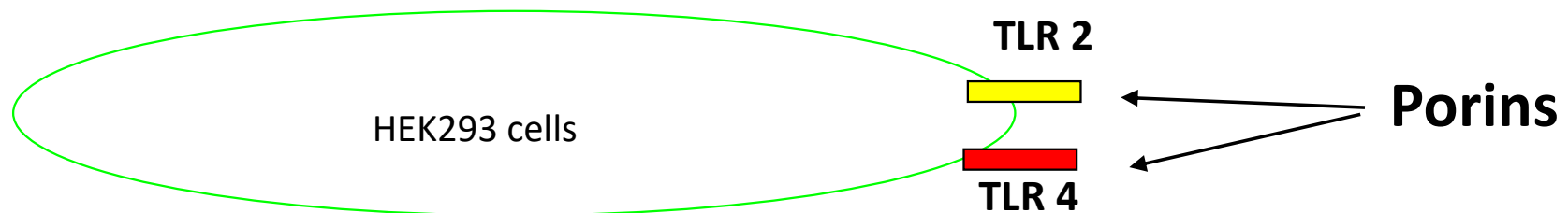


Why porins are strong immunogens?

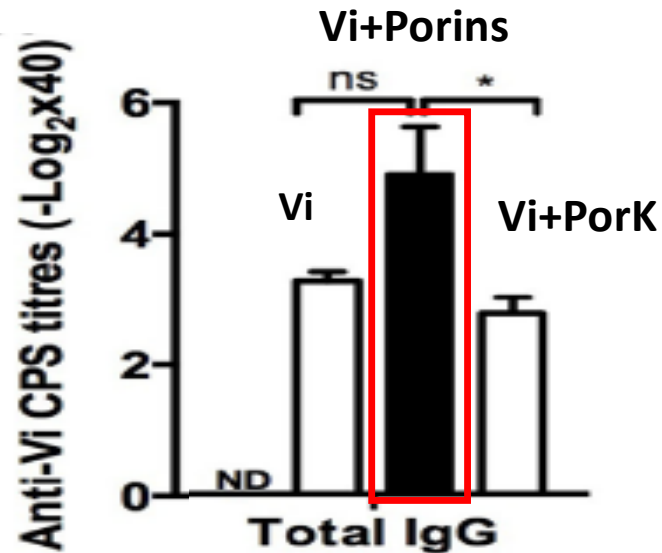
Pérez-Shibayama C., *et al.* JI 2014

N. Valero-Pacheco, J. Blight, *et al.*, submitted

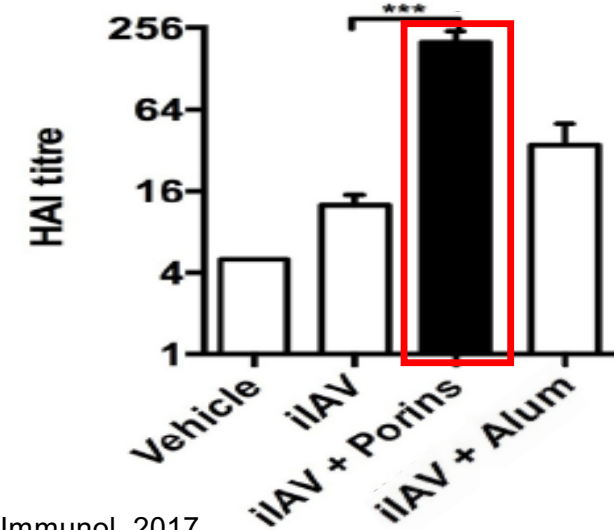
Porins are agonist of TLR2 and 4 and induced an adjuvant effect on the antibody responses to co-immunised vaccines



Vi polysaccharide anti-Typhoid vaccine



Pandemic influenza inactivated virus



S. Typhi porins:

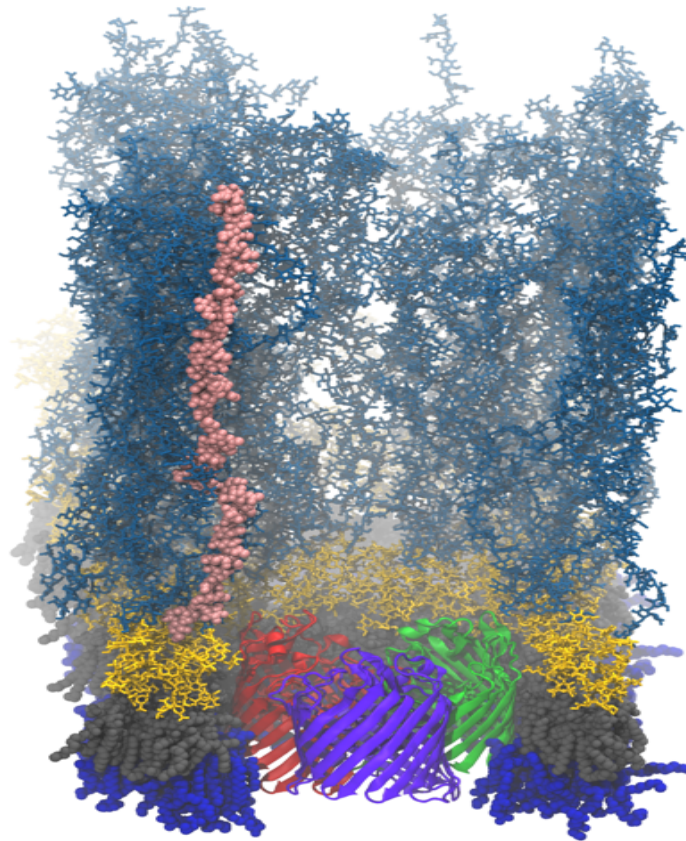
- **Porins vaccine is safe, well tolerated and immunogenic in humans**
- 1 dose induced a long-lasting (11years) antibody responses in humans
- Shared T cell epitopes among clinically relevant strains may maintain T cell responses for long time
- Intrinsic adjuvant properties of porins could promote long-lasting responses to itself and co-immunised antigens

Who is responsible for the induction of protection?

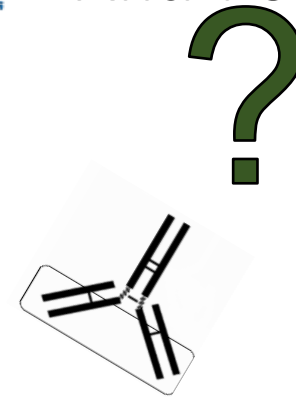
Anti-LPS



Prof. Adam Cunningham
University of Birmingham UK



Anti-Porins



In HIV patients, anti-LPS Ab block bactericidal anti-porins Ab



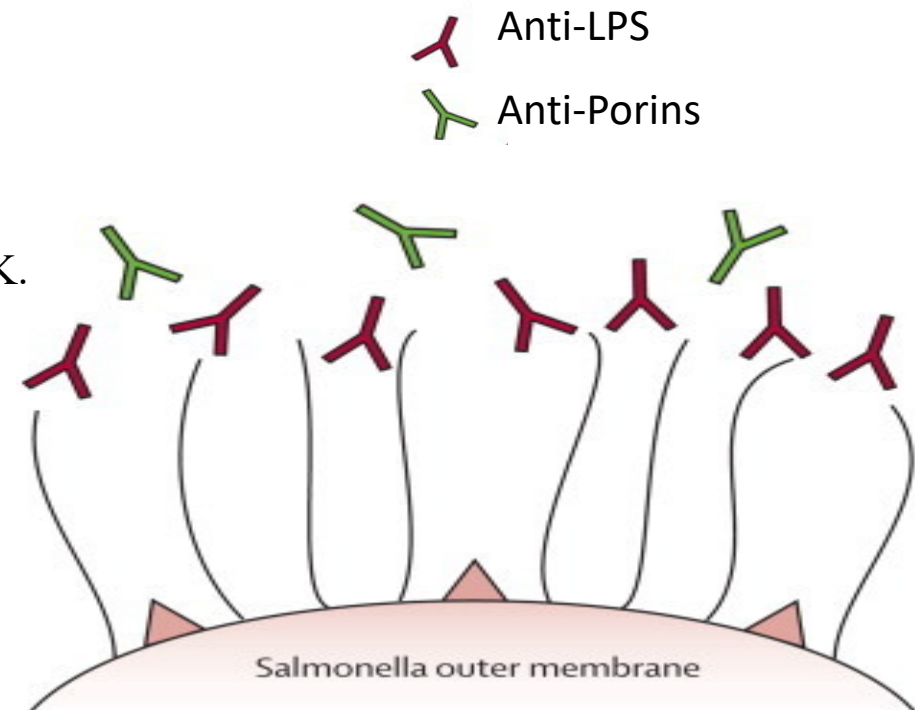
Prof. Cal MacLennan/U.Oxford Prof. Adam Cunningham/U. Bham. UK.



MacLennan, *et al.* Science 2010

Perspectives

S. Fauci. **Science 2010**

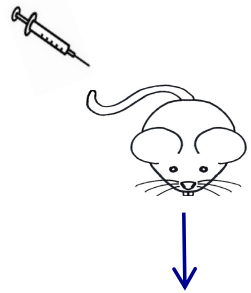


Feasey N *et al.* Lancet. 2012.

The porin OmpD from non-typhoidal *Salmonella* is a key target for a protective B1b cell antibody response

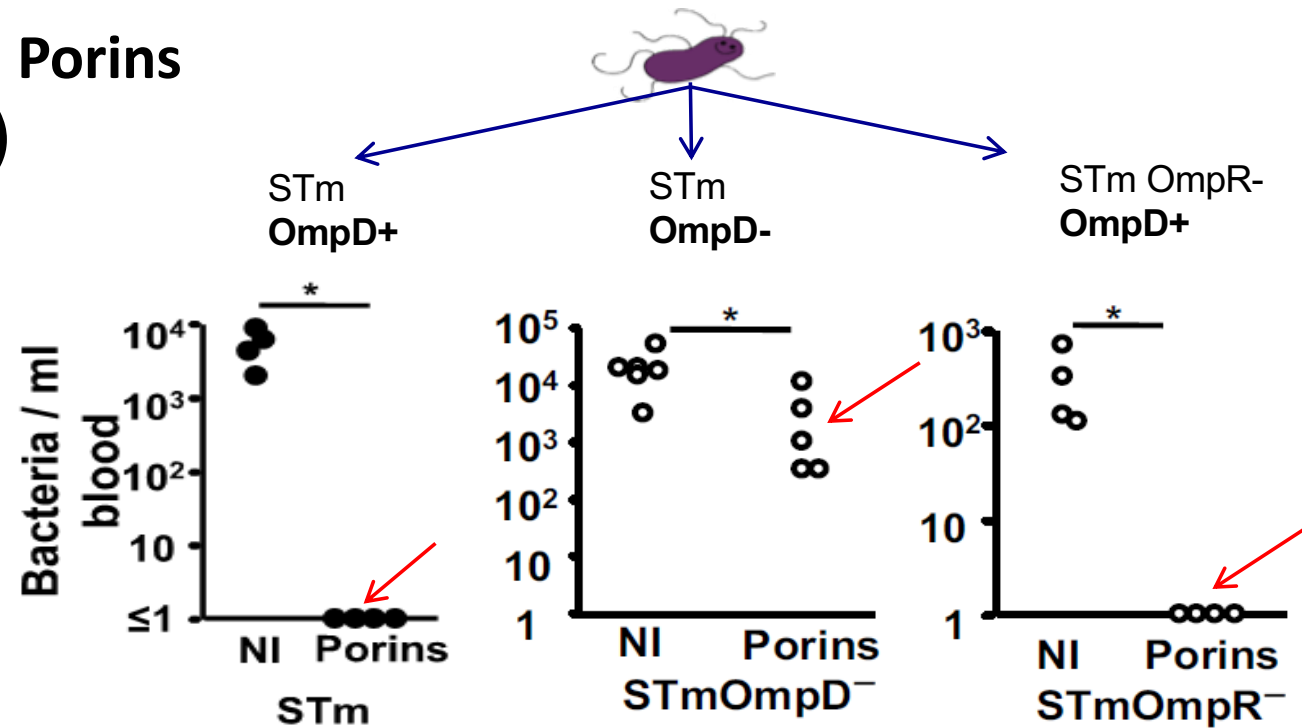
Immunisation

S. Typhimurium (STm) Porins
(OmpC, OmpF, OmpD)

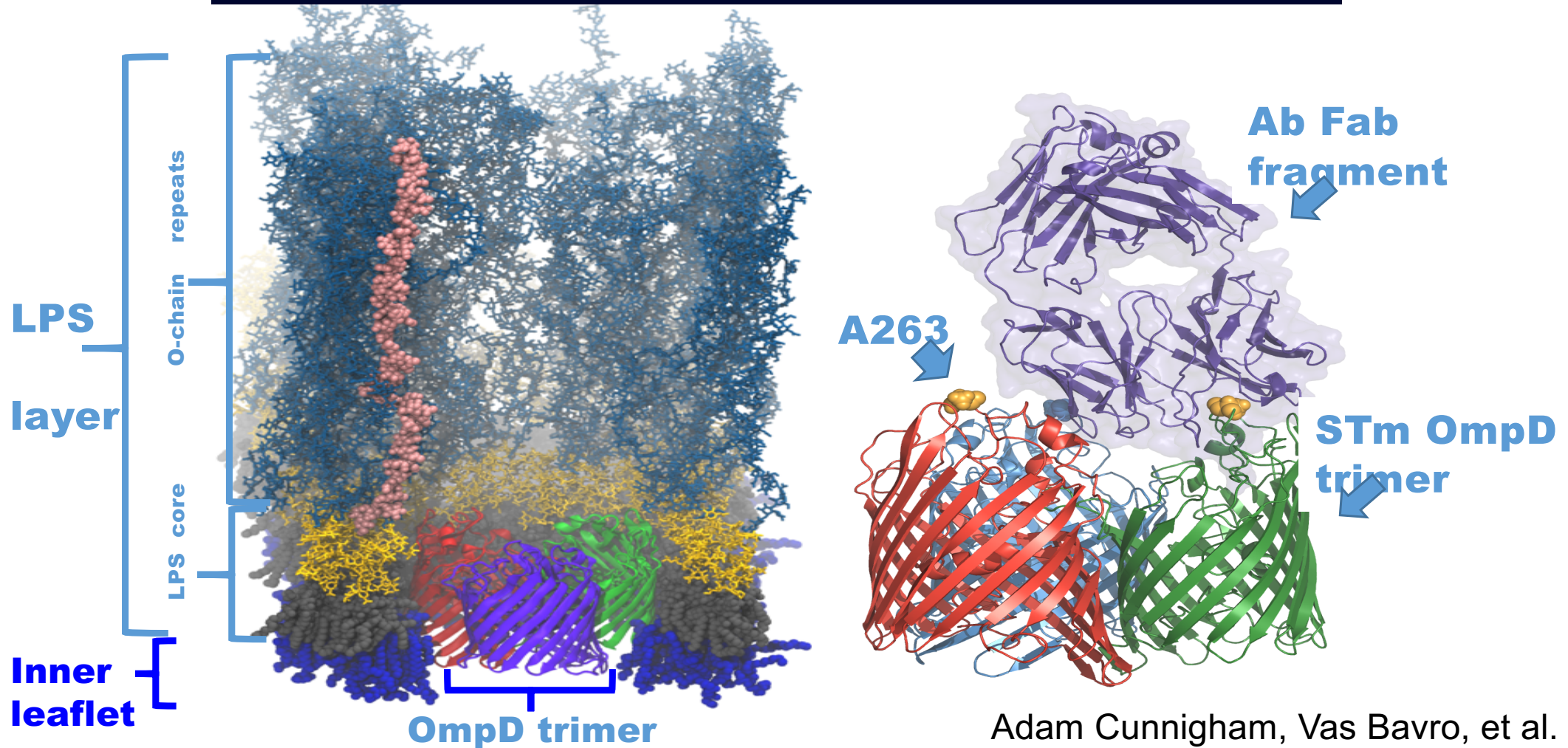


Bactericidal
antibodies

STm Challenge

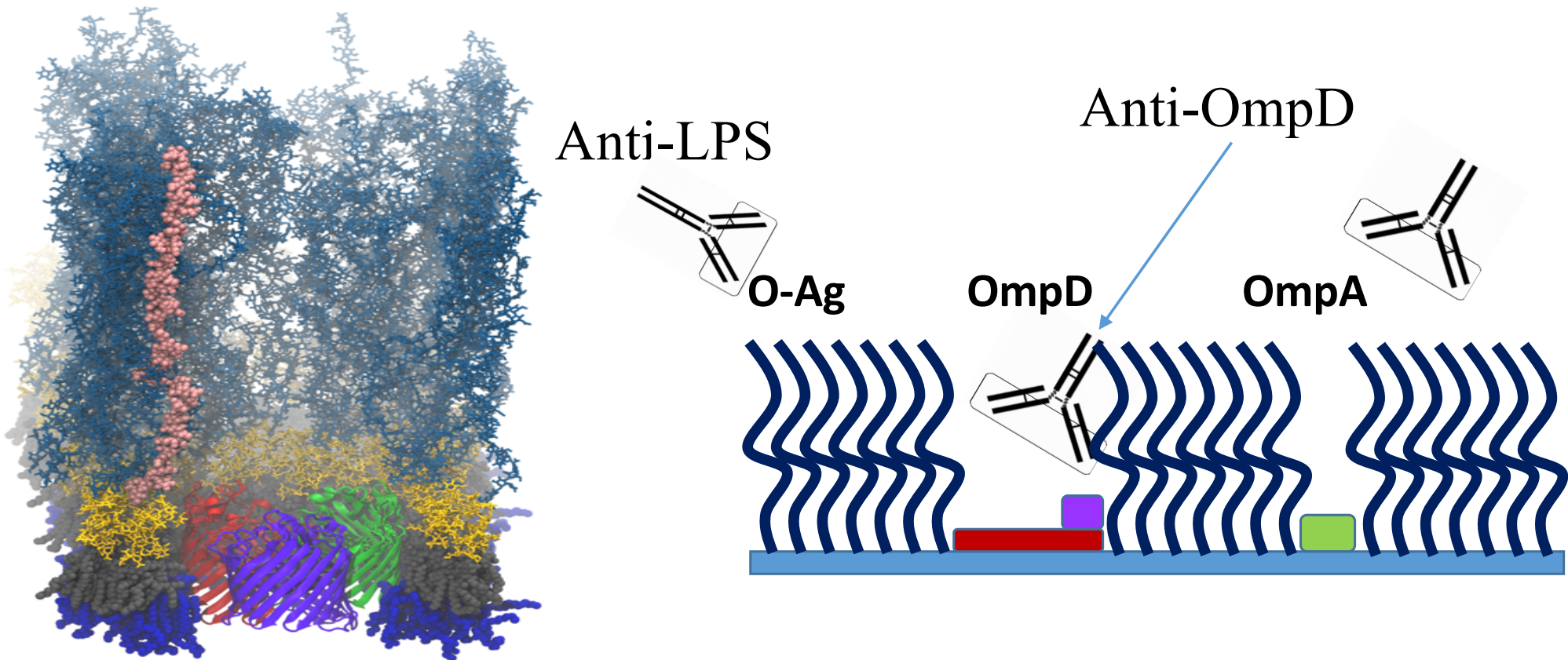


Modelling reveals the limited access O chain allows to the cell surface



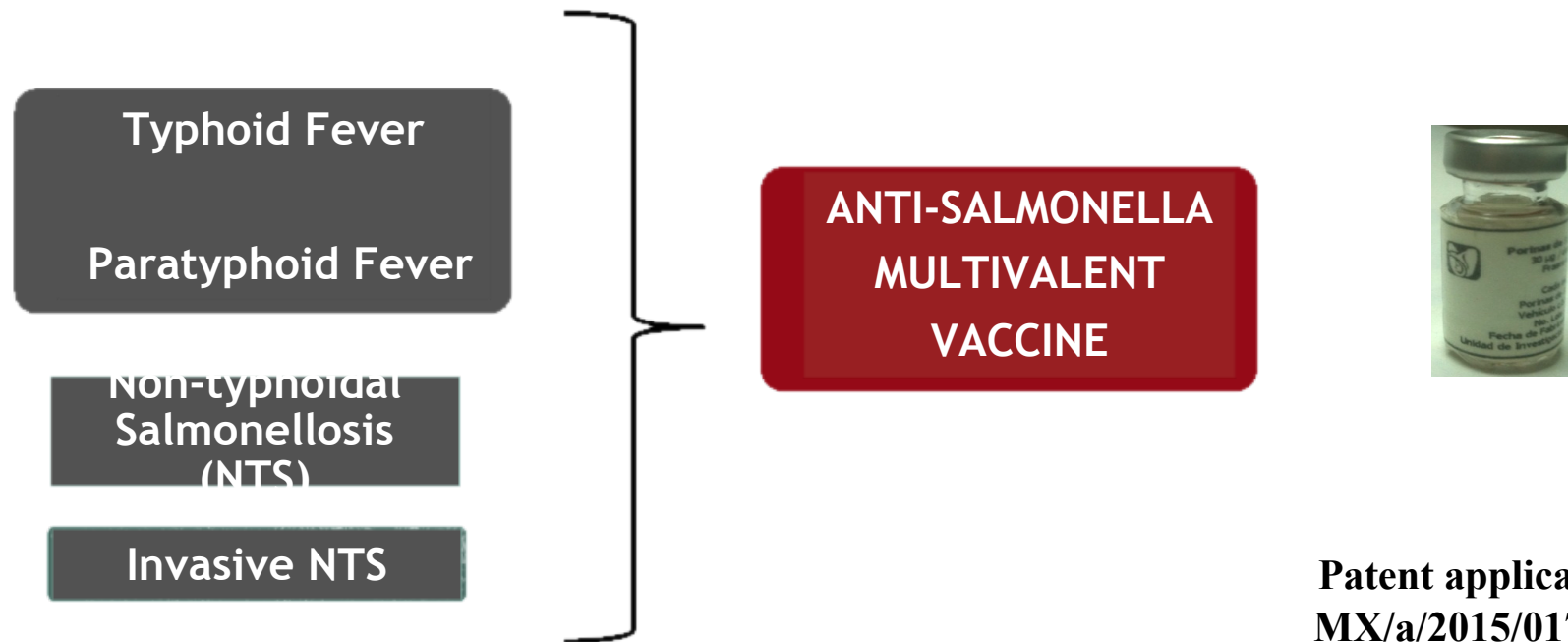
Adam Cunningham, Vas Bavro, et al.

Model of anti-OmpD porin Ab induction of protection



Adam Cunningham, Vas Bavro, et al.

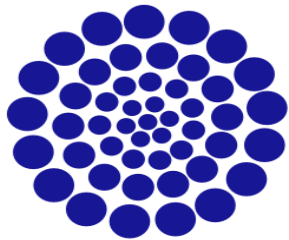
Development of a multivalent vaccine against the diseases produced by *Salmonella enterica*



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BIRMINGHAM



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