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MUCOSAL AND SYSTEMIC IMMUNE RESPONSE AGAINST *NEISSERIA MENINGITIDIS* B INDUCED BY SINGLE TIME VACCINATION STRATEGY

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Immunization have been helping to reduce child mortality, improving maternal health and combating infectious diseases. In spite of its undisputed past success and promising future, however, immunization remains an unfinished agenda because of them inadequate coverage. Several factors have been largely responsible of a difficulty to attain immunization coverage and have been recognized as a problems of current vaccines. To bear in mind these principals problems of current vaccines, a novel protocol for vaccination named Single Time Vaccination Strategy (SinTimVaS) was developed. Using female BALB/c mice, we induce systemic and mucosal immune responses against *N. meningitidis* with only one parenteral and one mucosal dose at the same time, employing the Finlay Adjuvants derivate from *N. meningitidis* (AFPL1 and AFCo1) respectively.

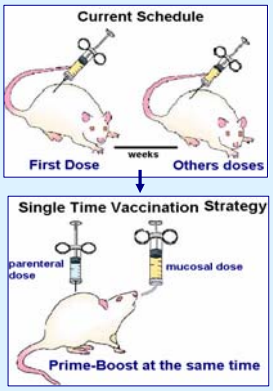
Introduction:

Vaccination is considered by the World Health Organization (WHO) to be the most cost-effective strategy for controlling infectious diseases. In spite of this, the global coverage of many vaccines are still inefficient.

For bacterial meningitis WHO estimates that 1.2 million cases occur annually and *Neisseria meningitidis* is the etiological agent in more than 40% of these cases although some meningococcal vaccines are available

Several factors have been responsible to attain immunization coverage such as: the number of dose, the excessive use of parenteral route, few adjuvants for use in human vaccines, higher reactogenicity and scanty feasibility to combined more than one antigen in the same formulation

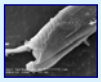
To bear in mind these principal problems of current vaccines a novel protocol for vaccination named Single Time Vaccination Strategy (SinTimVaS) is proposed.



We propose that with SinTimVaS the administration of one mucosal dose and one parenteral dose at the same time induce an efficient systemic and mucosal immune responses against the antigens immunized.

Finlay's vaccines formulations against *N. meningitidis*

AFPL1. Outer membrane vesicles obtained from live *N. meningitidis* B, the core antigen of the Cuban meningococcal vaccine, VA-MENGOC-BC™. Used by parenteral route.



AFCo1. Cochleate structure derived from AFPL1 by dialysis process.

Results

1- Mucosal and systemic immune response against *N. meningitidis* B induced by one intranasal dose of AFCo1 and one intramuscular dose of AFPL1 at the same time, (SinTimVaS).

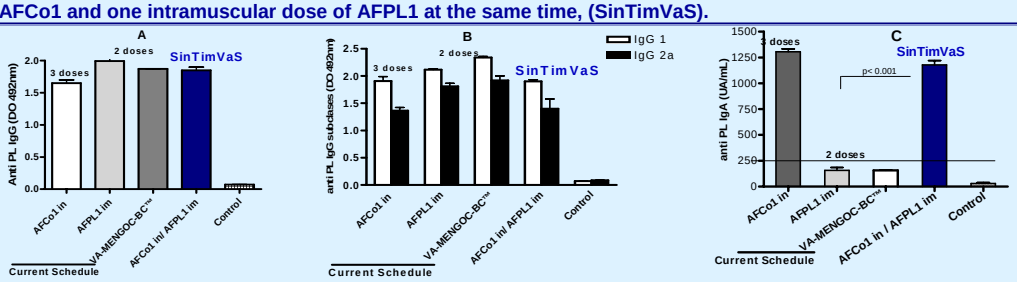


Figure 1. (A) anti PL specific IgG in sera, (B) anti PL specific IgG subclasses in serum and (C) anti PL specific IgA in saliva . A P-value <0.05 was considered statistically significant.

2- Mucosal and systemic immune response induced by SinTimVaS using others mucosal routs like oral (Or) and sublingual (Sl) at the same time with the intramuscular rout.

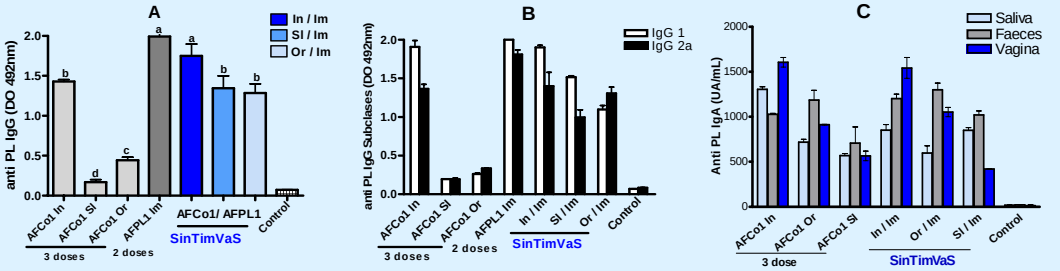


Figure 2. (A) anti PL specific IgG in sera, (B) anti PL specific IgG subclasses in serum and (C) anti PL specific IgA in saliva, faeces and vagina. A P-value of <0.05 was considered statistically significant and it is represent by different letters, a (p<0.001); b is (p<0.05) and c (p <0.01).

3- Mucosal and systemic immune response induced by SinTimVaS using other parenteral rout like subcutaneous (Sc) at the same time with others mucosal routs.

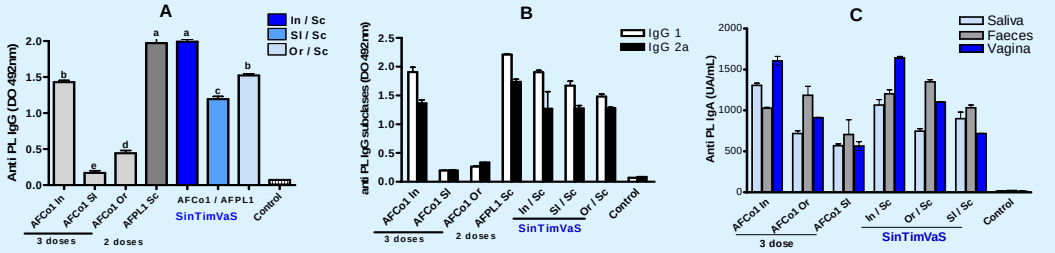


Figure 3. (A) anti PL specific IgG in sera, (B) anti PL specific IgG subclasses in serum and (C) anti PL specific IgA in saliva, faeces and vagina. A P-value of <0.05 was considered statistically significant and it is represent by different letters, a (p<0.001); b is (p<0.05) and c (p <0.01).

4- Mucosal and systemic immune response induced by SinTimVaS using the *Neisseria* derivates AFPL1 and AFCo1 as adjuvants against BSA and TT

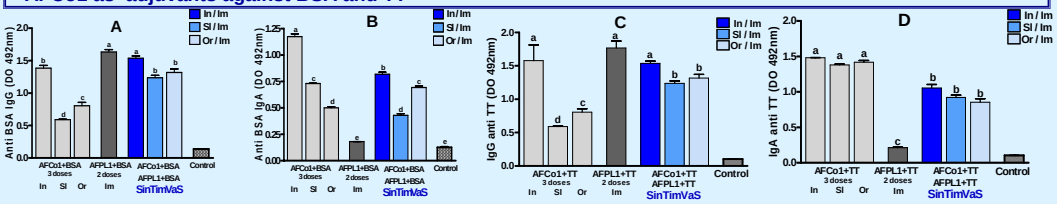


Figure 4. (A and B) anti BSA specific IgG in sera and IgA in saliva. (C and D) anti TT specific IgG in sera and IgA in saliva. A P-value of <0.05 was considered statistically significant and it is represent by different letters, a (p<0.001); b is (p<0.05) and c (p <0.01).

Conclusions:

- In SinTimVaS using the Finlay candidates and combining mucosal with parenteral rout at the same time, induce both systemic and mucosal immune responses against *N. meningitidis* B.
- With this proprietary new strategy of vaccination (Patent applied OCPI, CU/P/2008/215. November 19, 2008) one IN dose of AFCo1 simultaneously with one IM dose of AFPL1 , induce similar anti PL specific IgG antibodies titters in serum than two IM doses of AFPL1 or three IN doses of AFCo1, as well as it induces mucosal anti PL specific IgA response.
- In addition, the new strategy SinTimVaS is not restricted to the combination of IN / IM route but it also function by other mucosal route like Oral and Sublingual and by other parenteral rout like Subcutaneous.
- SinTimVaS induces an efficient systemic immune response as well as mucosal immune response at least in mice. Also SinTimVaS could increase the vaccination coverage and reduce the time-cost of vaccine campaigns.

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