

Title: Mechanisms of Protection in Gonococcal Infection and Disease: from Laboratory to Real-World Evidence of OMV-Based Vaccines

Authorship:

Ruiz García Y¹, Martinon-Torres F², Marrazzo J³, Workowski KA⁴, Giordano G⁵, Pizza M⁵, Sohn W-Y⁶

Affiliations:

¹ GSK, Madrid, Spain

² Hospital Clínico Universitario de Santiago, Santiago de Compostela, Spain

³ University of Alabama, Birmingham, AL, USA

⁴ Emory University, Atlanta, GA, USA

⁵ GSK, Siena, Italy

⁶ GSK, Rockville, MD, USA

Contact details for presenting author: Woo-Yun Sohn

Email address: woo-yun.w.sohn@gsk.com

Background

Neisseria gonorrhoeae is widespread globally and increasing in incidence. Primary prevention measures are not successful and antimicrobial resistance threatens optimal management. There is no specific vaccine and infection does not induce a protective immune response. Purpose: to review the evidence on the immunogenicity and efficacy of available vaccines against gonorrhoea to inform research and policy directions.

Aim/Methods

To address the unmet medical need to prevent gonococcal infection, we prospectively assessed the literature on immune response and gonorrhoea prevention.

Results

Natural infection studies show that *N gonorrhoeae* can avoid and suppress the immune response. In addition to extensive variation in the expression and specificity of many gonococcal surface antigens, it induces a robust inflammatory response through the Th17 pathway with a large influx of neutrophils and inflammatory cytokines but evades macrophages. The Th1 and Th2 mediated response is suppressed, resulting in low antibody titres of short duration. However, titres are higher in severe infection such as pelvic inflammatory disease, suggesting that the adaptive immune response might depend on gonococcal tissue penetration. Development of a stand-alone gonorrhoea vaccine has not been successful; challenges for conducting vaccine trials include frequent asymptomatic infections (notably pharynx and rectum) and social stigma leading to recruitment difficulties. Mouse immunogenicity studies and retrospective analyses reporting a decline in gonorrhoea cases and severe disease among recipients of meningitis B (MenB) vaccines containing outer membrane vesicle (OMV) provide support for a vaccine approach to gonococcal control.

Conclusion

Natural gonococcal infection does not reliably induce immunity and thus the classical approach of vaccine design, mimicking natural infection, is challenging. We need to understand how *N gonorrhoeae* avoids inducing an effective immune response to develop vaccines with a superior protective immune response than that induced by natural infection. Vaccines able to maintain a Th1 response might be promising. Investigation of an apparent protective effect of MenB OMV vaccines is a high priority.

Funding: GlaxoSmithKline Biologicals SA

Acknowledgement: Business & Decision Life Sciences c/o GSK. Mary Greenacre provided writing support.

Affiliations table:

First name	Last name	Email address	Position (max character 100)	Credentials (can be n/a)	Presenting author?	Have you presented at either the 2022 or 2018 IPNC meetings? (Y/N)	Biographical Sketch (no more than a few paragraphs in length.)	ORCID	Institution/ Organization	City	State/Province/Region	Country
Yara	Ruiz	yara.x.ruiz@gsk.com	MSc, PhD	-	N	-	-	0000-0003-4040-6139	GSK	Tres Cantos	-	Spain
Federico	Martinon-Torres	federico.martinon.torres@sergas.es	MD, PhD, Assoc. Prof	-	N	-	-	0000-0002-9023-581X	Hospital Clínico Universitario de Santiago	Santiago de Compostela	-	Spain
Jeanne	Marrazzo	jmarrazzo@uabmc.edu	MD, MPH	-	N	-	-	0000-0002-9277-7364	University of Alabama at Birmingham	Birmingham	AL	USA
Kimberly A	Workowski	kworkow@emory.edu	MD	-	N	-	-	0000-0002-9918-9493	Emory University	Atlanta	GA	USA
Giulia	Giordano	giulia.x.giordano@gsk.com	PhD	-	N	-	-	0000-0001-6425-7313	GSK	Siena	-	Italy
Mariagrazia	Pizza	mariagrazia.x.pizza@gsk.com	-	-	N	-	-	0000-0002-7800-1404	GSK	Siena	-	Italy
Woo-Yun	Sohn	woo-yun.w.sohn@gsk.com	MD	-	Y	-	-	0000-0002-	GSK	Rockville	MD	USA

								4034- 4735				
--	--	--	--	--	--	--	--	---------------	--	--	--	--