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Evaluation of a Novel *Treponema pallidum* Proteomic Array to Improve Understanding of Syphilis Immunology

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Syphilis

No syphilis vaccine

Syphilis is on the rise, across all populations

Congenital syphilis is a major public health problem

Why study *T. pallidum* antibody responses?

Differences in humoral reactivity to selected *T. pallidum* antigens in patients diagnosed with their first-ever syphilis episode versus those with a history of previous infection might inform vaccine development

Pathway to a vaccine against clinical manifestations

Novel 16 *T. pallidum* antigen proteomic array

Selected proteins from most highly expressed genes and/or putative surface antigens

IgG reactivity was assessed via enzyme-linked immunosorbent assay (ELISA) using sera from 58 patients collected at diagnosis

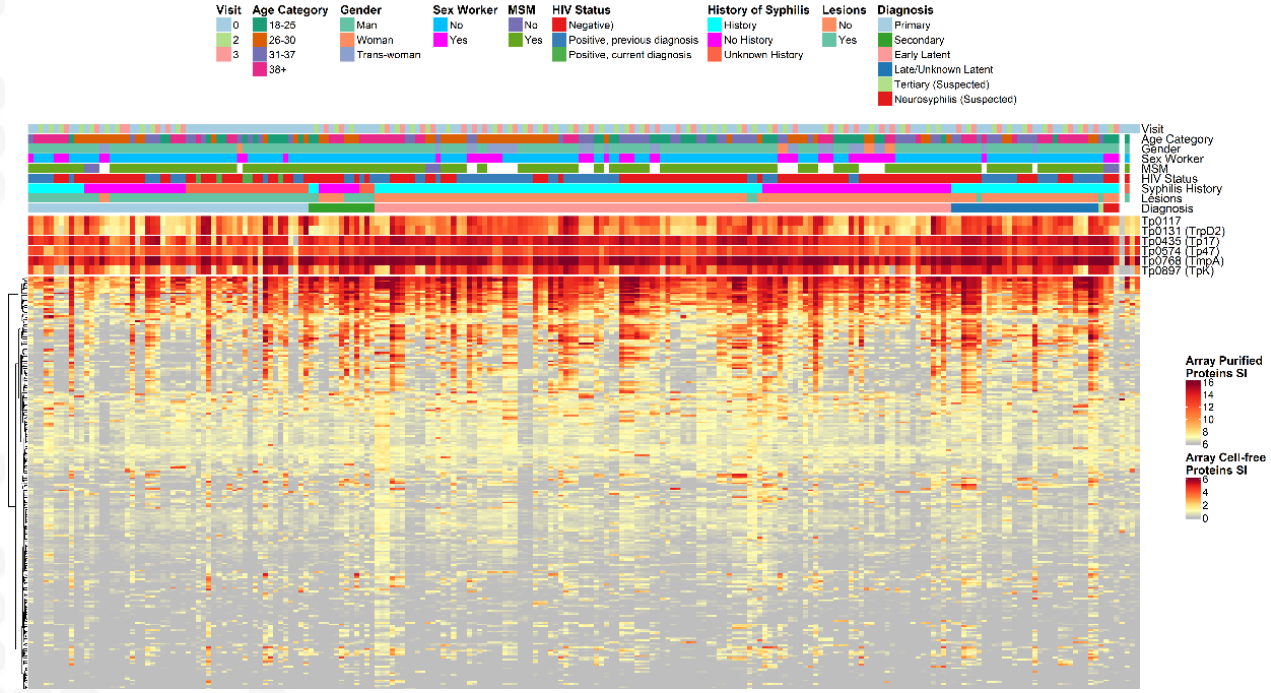
Differences analyzed using ANOVA, $p<0.05$

Lipoproteins (LPs)	Putative surface-exposed proteins (SEPs)	Ligand binding proteins (LBPs)
TP0435 Tpp17	TP0117 (TprC)	TP0163 TroA (Periplasmic binding protein)
TP0574 47kDa Carboxypeptidase	TP0548 (FadL homolog)	TP1038 Bacterioferrin
TP0751 Pallilysin	TP0621 (TprJ, NH_2-region)	
TP0768 TmpA	TP0733 (OmpA)	
TP0769 TmpB	TP0859 (FadL homolog)	
TP0954 (Placental Adhesin)	TP0865 (FadL homolog)	
	TP0897 (TprK conserved region)	
	TP1031 (TprL conserved region)	

Key findings

Serum samples from syphilis-experienced patients showed significantly lower reactivity to the Tp0548, TprJ, and TprL

Considered putative outer membrane proteins



Conclusions

Given that immunity to outer membrane proteins is pivotal for pathogen clearance though opsonophagocytosis, a decrease in serum reactivity against these key proteins could facilitate patient re-infection.

Additional information on the immune response to prior infection could help to identify possible vaccine candidates for syphilis that should be tested to evaluate their ability to generate protective immunity

Next steps

Created larger array looking at 1043 expressible open reading frames → proteins across *T. pallidum* genome (partners with Antigen Discovery, Inc).

Measuring IgG, IgA +/- IgM

Study in different patient populations: naive, repeat infection, untreated early, untreated late

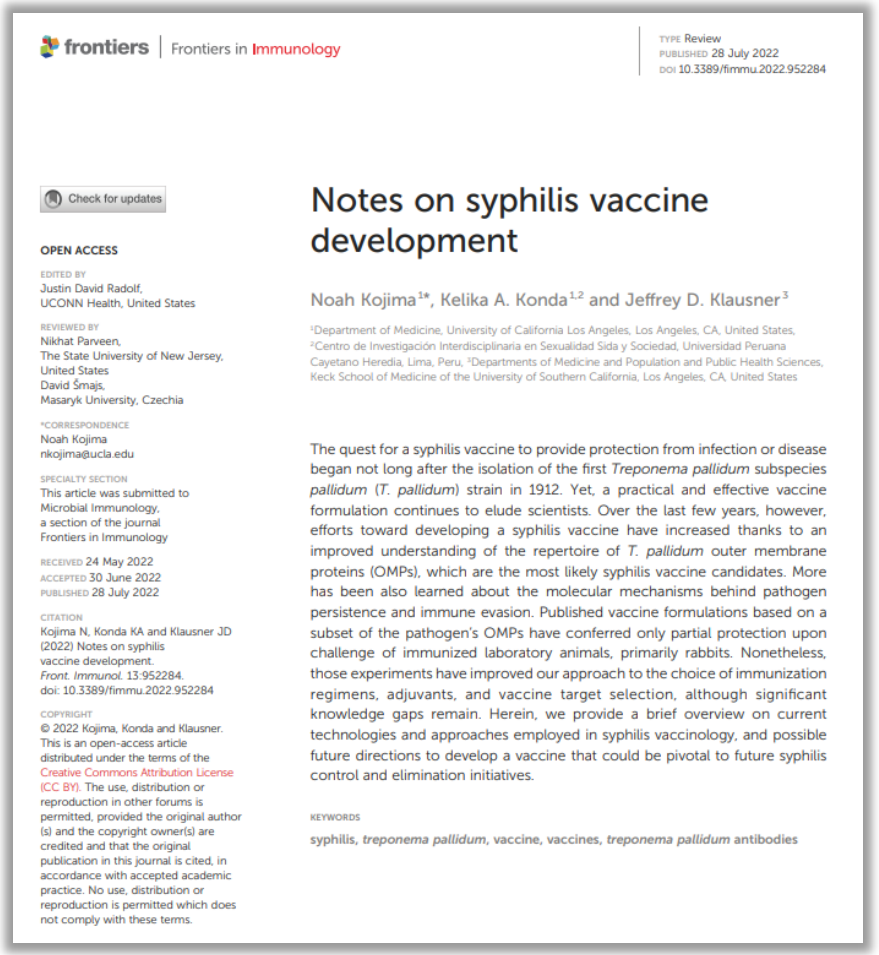
For More Information

T. Pallidum outer membrane proteins

Rabbit studies—partially protective

T. Pallidum protein array

“Omics”



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Notes on syphilis vaccine development

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The quest for a syphilis vaccine to provide protection from infection or disease began not long after the isolation of the first *Treponema pallidum* subspecies *pallidum* (*T. pallidum*) strain in 1912. Yet, a practical and effective vaccine formulation continues to elude scientists. Over the last few years, however, efforts toward developing a syphilis vaccine have increased thanks to an improved understanding of the repertoire of *T. pallidum* outer membrane proteins (OMPs), which are the most likely syphilis vaccine candidates. More has been also learned about the molecular mechanisms behind pathogen persistence and immune evasion. Published vaccine formulations based on a subset of the pathogen's OMPs have conferred only partial protection upon challenge of immunized laboratory animals, primarily rabbits. Nonetheless, those experiments have improved our approach to the choice of immunization regimens, adjuvants, and vaccine target selection, although significant knowledge gaps remain. Herein, we provide a brief overview on current technologies and approaches employed in syphilis vaccinology, and possible future directions to develop a vaccine that could be pivotal to future syphilis control and elimination initiatives.

KEYWORDS
syphilis, *treponema pallidum*, vaccine, vaccines, *treponema pallidum* antibodies

[Frontiers | Notes on syphilis vaccine development (frontiersin.org)]