

Abstract

Delineating Humoral and Cellular Immune Responses Induced by a Peptide-Based Vaccine for Protection Against *Streptococcus pyogenes*[†]

Despena Vedis *, Ailin Lepletier *, Victoria Ozberk , Simone Reynolds, Ainslie Calcutt, Darrell Bessette, Michael F. Good and Manisha Pandey *

Institute for Biomedicine and Glycomics, Griffith University, Gold Coast, QLD 4222, Australia; v.ozberk@griffithuni.edu.au (V.O.); simone.reynolds@griffith.edu.au (S.R.); a.calcutt@griffith.edu.au (A.C.); darellbessette@hotmail.com (D.B.); michael.good@griffith.edu.au (M.F.G.)

* Correspondence: despena.vedis@griffithuni.edu.au (D.V.); a.lepletierdeoliveira@griffith.edu.au (A.L.); m.pandey@griffith.edu.au (M.P.)

[†] Presented at the 22nd Lancefield International Symposium on Streptococci and Streptococcal Diseases, Brisbane, Australia, 1–5 June 2025.

Keywords: *Streptococcus pyogenes*; HLA transgenic mice; M-protein based vaccine; long term-protection; IL-1 β knockout mice; *S. pyogenes* M75 strain; IL-1 β cytokine; peptide-based vaccine

Despite the substantial burden of *Streptococcus pyogenes* infections and their associated sequelae, there is currently no Strep A vaccine. To address this global human health issue, we have developed a combination peptide-based vaccine that utilises conserved epitopes—p*17 from the M protein and K4S2 from SpyCEP, an anti-neutrophil protease—, each conjugated to diphtheria toxoid and adjuvanted with Alum. This vaccine is now in a phase 1 clinical trial.

Transgenic mice expressing human HLA-DR3-DQ2 (HLA-II) were intramuscularly immunised at days 0, 21, and 42, leading to the induction of p*17- and K4S2-specific serum IgG antibodies, which are capable of binding multiple clinical isolate strains of *StrepA*. However, following a 5-month resting period, a decline in antibody levels and *S. pyogenes* binding capabilities was observed. To investigate the efficacy of the vaccine in vivo, vaccinated HLA-II mice were challenged intranasally with the *S. pyogenes* M75 strain. Protection was assessed by measuring bacterial burden in the nasal-associated lymphoid tissue and lungs, as well as via throat swabs, at two time points post-final booster—2 weeks and 5 months. Notably, significant protection against *S. pyogenes* was maintained in all tissues analysed, regardless of the levels of antigen-specific antibody. Immunological analyses revealed increased systemic IL-1 β levels in 5-month-rested vaccinated mice, suggesting a role for sustained innate and cytokine-mediated responses in long-term protection against infection. To further validate these findings, vaccination and challenge studies involving IL-1 β knockout mice revealed a loss of vaccine efficacy compared to wild-type controls, despite comparable antibody levels, emphasising the role of IL-1 β in mediating vaccine-induced immunity.



Academic Editors: Joshua Osowicki and Theresa Lamagni

Published: 18 August 2025

Citation: Vedis, D.; Lepletier, A.; Ozberk, V.; Reynolds, S.; Calcutt, A.; Bessette, D.; Good, M.F.; Pandey, M. Delineating Humoral and Cellular Immune Responses Induced by a Peptide-Based Vaccine for Protection Against *Streptococcus pyogenes*. *Proceedings* **2025**, *124*, 19.

<https://doi.org/10.3390/proceedings2025124019>

Copyright: © 2025 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

Author Contributions: Conceptualization, M.F.G., M.P. and A.L.; methodology and experiments, A.L., D.V., D.B., V.O., A.C. and S.R.; formal analysis, D.V., A.L. and D.B.; investigation, A.L., D.V., D.B., V.O., A.C. and S.R.; resources, M.F.G. and M.P.; data curation, A.L. and D.V.; writing—original draft preparation, D.V. and A.L.; writing—review and editing, D.V., A.L., M.F.G. and M.P.; visualization, D.V., A.L., M.P. and M.F.G.; supervision, A. L., M.F.G. and M.P.; project administration, M.F.G. and M.P.; funding acquisition, A.L., M.P. and M.F.G. All authors have read and agreed to the published version of the manuscript.

Funding: This work was supported by the National Health and Medical Research Council (NHMRC), Australia, Program Grant APP1083548 (M.F.G.) and NHMRC Australia, Investigator Fellowship APP1174091 (M.F.G.), NHMRC Project Grant APP1160379 (M.P.), Heart Foundation Vanguard Grant (108443-2024) and Griffith University internal grant to A.L.

Institutional Review Board Statement: All animal protocols were reviewed and approved by the Griffith University Animal Ethics Committee (GU-AEC) in accordance with the National Health and Medical Research Council (NHMRC) of Australia guidelines. All mice were housed. In a PC2-certified animal facility in individually ventilated cages (IVC) with a maximum of 5 mice/cage. The relative humidity ranged between 45–65% and temperature 20–24 °C. Mice were exposed to a 12-h light-dark cycle.

Informed Consent Statement: Not applicable.

Data Availability Statement: The data presented in this study are available upon request from the corresponding author.

Conflicts of Interest: The authors declare no conflict of interest.

Disclaimer/Publisher’s Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.