

University of Adelaide
Department of Medicine
Adelaide Health and Medical Sciences building,
Cnr North Terrace & George Street
Adelaide, SA 5000
Australia

Selection Committee for Australian Women in Endocrinology (AWE) Travel Awards
Endocrine Society of Australia

June 13, 2025

Dear members of the selection committee,

Thank you for your consideration of my application for the AWE Travel Award.

I am an endocrinologist and PhD candidate in my final year. The main topic of my PhD was mass spectrometric analysis of corticosteroid binding globulin (CBG) in septic shock. Whilst it had a significant scientific and laboratory component and hence not without its challenges, it has been greatly rewarding and has resulted in exciting research achievements, such as first-time demonstration of neutrophil elastase cleavage phenomenon of CBG *in vivo*; elucidation of limitations of existing immunoassays in detecting CBG affinity forms; and the significant discovery that certain glycoforms of CBG are uniquely associated with septic shock mortality which has important implications with regards to future therapeutic development.

My abstract has been selected for rapid fire oral presentation at the US ENDO 2025, which is an exciting opportunity to share my research findings with the broader international endocrine community; it would also be an invaluable networking opportunity as our research group is working towards a multicentre trial; a chance to meet potential collaborators and funders for furtherment of the CBG project would be extremely valuable.

The US ENDO conference is being held in San Francisco this year, which would entail travel from Adelaide via Melbourne, and via Sydney on the way back. My PhD has extended beyond the initially intended three years due to inevitable delays in procuring necessary antibodies, which I had to produce myself due to unforeseen contamination of existing reagents. As a result, there is no project funding available from the university for conference travel, and hence I will be self-funding the entire costs of attending US ENDO. Having been a full time PhD student in the past few years, any financial support in funding this travel would be a significant and valuable help.

Sincerely,

Dr Jessica (Hee Jong) Lee
MBChB FRACP PhD candidate

Department of Medicine
University of Adelaide, Adelaide SA
Email: jessica.lee@adelaide.edu.au

US ENDO 2025 Abstract

Abstract Title:

Deficiency of Triantennary Asn347 Site Glycoforms of Corticosteroid binding globulin (CBG) is Associated with Septic Shock Mortality and Morbidity

Authors:

Jessica H. Lee¹, Zeynep Sumer-Bayraktar², R. Louise Rushworth³, Marni Nenke^{4,5}, Morten Thaysen-Andersen^{2,6}, Emily J. Meyer^{4,5}, David J. Torpy^{4,5}.

Author Institutions:

1. Department of Medicine, University of Adelaide, Australia
2. Endocrine and Metabolic Unit, Royal Adelaide Hospital, Australia
3. School of Natural Sciences, Macquarie University, Australia
4. Institute for Glyco-core Research, Nagoya University, Japan
5. School of Medicine, Sydney, The University of Notre Dame, Australia

Low serum corticosteroid binding globulin (CBG) concentration (<200 nmol/L) is independently associated with 3-fold greater intensive care unit (ICU) mortality in septic shock patients. CBG deficient mice have greater mortality on sepsis simulation via lipopolysaccharide (LPS) administration; restoration of CBG reduced mortality to that of controls. CBG is variably glycosylated at six sites, and Asn347 site glycosylation affects susceptibility to neutrophil elastase (NE) cleavage. NE cleavage of CBG results in irreversible reduction in cortisol binding affinity by 90%. We hypothesized that CBG Asn347 glycosylation is associated with septic shock clinical outcome, possibly by affecting tissue cortisol delivery.

Asn347 site glycosylation profiling of CBG was performed by mass spectrometry following CBG immunoprecipitation from serum of 135 septic shock patients taken on day 1 and last day (up to day 7) of ICU admission. This was correlated with clinical outcome data including ICU mortality, requirement for mechanical ventilation, inotropes and renal replacement therapy, and Sequential Organ Failure Assessment (SOFA) score, a measure of sepsis severity.

Mean serum triantennary trisialylated (TS3) Asn347 CBG glycoform concentrations were lower in septic shock non-survivors compared to survivors (29.74 vs 45.16 nmol/L, $P=0.007$). Lower triantennary trisialylated core-fucosylated (TS3F) glycoform concentrations were associated with mechanical ventilation requirement (37.9 vs 52.6 nmol/L, $P=0.002$), and higher total SOFA score ($r = -0.335$, $P < 0.001$), indicative of greater illness severity. No clinical associations were seen with other CBG Asn347 glycoforms. Throughout ICU admission, concentrations of TS3 and TS3F CBG Asn347 glycoforms showed the most pronounced reduction of 38.8% (42.3 vs 25.9 nmol/L, $P < 0.001$) and 22.9% (44.2 vs 34.1 nmol/L, $P=0.002$), respectively, compared to 13.2% reduction in BS2 (101.8 vs 88.4 nmol/L, $P=0.03$), and no change in BS2F (22.4 vs 22.4 nmol/L, $P=0.99$).

Low concentrations of CBG Asn347 TS3 and TS3F glycoforms are associated with mortality and morbidity in septic shock, respectively. Hence, the association between low total CBG and septic shock mortality reported previously seem to be attributable to the depletion of the TS3/TS3F Asn347 CBG glycoforms, specifically. This has significant therapeutic implications in considering CBG administration as treatment for septic shock.

Curriculum Vitae: **DR. JESSICA (HEE JONG) LEE** MBChB FRACP & PhD Candidate

EMPLOYMENT/QUALIFICATIONS

01/2025- current	Research Commercialisation Associate	AusHealth (CALHN commercialisation agency)
11/2024- current	Hon. Clinical Senior Lecturer	University of Adelaide
02/2022- current	Endocrinologist	Norwood Specialist Clinic
02/2021- current	PhD Candidate	University of Adelaide
03/2020	FRACP Endocrinology/Gen Medicine	RACP
11/2011	Bachelor of Medicine & Surgery (MBChB)	University of Auckland (New Zealand)

AWARDS & PRIZES

2025	Outstanding Abstract Award	Endocrine Society (US)
2025	Excellent Oral Presentation Award	SICEM 2025
2025	ESA-KES Exchange Travel Award	ESA
2023	Margorie Hooper Scholarship	RACP Foundation
2021	Dawes Scholarship	Central Adelaide Health Network (CALHN)
2008	Senior Prize in Medicine and Surgery	University of Auckland, School of Medicine

PRESENTATIONS

2025	Seoul International Congress of Endocrinology and Metabolism (SICEM)	CBG in septic shock patients: CBG glycosylation & impact on mortality
2024	ESA-SRB-ANZBMS 2024 - Bryan Hudson Clinical Awards Session	M/S analysis of CBG in septic shock patients: detection of NE cleaved CBG; association between Asn347 glycosylation and mortality
2018	NZSE Clinical Endocrinology Conference	A Case of Familial Aches: Camurati-Engelmann Disease
2017	International Diabetes Federation Congress	DKA at Middlemore Hospital (first author for poster)

PUBLICATIONS

- Chernykh, A., Sumer-Bayraktar, Z., **Lee, J. H.**, Meyer, E. J., Torpy, D. J., & Thaysen-Andersen, M. (2025). RCL glycosylation of serum corticosteroid-binding globulin: implications in cortisol delivery and septic shock. *Glycobiology*, cwaf013.
- Lee, J.H.**, Sumer-Bayraktar, Z., Mittal, P., Donnellan, L., Young, C., Rushworth, R.L., Lewis, J.G., Nenke, M., Rankin, W., Klingler-Hoffman, M., Hoffmann, P., Thaysen-Andersen, M., Torpy, D.J., Meyer, E.J. (2025). Mass spectrometric detection of neutrophil elastase cleaved corticosteroid binding globulin and its association with Asn347 site glycosylation, in septic shock patients. *Clinica chimica acta; international journal of clinical chemistry*, 567, 120108.
- Lee, J. H.**, Meyer, E. J., Nenke, M. A., Lightman, S. L., & Torpy, D. J. (2024). Cortisol, Stress, and Disease-Bidirectional Associations; Role for Corticosteroid-Binding Globulin?. *The Journal of clinical endocrinology and metabolism*, 109(9), 2161–2172.
- Lee, J. H.**, Meyer, E. J., Nenke, M. A., Falhammar, H., & Torpy, D. J. (2023). Corticosteroid-binding globulin (CBG): spatiotemporal distribution of cortisol in sepsis. *Trends in endocrinology and metabolism: TEM*, 34(3), 181–190.
- Lee, J. H.**, Nenke, M. A., Flabouris, K., Torpy, D. J., & Meyer, E. J. (2023). Plasma corticosteroid-binding globulin concentrations are preserved in mild cirrhosis. *Liver international: official journal of the International Association for the Study of the Liver*, 43(3), 740–741.
- Lee, J. H.**, & Torpy, D. J. (2023). Adrenal insufficiency in pregnancy: Physiology, diagnosis, management and areas for future research. *Reviews in endocrine & metabolic disorders*, 24(1), 57–69.
- Lee, J. H.**, Jaung, R., Beban, G., Evennett, N., & Cundy, T. (2020). Insulin use and new diabetes after acceptance for bariatric surgery: comparison of outcomes after completion of surgery or withdrawal from the program. *BMJ open diabetes research & care*, 8(2), e001837.
- Lee, J. H.**, & Orr-Walker, B. J. (2020). Diabetic ketoacidosis admissions at Middlemore Hospital: observational study of cause and patient demographics. *The New Zealand medical journal*, 133(1525), 34–40.
- Hughes, P., Hassan, I., Que, L., Mead, P., **Lee, J. H.**, Love, D. R., Prosser, D. O., & Cundy, T. (2019). Observations on the Natural History of Camurati-Engelmann Disease. *Journal of bone and mineral research: the official journal of the American Society for Bone and Mineral Research*, 34(5), 875–882.

GRANTS/FUNDING

- Torpy D, Meyer E, **Lee J**, Anderson M. CBG as a Novel Therapeutic for Septic Shock. AusHealth 2023-24. \$250,000
- Torpy D, Meyer E, **Lee J**. *Development of new approaches to measure proteolysis and glycosylation profiling of high and low affinity corticosteroid-binding globulin (CBG) in septic shock using mass spectrometry.* Royal Adelaide Hospital, Gum Bequest, HSCGB funding. 2022-24 \$70,000.
- Torpy D, **Lee J**. Simultaneous measurement of therapeutic and endogenous glucocorticoids using a novel hair assay. Towards optimisation of glucocorticoid therapy for inflammatory disease. Royal Adelaide Hospital, Gum Bequest, HSCGB funding. 2022-23 \$15,000.

4 June 2025

Reference for Dr Jessica (Hee Jong) Lee MBChB FRACP, PhD candidate University of Adelaide, Australia

To whom it may concern,

I have been asked to write a reference for Dr Jessica Lee, in relation to her application for an Australian Women in Endocrinology (AWE) to assist her travel to ENDO 2025 where she will present her novel and impactful data in corticosteroid binding globulin glycosylation variants with respect to septic shock outcomes.

I am honoured to have worked with Jessica. She is a fine physician. During many interactions regarding complex patients, it is clear she has excellent medical/endocrine knowledge, further bolstered by her excellent judgment and keen awareness of patient priorities.

Jessica has excelled in her PhD studies. Her thesis will be submitted within the several months and is likely to be among the best thesis submissions at our university and competitive internationally. Her academic track record, including publications is very impressive.

Dr Lee has solved some important research questions working in the field of corticosteroid binding cleavage, showing that neutrophil elastase cleavage is a genuine process *in vivo* in humans, a novel finding. The subject of this abstract, involving the CBG glycosylation forms and their relation to acquired CBG deficiency is both novel and crucial in understanding the pathogenesis of septic shock, with potential therapeutic implications.

Dr Lee's is an engaging speaker making complex subjects very approachable to the non-expert, especially in endocrine methodology such as mass spectrometry. Jessica has been highly involved in commercialisation of her findings and is learning about the research/commercial interface, an area where she is acquiring unusual skills, and I can see her reaching a leadership position in the endocrine research/commercialisation space. Without doubt Jess will make a valuable and continuing contribution to Australian endocrinology and I wholeheartedly support her application for the AWE travel award.

Yours sincerely,



Professor David J. Torpy

University of Adelaide

Senior Consultant Physician

Royal Adelaide Hospital

Budget Justification

I will be flying from Adelaide to San Francisco to present at the US ENDO 2025.

The costs associated with the travel are as follows:

Flights	\$3069.54
Adl->Mel->San Fran, then San Fran->Syd->Adl	
Accommodation	\$1256.12 USD
Westin St. Francis Hotel (Housing partner for US ENDO) 11-15 July2025	(~ \$1,938.37 AUD)
Conference Registration	\$436 USD
	(~\$672.87 AUD)
<hr/>	
Total Cost	\$ 5680.78 (AUD)

As my PhD has extended beyond 3 years, there is no project funding for the travel through the University. At present I do not hold a public hospital position and hence there is no professional development fund available. Therefore, the entirety of the travel costs is self-funded.